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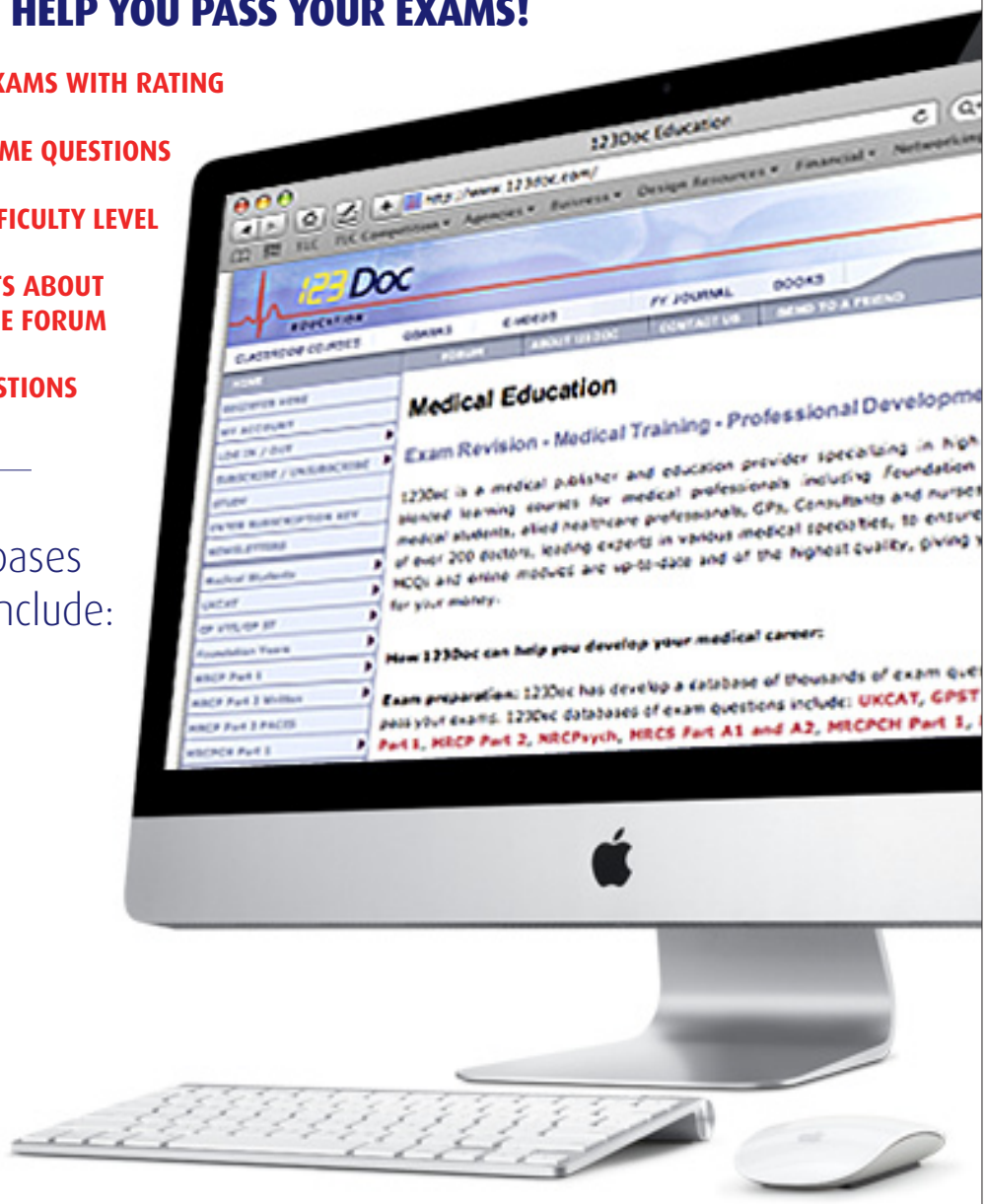

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A CASE OF LEAKING CLEAR FLUID FROM SKIN AROUND THE EYE

J Myneni, E Gajdosova, A McCormick

Abstract

A case of a two year old girl with discharge of clear fluid from the skin adjacent to her left eye. This presented a diagnostic dilemma of whether the origin of the leak was cerebrospinal fluid (CSF) or ectopic lacrimal tissue. Biochemical analysis of the fluid and neuroimaging can aid in differentiating CSF from other fluids. It is important to rule out CSF leaks which can have potential life threatening complications.

Case History

Two year old girl presented to eye clinic with her foster carer who gave a history of discharge from the skin adjacent to her left eye. She reported that onset was from birth and they could not recollect any significant trauma in the past. The leaking fluid was always clear, which was made worse on crying. They did not report any pain or episodes of redness or swelling of the surrounding skin.

On examination, there was a pinpoint area on left temple about 2.5cm from the lateral canthus , with drops of clear fluid. There was a definite increase in leakage when the child was upset and crying. The surrounding skin appeared non inflammed, non tender to touch, soft on palpation and there was no underlying swelling. She could fix and follow small objects with both eyes. There was an alternate exotropia on orthoptic examination and refraction showed hypermetropic astigmatism in both eyes. Her ocular movements were full and her lids were normal to examine. Her anterior segments and fundus examinations were normal.

Our differential diagnosis was ectopic lacrimal tissue or leak of cerebrospinal fluid (CSF). The site of leak was unusual for either of the diagnoses. Though the history of onset since birth was more supportive of the former diagnosis, CSF fistula needed to be excluded due to the location of the leak and the secondary complications of unidentified CSF leak can be life threatening. Fluid was collected in a sterile syringe and sent for biochemical analysis. This was analysed for glucose levels which were reported as negligible,suggesting the fluid was tears. Further tests for assay of ß 2 Transferrin and contrast radiography are planned for this child for confirmation of diagnosis.

Discussion

CSF fistulas subsequent to trauma are not uncommon and present as rhinorrhea or otorrhea. Cranio-orbital fistulas leaking cerebro-spinal fluid, termed CSF oculorrhea, are a rare complication of penetrating or blunt trauma. The nature of trauma may be mild (1) to severe.

There are case reports of chronic (2) and delayed (3) CSF oculorrhea masquerading as epiphora or excessive watering. CSF fistulas which are non-traumatic in origin are very rare, with a few cases reported secondary to pituitary tumours (4), dermoids (5), idiopathic intracranial hypertension (4).

CSF fistulas are not easy to diagnose. It is important to rule these out to avoid complications of chronic CSF leak and meningitis. Several tests can be done to differentiate CSF from tears. Simple biochemical analysis is the first step. Detection of glucose in the fluid to determine CSF leak is a very helpful test. Glucose levels in CSF are 2/3rd of serum glucose levels, whereas tears have negligible glucose levels (6).

ß 2 Transferrin is a protein specific to CSF. Tests to detect this protein are highly sensitive, specific, non- invasive and very useful in identifying CSF leaks. (7)

Neuroimaging with or without contrast can help localise the site of the fistula. Treatment of CSF fistula can be conservative as a proportion of the fistulas spontaneously resolve. Surgical repair is done in some cases to reduce risks of chronic leakage and meningitis.

Tear flow from an ectopic site could be due to anomalous lacrimal ductule (lacrimal gland fistula) or functioning ectopic lacrimal gland tissue. Lacrimal gland fistulae are rare and have been previously described as tarsal group where the opening is on the upper lid and lateral group where the opening is on the skin lateral to external canthus. After radiological confirmation, these can be excised or the opening of the duct can be redirected into the fornix or managed conservatively (8).

Ectopic lacrimal gland tissue or lacrimal choristomas are most commonly found on epibulbar conjunctiva. Orbital and intraocular involvement are uncommon. There are case reports of localisation in other sites such as eyelids and nasal mucosa. (9)

In our patient, the fluid discharge was tears and not CSF and is likely to be due to congenital lacrimal gland fistula.

Conclusion

In cases of persistent leakage of clear fluid from eyes, nose or ears, CSF fistulas need to be ruled out. They can sometimes be as a result of mild trauma and can have delayed presentation. Biochemical analysis for glucose levels, will aid in diagnosis. Detection of ß 2 Transferrin is a confirmatory test. Imaging to localise the leak can help in further surgical management, where necessary.

5 MCQs

1. What is the glucose level of CSF?

a. 2/3 rd of serum glucose levels
b. 1/3 rd of serum glucose levels
c. Equal to serum glucose levels
d. Negligible
e. ½ of serum glucose levels

2. What is the commonest cause of CSF oculorrhea/ cranio-orbital fistula?

a. Congenital
b. Trauma
c. Benign intracranial hypertension
d. Tumour
e. Latrogenic

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3. What is the commonest site of ectopic lacrimal gland tissue?

a. Orbit
b. Intraocular
c. Extra-orbital area
d. Conjunctiva
e. Lids

4. Immunoassay can be done for this protein which is specific for CSF-

a. Lysozyme
b. ß 2 Transferrin
c. Lactate Dehydrogenase
d. Creatine Kinase
e. Albumin

5. What is the complication of ectopic/anamolous lacrimal gland ductule?

a. Epiphora
b. Inflammation
c. Cyst formation
d. Abscess formation
e. All of the above

Answers for MCQs

1. a. 2/3rd of serum glucose levels

Glucose levels of CSF are approximately 2/3rd of serum glucose levels. Tears have insignificant glucose levels. (2.5-4.1 mg/dl).

2. b. Trauma

Commonest cause of CSF fistulas is trauma- penetrating or blunt. Non traumatic CSF fistulas are reported secondary to pituitary tumours, dermoids, benign raised intracranial hypertension, congenital defects.

3. d. Conjunctiva

Ectopic lacrimal gland tissue is commonly found on temporal epibulbar conjunctiva or limbal area. Often, a proplapsed lacrimal gland can be mistaken for ectopic lacrimal gland tissue.

4. b. ß 2 Transferrin

Detection of ß 2 Transferrin in suspect fluids can help differentiate CSF from other fluids in cases of head trauma.

5. e. All of the above

Ectopic lacrimal ductules can cause continuous epiphora and sometimes develop complications like inflammation, infection and cyst formation.

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ATYPICAL PRESENTATION OF ACUTE ANGLE CLOSURE GLAUCOMA

PY Chua, O Chadwick, AE Pyott

Case History

A 64-year-old lady with a significant history of poorly controlled type 2 diabetes mellitus was admitted to the intensive care unit following an elective below knee amputation. Her co-morbidities included ischaemic heart disease, chronic kidney disease, non-convulsive episodes and chronic obstructive pulmonary disease.

During this admission she had reduced consciousness, and initially this was thought to be due to opiate toxicity. Later, multiple episodes of delirium were due to sepsis, hypoglycaemia, and constipation. Management included a number of anti-convulsants including phenytoin, pregabalin, sodium valproate, levitiracetam and venlafaxine.

Around 6 weeks after admission she developed a red painful right eye. This was presumed to be secondary to trauma during a delirious episode. A referral was made to ophthalmology and she was reviewed on the medical ward by a consultant ophthalmologist who elicited a history of reduced vision for an uncertain period, hypermetropia (long-sightedness) and a family history of glaucoma.

Examination revealed that she had a corneal abrasion on the right eye, but that her intraocular pressure was raised in both eyes. The following day she was reviewed in clinic on a slit lamp where the visual acuities were found to be 6/18 on the right and Counting Fingers at 1 metre on the left.

The intraocular pressures (IOP) were found to be 38mmHg on the right and 40mmHg on the left (normal range 10-21mmHg), there was right sided corneal oedema, the anterior chambers of both eyes were very shallow and there were abnormal iris vessels on the right side. She had bilateral cataracts and the optic discs had a 'cupped' glaucomatous appearance. The impression was bilateral acute angle closure glaucoma.

The patient was treated medically with topical IOP lowering drops to both eyes (pilocarpine, latanoprost, dorzolamide and timolol) and YAG peripheral iridotomies. The following day the IOP had reduced to 21mmHg in the right and 13mmHg on the left.

Unfortunately, during follow up, the IOP in both eyes increased further despite being on maximal treatment. She was listed for phacoemulsification with intraocular lens implant to deepen the anterior chamber and this has been successful in reducing the intra-ocular pressure.

Discussion

Acute angle closure glaucoma (AACG) is an acute onset of increased intraocular pressure secondary to closure of the anterior chamber drainage by the blockage of trabecular meshwork. The prerequisites are the underlying anatomy of the anterior segments together with mechanism(s) that induce apposition or synechial closure.

The process of angle closure is dynamic and the mechanisms can be multiple. Whilst pupil block is considered to be the most common mechanism, other mechanisms are plateau iris, lens block and ciliary effusion.

Pupillary block mechanism involves lens-iris apposition at the pupil, with resultant bowing forward of the peripheral iris as aqueous pressure builds up in the posterior chamber. This condition is known as 'iris bombe'. In anatomically predisposed eyes (i.e hypermetropia), the iris bombe closes the angle and compromises aqueous drainage, causing IOP to rise.

Pupillary block may present as a sole mechanism or it may be mixed with others. However, it is not in the scope of this article to explain all different mechanisms. Signs and symptoms of AACG1 are shown in table 1.

Signs	Symptoms
Corneal oedema	Ocular or peri-ocular pain
Unreactive mid-dilated pupil	Nausea / vomiting
Iris bombe	Blurring of vision
Conjunctival injection	Antecedent history of intermittent blurring of vision with haloes.
IOP ≥ 30 mmHg	

Table 1: Signs and symptoms of acute angle closure glaucoma

It is important to highlight that in AACG, the pupil is semi-dilated, fixed and does not react to light. Figure one shows fixed, semi-dilated pupil and hazy cornea in a patient with AACG.

During the attack of AACG, the high IOP can cause irreversible glaucomatous optic nerve damage and/or retinal vascular occlusion. The immediate goal of treatment is to reduce IOP which can be achieved by medical therapy like oral/topical carbonic anhydrase inhibitors, topical beta-blockers and topical alpha-2 adrenergic agonist.

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Sometimes, an intravenous carbonic anhydrase inhibitor (acetazolamide) or an hyperosmotic agent like mannitol is required if topical treatments are unsuccessful. Once IOP is <40mm Hg, a cholinergic agent (pilocarpine) is used to constrict the pupil and break the pupillary block.

Once the attack is broken, laser iridotomy is performed to normalise the pressure gradient between the anterior and posterior chambers. As a result, the anterior chamber deepens and the angle opens. If the IOP is still high, further interventions like phacoemulsification with intraocular lens implant or surgical trabeculectomy are indicated.

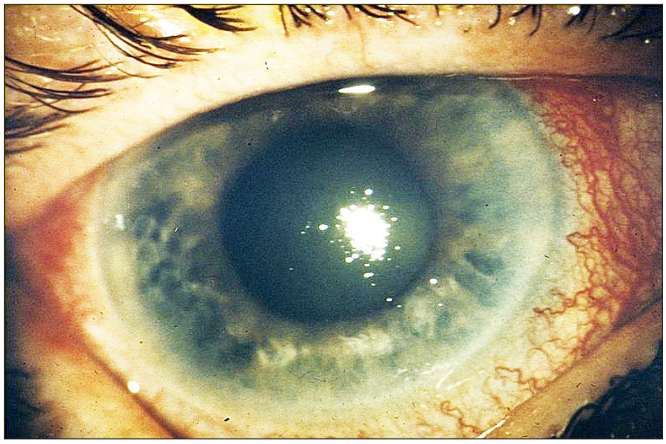

Figure 1: Fixed, semi-dilated pupil and hazy cornea in a patient with AACG.

AACG can be easily recognised by any health care professional with or without a slit lamp. Junior doctors and inexperienced clinicians often find it difficult to rule out AACG and differentiate it from conditions that cause pain and drop in vision. The differential diagnosis include, 3rd nerve palsy with pupil involvement, and migraine.

1. AACG vs 3rd nerve palsy with pupil involvement.

Pitfall: 3rd nerve palsy with pupil involvement can present with sudden onset of headache and a dilated pupil. This can be confused with AACG and leads to delayed investigation and treatment.

Tip: It was reported that up to 70% of cases of pupil involved 3rd nerve palsy associated with intracranial aneurysm have fixed, fully dilated and non-reactive pupil. (2,3)

However, these patients will have other signs of 3rd nerve palsy including ptosis and variable ophthalmoplegia. In AACG, there is no ophthalmoplegia, the eye is red and the cornea is usually hazy with semi-dilated pupil.

2. AACG vs migraine/ headache

Pitfall: Migraine can present as a sudden onset of unilateral eye pain, unilateral red eye and unilateral reduced vision.

Tip: The pupil in AACG is fixed, in the mid dilated position and by definition is not reactive to light. In contrast, the pupils in patients with migraine and headache are reactive. The pupil is best examined in ambient low light conditions.

An assessment can be made of the intra-ocular pressure by digital palpation. The unaffected eye will be soft, and the affected eye stony hard. This examination can be very uncomfortable for the patient, and other features should make the diagnosis clearly apparent.

Rarely patients with acute angle closure can present with systemic symptoms predominating. In this case a painless red eye can be mistaken for conjunctivitis. A sudden rise in intra-ocular pressure can increase vagal tone leading to nausea, vomiting and abdominal pain. Delayed diagnosis can lead to irreversible blindness from glaucomatous optic neuropathy.

These atypical presentations usually occur in the elderly, the confused, and debilitated patients. A previous case report has highlighted the importance of pupil examination in patients with reduced vision and red eye to rule out AACG (4).

The AACG attack in our patient went unnoticed because the patient was delirious and the red eye was thought to be related to trauma. The corneal erosion in the right eye was secondary to a decompensated cornea, secondary to prolonged cornea oedema resulting from raised intraocular pressure.

In retrospect, she had several risk factors for AACG. Firstly, she is hypermetropic, making her anatomically more predisposed to an AACG attack. Figure two shows an example of hypermetropic glasses. Secondly, she was on three drugs which can precipitate AACG, ie salbutamol, tiotropium and venlafaxine. Table 2 lists other medications which can provoke an episode of AACG (5).

ATYPICAL PRESENTATION OF ACUTE ANGLE CLOSURE GLAUCOMA

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Class of drug	Example of	Mechanism of action
Adrenergic agonists	Phenylephrine Ephedrine	Pupil block
Non-catecholamine adrenergic agonist	Naphazoline Salbutamol	Pupil block
Anticholinergics	Tropicamide Iprotropium bromide Promethazine	Pupil block
Medications with anticholinergics side effects	Tricyclic antidepressant Serotonin reuptake inhibitor	Pupil block
Sulfa-based agents	Topiramate	Ciliary effusion

Table 2: Medications that precipitate acute angle closure glaucoma.

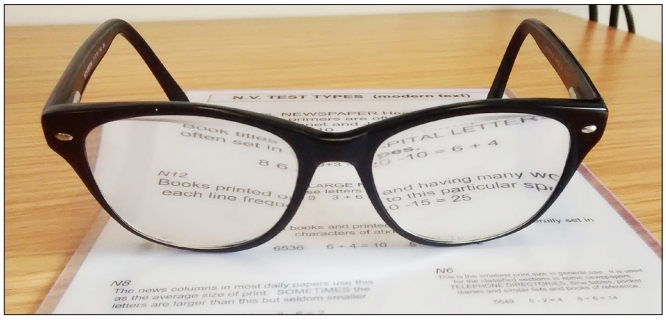

Figure 2: Hypermetropic glasses. Note that the image is magnified by hypermetropic glasses.

It is worth highlighting that some junior doctors are concerned about the risk of precipitating acute angle closure glaucoma by dilating pupils during fundoscopy examination.

A systemic review showed that of the 600,000 individuals who received mydriatic eye drops, only 33 (0.006%) developed AACG, giving estimated risk of 1 in 20,000 (6) of these 33 patients, they have long acting (atropine) or combined (tropicamide 1% & phenylephirine 2.5%)mydriatic drops. None of the patients developed AACG with tropicamide drop alone. Hence, tropicamide mydriatic eye drop is safe to use in primary care or casualty. (7)

In conclusion, there are two learning points in this case. Firstly, AACG should be suspected in any hypermetropic patient with red eye who has a fixed, semi-dilated pupil. The diagnosis can be made by bedside; a reactive pupil exludes AACG. Secondly, clinicians have to be mindful of medications that can potentially precipitate AACG.

Questions

1. Which of the following medication does not precipitate acute angle closure glaucoma?

a) Ipratropium inhaler

b) Amitriptyline hydrochloride

c) Fluoxetine

d) Risperidone

e) Topiramate

2. Of the following, what is the most common mechanism of acute angle closure glaucoma?

a) Pupil block

b) Ciliary effusion

c) Plateau iris

d) Forward displacement of lens-iris diaphragm

e) None of above

3. Of the following, which is the NOT a risk factor for acute angle closure glaucoma?

a) Chinese ethnicity

b) Long-sightedness

c) Hypermetropia

d) Myopia

e) Family history of glaucoma

ATYPICAL PRESENTATION OF ACUTE ANGLE CLOSURE GLAUCOMA

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4. The following are the management of acute angle closure glaucoma EXCEPT

a) YAG laser peripheral iridotomy

b) Argon laser peripheral iridoplasty

c) Paracentesis

d) Selective laser trabeculoplasty

e) Intraveneous mannitol

5. Which of the following statements is true regarding glaucoma?

a) Relative afferent pupil defect can be positive in unilateral glaucoma

b) Thick cornea over-estimates intra-ocular pressure.

c) Glaucoma can occur in patient with normal intraocular pressure.

d) Oral acetazolamide should be avoided in patients with sickle cell disease

e) All of above

Answers

1) d

2) a

3) c myopia is a risk factor for primary open angle glaucoma

4) d selective laser trabeculoplasty is applied to the trabecular meshwork to lower IOP.

In AACG, the angle is closed and trabecular meshwork is not visible on gonioscopy. In argon laser peripheral iridoplasty, the contraction burns of iridoplasty pull the peripheral iris stroma away from the angle structures to deepen the angle, it is useful to break the AACG attack in patient with hazy cornea.

5) e

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HOW TO BECOME AN OPHTHALMOLOGIST: OVERCOMING THE HURDLES OF APPLICATION

A Lewis, C Liu

Abstract

Recent changes have taken place to the application procedure for Ophthalmology. This article aims to give some practical tips and advice towards applying for a place on the Ophthalmology run-through programme.

Introduction

Ophthalmology is an exciting branch of surgery which requires dexterity and an interest in all things visual. It is a specialty which has seen huge technological advancement in recent years in both diagnostic and surgical techniques and medical therapies.

The ophthalmologist is both a surgeon and a physician. It is a career that involves the use of many gadgets on a weekly basis including microscopes, various types of lasers, optical lenses and ultrasound probes, to name but a few. If you have an eye for microscopic detail, a brain adept at visual pattern recognition and a steady hand then perhaps ophthalmology could be the specialty for you?

Ophthalmology is a busy and largely outpatient based specialty. Nearly 10% of all NHS outpatient appointments are for ophthalmic care (1). It is subdivided into eight sub-specialties including cornea and anterior segment, medical retina, glaucoma, oculoplastic surgery, paediatric ophthalmology, vitreo-retinal surgery, neuro-ophthalmology and primary care. Surgical procedures are largely carried out under local anaesthetic as day cases and therefore the need for inpatient beds has declined as surgical techniques, including phacoemulsification cataract surgery (see below), have advanced.

When can I apply?

Candidates can apply to ophthalmology after foundation year 2. It is a run-through specialty which lasts 7 years up to certificate of completion of training (CCT). This is advantageous as successful candidates do not need to reapply at ST3, as in many other specialties. Recruitment timescale involves application in November, interviews in February and offers in March.

Do I need previous experience?

No. Previous clinical experience in Ophthalmology is not essential. An elective in ophthalmology is a good way to gain experience and show commitment to the specialty. Evidence of a candidate's participation in audit or research, especially in an area relevant to ophthalmology is highly recommended.

How do I apply?

National recruitment is centralised and coordinated by health education south west (Severn) through an online 'Oriel' application system. Detailed information, including the online application procedure can be found at **https://www.oriel.nhs.uk/**

What does the application procedure involve?

Candidates are required to compile a portfolio of evidence prior to interview. The interviews for all UK posts takes place in February in Bristol and involve a series of stations, during which candidates will be scored according to his or her portfolio, clinical scenarios, critical appraisal of a paper and a station on improving patient care. Detailed information can be found at **http://www.severndeanery.nhs.uk.**

Isn't ophthalmology very competitive?

There are approximately 95 posts each year across all the deaneries within the UK. The exact number varies from year to year but specific details can be found on the Severn Deanery Website (See Helpful Resources: 1). Candidates rank each job in order of preference. Competition ratios are published each year by Health Education England (2). There were almost 4 applicants per post offered in 2015 for ophthalmology making it more competitive than most specialties.

What else can I do to increase my chances of getting a job?

Candidates should look at the personal specification for ophthalmology and direct CV activities towards this (See Helpful Resource: 4). Attending a microsurgical skills course is both good for the CV and helps candidates decide if ophthalmology is the right specialty for them. Courses can be booked via the Royal College of Ophthalmologists (RCOphth) website. Please note, these courses become fully booked very quickly.

Interview preparation is very important. Start by reading a book such as Picard's book on medical interviews (Helpful Resources: 6). It may be useful to find someone who has been through the process and have them carry out a mock interview prior to the real one. In addition to these suggestions, evidence of a hobby involving manual dexterity is another way of showing interviewers that you are a good candidate for a microsurgical post!

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What happens if I don't get in?

Firstly, don't despair! There are many successful ophthalmologists who didn't get in the first time around. Revisit the personal specification and see what areas of the portfolio could be improved upon. There are other ways of gaining ophthalmology experience. For instance, application to a fixed term specialty training appointment (FTSTA) in ophthalmology is one option of gaining clinical experience.

NB According to the personal specification, candidates should have a maximum of 18 month's experience in Ophthalmology prior to application. Applying for a clinical or teaching fellowship or an MSc run by the UCL institute of Ophthalmology are other options available. Don't forget that as applications take place in November, doing an MSc or fellowship may require a two years out of programme.

Do I need good eyesight?

Although stereopsis is no longer an application requirement it is certainly recommended that candidates should have good corrected vision (i.e. when wearing glasses) in both eyes. The rationale for this is that a lot of ophthalmology requires binocular vision. Both the slit lamp and the operating microscope require use of both eyes.

This allows perception of a three dimensional image which helps the diagnostician to ascertain which microscopic layer of the eye is pathologically involved during examination and facilitates dextrous use of surgical instruments.

It is advisable that candidates should see a trained orthoptist (an ophthalmic allied health professional with an interest in binocularity) for stereopsis testing prior to application. A copy of the orthoptist's report should be filed in the portfolio. This shows both initiative and commitment to the specialty.

If I am successful at application, when shall I start operating?

Phacoemulsification for removal of cataracts during lens exchange surgery remains the mainstay of ophthalmic surgery. It is a technique which is taught both in wet-labs using artificial and cadaveric eyes and Eyesi (3) computerised simulators.

Wet-lab training runs in tandem with supervision by a consultant ophthalmologist in theatre. Almost all of the run-through jobs in UK Ophthalmic specialist trainees (OST) start surgical training from OST1 are expected to have completed 50 cases by the end of their OST2 year. Trainees will perform surgery in other sub-specialties as they progress through the run-through programme.

Finally, I would encourage anyone who is considering applying to ophthalmology to do so. It is a hugely rewarding speciality with a great variety of skills and an interesting case-mix. It is well worth the hard work necessary to secure a post against the competition.

"There is no comparison between that which is lost by not succeeding and that which is lost by not trying".

Francis Bacon

Multiple choice questions:

1) What percentage of NHS outpatient appointments are for ophthalmic care?

A 1%

B 25%

C 60%

D 8%

E 3%

2) Which of the following is not a sub-specialty of ophthalmology?

A Orthoptics

B Medical retina

C Glaucoma

D Cornea and anterior segment

E Oculoplastic surgery

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3) Which of the following is not a requirement to apply to ophthalmology run-through programme?

A MBBS or equivalent

B Previous experience in Ophthalmology

C Completion of foundation competencies

D Capacity to use logical thinking to solve problems

E Demonstrates an understanding of research and audit

4) Which of the following are instruments is not commonly used by Ophthalmologists?

A YAG Laser

B OCT scanner

C Indirect Ophthalmoscope

D Ultrasound

E Hickman line

5) In which month do candidates need to be prepared to apply for a post in Ophthalmology?

A February

B June

C November

D March

E July

Answers

1) D

See Reference 1.

2) A

Orthoptics is an allied health specialty, not a medical specialty within ophthalmology.

3) B

Previous experience in Ophthalmology is not necessary prior to application. All the others are essential attributes of applicants according to the personal specification. See Helpful Resources: 4.

4) E

An ophthalmologist would be unlikely to insert a Hickman line without multidisciplinary involvement.

5) C

Candidates need to make application in November / early December prior to interview in February and offers in March.

Helpful Resources

1) The official website for application. Click tabs "job description" and "resources" for the most useful information. **http://www.severndeanery.nhs.uk**

2) Royal College of Ophthalmologists (RCOphth) Website: **http://www.rcophth.ac.uk**

3) Royal College of Ophthalmologists: Applicant guide to specialty training in ophthalmology- Oriel: **https://www.pathway.oriel.nhs.uk/Web/Sys_Documents/4867ee1e-73bd-44bb-8b97-30ecd4fd4b6d_Ophthalmology%20-%20Information%20Sheet.pdf**

HOW TO BECOME AN OPHTHALMOLOGIST: OVERCOMING THE HURDLES OF APPLICATION

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4) Personal specification: **http://specialtytraining.hee.nhs.uk**

5) Eye docs: An informative online community run by junior ophthalmology doctors. **https://www.eyedocs.co.uk/**

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2) Health Education England competition ratios. **http://specialtytraining.hee.nhs.uk**

3) Eyesi surgical simulator. h**ttps://www.vrmagic.com/simulators/eyesi-surgical**

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PERIOCULAR CAPILLARY HAEMANGIOMA

R Johnston, R Brennan

Abstract

Periocular capillary haemangiomas are the most common orbital tumour of childhood. They are mainly diagnosed on clinical history and examination. The majority will undergo spontaneous involution with no sequelae.

However, they can cause significant complications, most commonly amblyopia as a result of visual deprivation. More rarely they could cause potentially fatal complications if part of PHACES syndrome.

Propranolol has been shown to be a safe and effective first line therapy, promoting both a rapid reduction in size and permanent regression. Topical timolol is currently emerging as an option for smaller, well defined, superficial lesions.

Case History

Presenting complaint

15 week old boy with a vascular lesion involving his left upper lid, resulting in ptosis.

Background

Upper lid swelling was first noticed at 3 weeks old, and had increased in size over time. There were no other skin lesions elsewhere, and no other health issues of note.

Ocular examination

Red purple mass on left upper eyelid measuring 12mm by 15mm (see figure 1).

Refraction

R +2.00 -1.50 @ 180°. L +3.5 -4.5 @ 10°. Note the left eye has significant astigmatism.

Diagnosis

The examination findings and history are consistent with a capillary haemangioma of the left upper eyelid, resulting in partial occlusion of the left pupil. Due to the severity of the ptosis and the degree of induced astigmatism, amblyopia is a serious concern.

Management

Patching of the right eye for one hour per day for 10 days was commenced to treat left amblyopia. Propranolol treatment was initiated at a dose of 0.5mg/kg/day for one week and then increased to 1mg/kg/day for one week. He was then given the maintenance dose of 2mg/kg/day. A preliminary heart rate, blood pressure and blood glucose were checked before initiation of treatment. On first dose and at dose increases blood sugar, blood pressure (BP) and heart rate (HR) were checked every 30 minutes for 6 hours as hypoglycaemia, bronchospasm and bradycardia can occur. Blood pressure and pulse rate were checked by the community nurse weekly thereafter.

His mother administered the medication and gave a night time feed for the first 3 months, to help prevent hypoglycaemia.

Key points to tell parents (1)

- *Propranolol should be administered during daytime hours.*
- *Always give with a feed to reduce risk of hypoglycaemia.*
- *Do not give if child unwell or vomiting.*
- *Counsel parents on signs of hypotension, bradycardia and hypoglycaemia.*

Doctor's notes

- *Propranolol should not be given with salbutamol or any other selective B2 agonist. If bronchodilation required use ipratropium bromide.*
- *If child is undergoing a procedure and requires fasting, IV fluids containing glucose should be given. (1)*
- *Extra care must be taken in preterm infants, those on concurrent medications that can reduce blood glucose and children with other medical conditions associated with hypoglycaemia. (1)*

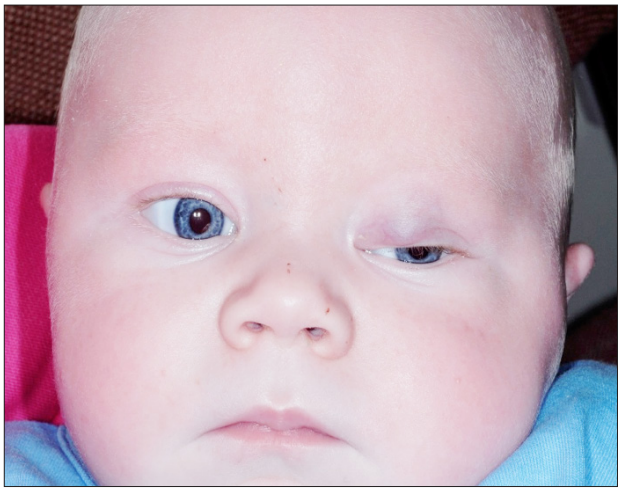

Figure 1: Before Treatment.

Figure 2: After 6 months on treatment.

PERIOCULAR CAPILLARY HAEMANGIOMA

R Johnston, R Brennan

Follow-up at 6 weeks after starting propranolol:
The lesion was smaller in size.

Refraction was improving
R +1.25 -1.0^0 @ 10^0. L +2.00 -3.25 @ 15^0

After 6 months on treatment lesion no longer visible (figure 2).

Refraction at 6 months
R +0.25, L +0.25 -0.50@ 15^0.

Note the left astigmatism has resolved as the globe is no longer being compressed.

How to stop propranolol
Aim when 12 months old to wean off over a period of weeks being aware of the risk of rebound growth if propranolol stopped too early or too quickly.

Discussion

Capillary haemangiomas have a very typical history and features. The case chosen illustrates this and also details the first line treatment. These benign vascular lesions are one of the most common periorbital tumours of infancy, present in 1 – 2% of neonates.

They generally appear in the first few weeks of life and are associated with rapid enlargement. The majority reach 80% of their full size by 5 months of age. This is followed by a period of slowed growth and finally regression. (2) Approximately 50% of haemangiomas regress by age 5, and by 10 years of age 90% have completely regressed. (3) A small proportion of these lesions can leave scars as they involute.

They are hamartomas created by abnormal growth of vascular endothelial cells. 50 – 60% are superficial, 15% subcutaneous and 25 – 35% mixed. The history and presentation combined is generally diagnostic. Parents will usually describe a red or purple area, not present at birth, which has become larger and thicker over the first few months of life. It blanches with pressure, which helps distinguish it from the port-wine stain of Sturge-Weber syndrome. (4)

Systemic complications

Doctors should be aware that the size and location of capillary haemangiomas dictates the possible morbidity. Large, segmental facial haemangiomas (generally over 5cm) can be associated with PHACES syndrome (posterior fossa malformations, hemangioma, arterial anomalies, cardiac abnormalities, eye abnormalities and sternal clefting).

Patients with this condition can have seizures, speech delays, headaches and very rarely ischaemic strokes. Additionally, they are much more likely to have a permanent cosmetic deformity due to the extensive nature of the haemangioma. Children with larger segmental lesions with extensive facial involvement and / or multiple lesions elsewhere need a more extensive pre-treatment work-up than the example given in our case. (5)

Another systemic association is Kasabach-Merritt syndrome, which should be considered in children with large visceral capillary haemangiomas who then develop thrombocytopenia. Mortality from this condition is high as a sudden massive haemorrhage can occur, with subsequent cardiovascular collapse. (5) Patients with lower facial and neck haemangiomas can have associated airway haemangiomas, which can bleed significantly during intubation. (4)

Propranolol now primary treatment for capillary haemangiomas

Propranolol has been used for several decades in children for cardiac and neurological diseases, with a good safety record. It is a non-selective beta-block which inhibits the action of adrenaline and noradrenaline on ß1 and ß2 receptors. Initial reports supporting the use of propranolol came from Chrsitine Leate-Labreze and colleagues.

Two children with capillary haemangiomas were noted to have reduction of their capillary haemangiomas lesions when started on propranolol for cardiac disease. This team subsequently went on to treat a further nine children with capillary haemangiomas but no cardiac disease. All had changes within the lesion in 24 hours and resolution during the course of treatment. (6)

Other treatment options

Observation is an option for lesions that are not interfering with vision or causing any marked cosmetic deformity.

Topical timolol has also been used with good effect (timolol maleate gel 0.25% twice a day). Works best on small, well defined, superficial haemangiomas. (4)

Prior to the serendipitous discovery of propranolol's efficacy, 1st line therapy was intralesional steroid injection. Most haemangiomas responded with a single injection. Possible side effects of this treatment include soft tissue atrophy, hypopigmentation, glaucoma, central retinal artery occlusion resulting in blindness and systemic absorption. A meta-analysis was performed by Izadpanah et al in 2013 comparing corticosteroids versus propranolol. Results showed a response rate to treatment of 69% using corticosteroids versus 97% using propranolol. (7)

In addition surgical excision, oral steroids, embolization and laser have all been used.

Amblyopia

Reported, in 40–60% of patients with periocular capillary haemangiomas. It is the most common ocular complication associated with these lesions and is due to visual deprivation and or induced astigmatism. This high rate of amblyopia occurs, as very young children are extremely susceptible to visual deprivation amblyopia. This is why early intervention for these histopathologically benign lesions is vital. (5)

PERIOCULAR CAPILLARY HAEMANGIOMA

R Johnston, R Brennan

Conclusions

- **Capillary haemangiomas are the most common periocular tumour of childhood.**
- **Diagnosis is largely clinical, hence the importance of being familiar with key features.**
- **Most will undergo spontaneous resolution, therefore watch and see is an option, if no complications.**
- **It is vital to refer any infant promptly with a vascular lesion obscuring the visual axis, as they are at high risk of amblyopia.**
- **Treatment with oral propranolol is now considered first line. It has been found to be both safe and effective.**
- **Potentially serious systemic associations such as PHACES; should be considered in very large lesions.**
- **Counselling parents on the administration of propranolol is very important to help avoid hypoglycaemia.**

Questions

1. What is the most common periocular tumour of childhood?

A Rhabdomyosarcoma

B Dabska tumour

C Capillary haemangioma

D Lymphangioma

E Cavernous haemangioma

2. At what age are capillary haemangiomas typically first noticed?

A Birth

B 4 months of age

C First few weeks of life

D After 6 months of age

E After one year of life

3. Which of the following is not currently a treatment option for capillary haemangiomas?

A Oral propranolol

B Topical timolol

C Surgical excision

D Intralesional and systemic corticosteroids

E Oral diamox

4. What is the most common ocular complication of periocular capillary haemangiomas?

A Raised intraocular pressure

B Strabismus

C Dry eye

D Amblyopia

E Red eye

5. Which of the following options is not associated with periocular capillary haemangiomas?

A PHACES syndrome

B Kasabach-Merrit syndrome

C Microangiopathic haemolytic anaemia (MAHA)

D Paratracheal haemangioma

E Chediak Higashi Syndrome

Answers

1. C

Capillary haemangiomas are the most common periocular tumour of childhood. (4)

Rhabdomyosarcoma - soft tissue sarcoma. In patients with localised disease overall 5 year survival rates have improved to more than 80%. (8)

Dabska tumour - rare low grade angiosarcoma.

PERIOCULAR CAPILLARY HAEMANGIOMA

R Johnston, R Brennan

Lymphangiomas are rare benign hamartomatous lesions of the lymphatic system.

Cavernous haemangioma is a benign, slowly progressive vascular neoplasm of endothelial-lined spaces surrounded by a fibrous capsule. It most commonly presents in middle-aged adults. Typically occurs within the muscle cone, lateral to the optic nerve.

2. C

First few weeks of life (3)

3. E

Propranolol has been seen to have a dramatic effect on the growth of infantile haemangiomas. (4)

Corticosteriods - until recently both intralesional and systemic steroids had been the mainstay of treatment. However they have potentially serious side effects such as adrenal suppression, growth retardation and immunosuppression. Live vaccines cannot be given while on oral steroids.

Topical timolol – good results on small, well-defined haemangiomas. (9)

Surgical excision – they can be excised with good results. Intraoperative bleeding can be an issue with these vascular lesions.

4. D

Most common ocular complication of periocular hemangiomas in childhood is visual loss secondary to amblyopia. (5)

Strabismus can also occur due to extraocular muscle infiltration

5. E

PHACES should be considered in segmental lesions over 5 cm in size, full workup prior to commencing treatment.

Kasabach-Merrit syndrome is a rare haematologic abnormality associated with extensive capillary haemangiomas. Clinically thrombocytopenic purpura is visible, along with ecchymoses surrounding the haemangioma.

MAHA – erythrocytes are destroyed from coagulation. Important to rule out visceral involvement as this carries a significant morbidity and mortality. Chediak Higashi syndrome is associated with an oculocutanous albinism phenotype and abnormal platelet aggregation causing a mild bleeding tendency. It is not associated with capillary haemangiomas.

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CASE BASED DISCUSSION: AN UNUSUAL CASE OF SUDDEN BILATERAL VISION LOSS

JL Yeong, C Collins

Abstract

This is a case of a 27 year old woman with no significant past medical or ophthalmic history who presented with acute bilateral painless loss of vision along with severe vomiting, headaches and extreme lethargy. She was diagnosed with megaloblastic anaemia secondary to folate deficiency. Fundal examination showed bilateral pre-retinal haemorrhages, which is thought to be due to Valsalva retinopathy on the background of anaemia related retinopathy. Her vision subsequently improved after 4 weeks with no active intervention apart from treatment of her anaemia.

This case discusses about an unusual cause of retinal haemorrhage and the management options available.

A 27 year old woman presented to A&E with bilateral painless sudden loss of central vision 10 days prior. This was associated with 3 weeks' history of headaches, 1 week's history of intermittent vomiting and lethargy. Her vomiting became more persistent 3 days prior to presentation, transforming from bilious vomitus to hematemesis. There was no preceding trauma prior to onset of symptoms.

Her past medical history includes H.pylori infection (2012), depression and myopia. She is not on any regular medications. Table 1 shows the relevant blood results on initial assessment in A&E.

Blood tests	*Value (units)*	*Reference Range*
Haemoglobin (Hb)	46 (g/L)	115-165 (g/L)
Platelets	90 (x10^9/L)	150-450 (x10^9/L)
Mean Corpuscular Volume (MCV)	122.9 (fL)	76-100 (fL)
Total White Cell Count	6.31 (x10^9/L)	4-11 (x10^9/L)
B12	211(ng/L)	191-663 (ng/L)
Folate	2.6 (µg/L)	4.6-18.7 (µg/L)
Total Iron	34 (µmol/L)	13-30 (µmol/L)
Ferritin	462 (µg/L)	13-150 (µg/L)
Transferrin	2 (g/L)	1.8-3.8 (g/L)

Table 1: Blood results at presentation showing megaloblastic anaemia, thrombocytopaenia and folate deficiency.

She was treated initially with blood transfusions and subsequent oesophagealgastroduodenalscopy (OGD) showed gastritis with no evidence of occult bleeding. She was treated for megaloblastic anaemia secondary to folate deficiency with folate and thiamine supplements, along with H.pylori eradication therapy.

She presented to the eye casualty 2 days later having no improvement in her vision since the onset of all her symptoms. On examination, her visual acuity was 6/36 both eyes aided with no improvement with pin-hole. There was no afferent pupillary defect and colour vision was normal. Visual fields to confrontation showed a paracentral visual field defect bilaterally.

Slit lamp examination of the anterior segments up to the lens was unremarkable. Fundal examination showed bilateral pre-retinal haemorrhages overlying the macula and flame haemorrhages on the superior and inferior arcades. Initial Optical Coherence Tomography (OCT) scans showed masking of the outer retinal layers as a result of the overlying haemorrhage (Figure 1).

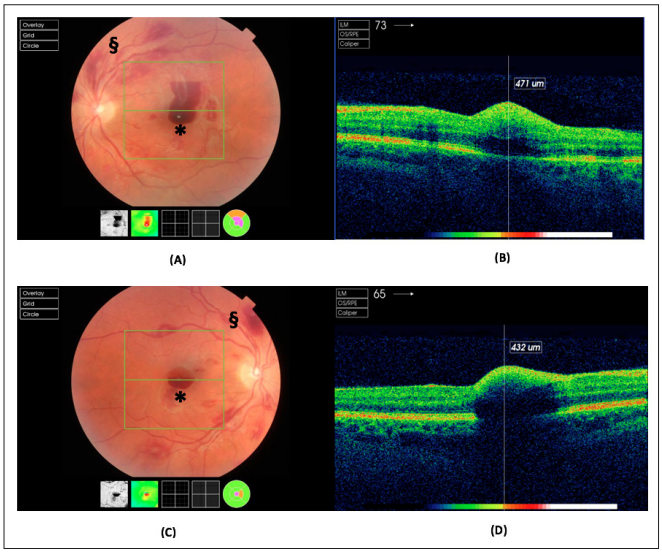

Figure 1: Fundal view and accompanying OCT scans on initial examination. (Left Eye-A,B; Right Eye-C,D). Note bilateral pre-retinal haemorrhages overlying the macula and flame haemorrhages on the superior and inferior arcades. Associated OCT scans showed masking of the outer retinal layers where the haemorrhage is overlying.

**pre-retinal haemorrhage; § flame haemorrhage*

The patient was diagnosed with Valsalva retinopathy on the background of anaemia related retinopathy and we observed her progress every fortnight. No active intervention was taken at this point.

CASE BASED DISCUSSION: AN UNUSUAL CASE OF SUDDEN BILATERAL VISION LOSS

JL Yeong, C Collins

Over the next month, she noticed gradual improvement in her vision and this was reflected on fundoscopic examinations and the accompanying OCT scans (Figure 2 and Figure 3). Her visual acuity improved to 6/18 (right) and 6/36 (left) on week 2 and 6/12 (right) and 6/24 (left) on week 4. She will be reviewed again in 1 month. Her most recent haemoglobin level was 121 g/L and MCV was 101.1 fL.

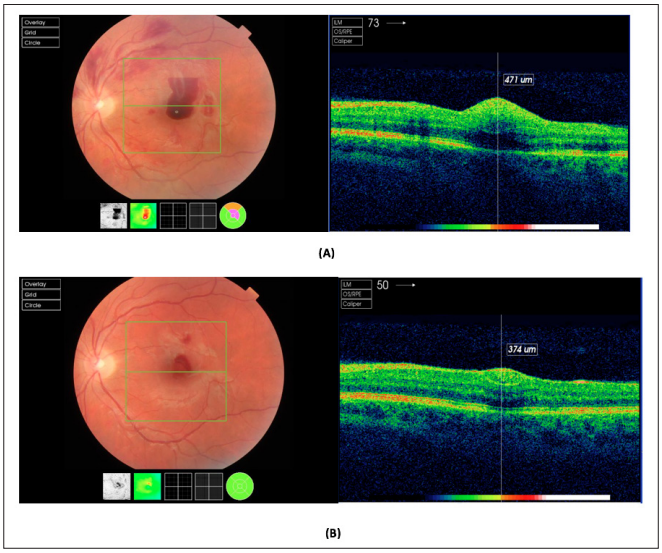

Figure 2: Comparison of the left fundus and OCT scans between initial assessment (A) and week 4 (B). There is less haemorrhage at week 4.

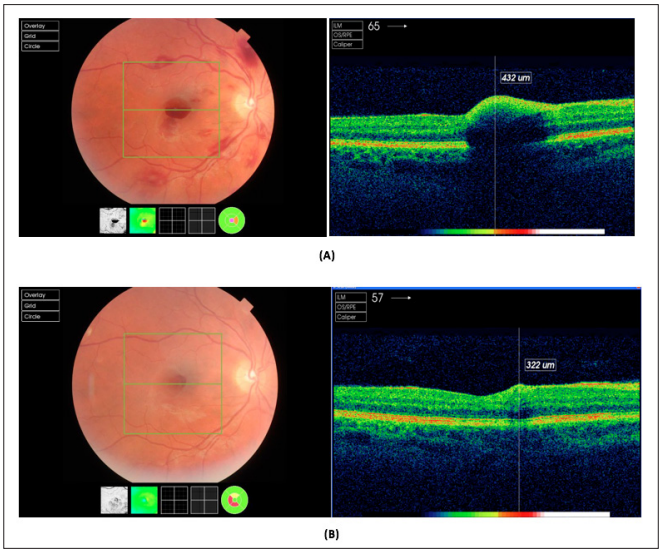

Figure 3: Comparison of the right fundus and OCT scan between initial assessment (A) and week 4 (B). There is again clinical improvement at week 4.

Discussion

Retinal haemorrhages can be broadly classified into pre-retinal or vitreous, retinal and sub-retinal. In this case, the patient presented with bilateral pre-retinal haemorrhages overlying the macula causing central visual loss with no recent trauma.

The three main pathologic mechanisms of vitreous haemorrhages are bleeding from abnormal retinal vessels, rupture of normal retinal vessels or extension of haemorrhage through the retina from adjacent sources. (1) The most common causes associated with each mechanism are summarized in Table 2. Other less common causes described in the literature are Valsalva retinopathy (3,4) and anaemia associated retinopathy. (5-7)

Mechanisms of Vitreous Haemorrhage
Abnormal Vessels
Proliferative Diabetic Retinopathy (31-54%)
Neovascularisation from retinal vein occlusions (4-16%)
Sickle Cell Retinopathy (0.2-6%)
Rupturing of Normal Vessels
Retinal tear (11-44%)
Trauma (12-19%)
Posterior Vitreous Detachment with Retinal Vascular Tear (4-12%)
Retinal Detachment (7-10%)
Terson's Syndrome (0.5-1%)
Blood from Adjacent Source
Macroaneurysm (0.6-7%)
Age Related Macular Degeneration (0.6-4%)

Table 2: Common causes of vitreous haemorrhage (1,2)

In this case, the haemorrhages occurring as a result of proliferative diabetic retinopathy or neovascularisation from previous retinal vein occlusion could be excluded from the history itself. Rupturing of normal blood vessels due to retinal tear, retinal detachment or posterior vitreous detachment are excluded as well as there were no associated symptoms (flashes and floaters) or clinical findings.

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There was also no history of trauma that could have caused the haemorrhages. Based on her history of severe vomiting, clinical findings and blood results, both Valsalva retinopathy and anaemia related retinopathy were the most likely causes of the haemorrhages.

Valsalva retinopathy is defined as an acute sudden painless loss of vision due to straining, causing retinal capillary rupture secondary to sudden spike of retinal venous pressure. Activities that have been described in literature to cause Valsalva retinopathy include weight lifting, vomiting, sexual activity, labour and general anaesthesia. (8-10)

On the other hand, retinal haemorrhages secondary to anaemia are well known, with various studies reporting highest prevalence in patients with concurrent severe anaemia (<80 g/L) and severe thrombocytopaenia (<50 x 10^9/L). Although most of the recent case reports are of patients diagnosed with idiopathic thrombocytopaenic purpura, a case series performed by Carraro et al demonstrated that other forms of anaemia and thrombocytopaenia, including B12 and folate deficiency could present with retinal haemorrhages as well. (5-7), (11,12) This corresponds with our patient's findings.

The pre-retinal haemorrhages associated with Valsalva retinopathy or anaemia related retinopathy usually resolves spontaneously with time if the size of the haemorrhage is small (<1 disc diameter), which is the case for our patient.

Therefore, we have decided to observe the patient in the beginning whilst she was treated for folate deficiency. However, a larger (≥3 disc diameter) or denser pre-retinal haemorrhage might not resolve spontaneously and will cause permanent structural damage to the eye, such as haemosiderosis, epiretinal membrane formation, proliferative vitreoretinopathy and secondary glaucoma if left for long periods. (1,13)

For these cases, Nd:YAG membranatomy (laser to create an opening at the hyaloid membrane, causing the haemorrhage to drain inferiorly away from the macula) can be utilised to drain the haemorrhage. (13) Pars plana vitrectomy (PPV) surgery is an effective procedure mainly used for non-resolving cases after a period of observation or post-Nd:YAG membranotomy. (14,15)

Both of these procedures have their associated risks. The risks of Nd:YAG membranotomy include macular hole formation, thermal damage to the macula, epiretinal membrane formation and retinal detachment although the risks are minimal according to recent studies. (13) The risks of PPV are similar to cataract surgery along with earlier formation of cataracts.

The main management challenge in this case was to manage the patient's anxiety. She is a young patient with previously perfect vision bilaterally who suddenly developed marked central visual loss. Understandably, she was worried about permanent visual loss. We discussed possible interventions and agreed to observe for 2 weeks (good likelihood of spontaneous recovery due to small size of haemorrhages) and the risks associated with Nd:YAG membranotomy and PPV surgery.

In conclusion, this unusual case of bilateral pre-retinal haemorrhage is due to a combination of severe anaemia and Valsalva-related complications. It highlights the causes of anaemic retinopathy and with conservative management many of these cases make a good recovery.

Multiple Choice Questions

1. As an FY2 in GP placement, you diagnosed a 50 year old patient with Type 2 Diabetes Mellitus and decided to manage with diet control initially for 3 months. As per NICE guideline, when will this patient need to be referred for diabetic retinopathy screening?

A. After 3 months if he is started on oral hypoglycaemics

B. No referral is needed as he does not have visual symptoms

C. At time of diagnosis

D. Urgent referral to ophthalmologist

E. After 1 year from diagnosis

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2. As an FY2 in the emergency department, you have just seen a 67 year old male patient with painless visual loss on his right eye. He has no significant past medical history but has extensive family history of cardiovascular disease.

He is a smoker. Examination showed a right central retinal vein occlusion. What is the most likely systemic condition associated with this finding?

A. Atrial fibrillation

B. Hypertension

C. Hyperlipidaemia

D. Haematological disorders

E. Diabetes Mellitus

3. As an FY2 in ophthalmology, you have just seen a 22 year old girl with poorly controlled type 1 diabetes who presented with a sudden visual loss in her left eye.

She has had previous pan-retinal photocoagulation (PRP) to the left eye for proliferative diabetic retinopathy (PDR). Fundal examination showed a dense vitreous haemorrhage. What will you do?

A. Consult your registrar with regards to immediate PRP to the left eye on the same day

B. Discharge home and emphasise better glycaemic control. No further ophthalmology follow up is needed as this is expected in PDR

C. Perform an ultrasound B-scan. If no evidence of retinal detachment, follow up patient in 4-6 weeks' time with a view of further PRP

D. List the patient for urgent pars plana vitrectomy surgery

E. Refer to diabetic team for optimization of diabetic treatment. No further follow up is required from ophthalmology

4. Which diabetic retinopathy grade listed below must be referred to the ophthalmology services?

A. Mild diabetic retinopathy or worse

B. All grades of diabetic retinopathy

C. Severe diabetic retinopathy or worse

D. Only proliferative diabetic retinopathy

E. Moderate diabetic retinopathy or worse

5. In patients with pre-retinal haemorrhages secondary to Valsalva retinopathy, what interventions can the ophthalmologist consider in cases with dense haemorrhages or non-resolving after 4 weeks of observation?

A. Observe for another 4 weeks as it may take longer to resolve

B. Nd:YAG membranatomy (laser to create an opening in the hyaloid membrane to drain the haemorrhage)

C. Pars plana vitrectomy surgery

D. Pan retinal photocoagulation

E. YAG capsulotomy

CASE BASED DISCUSSION: AN UNUSUAL CASE OF SUDDEN BILATERAL VISION LOSS

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Teaching Notes

1. Answer: C

Diabetic retinopathy is a complication of poorly controlled Type 1 or Type 2 diabetes. It is also dependent on the duration of diabetes. Patients are normally asymptomatic before having proliferative changes, therefore all diabetic patients are screened annually so that those at risk of progress are followed up more closely by the ophthalmology service.

NICE has recommended that all diabetic patients (Type 1 and Type 2) should be referred to the screening service at the time of diagnosis.

2. Answer: B

Retinal vein occlusion is an important cause of painless visual loss, especially in the elderly population with long-term consequences. It is strongly associated with age-related local and systemic factors. It is normally precipitated by arterioloscelortic thickening of a retinal arteriole with subsequent compression of a venule at an arteriovenous junction.

This causes thrombus formation as a result of endothelial cell loss and turbulent flow in the venules. The most significant systemic association of retinal vein occlusion is hypertension. It is present in more than two-thirds of these patients over age 50 and 25% in younger patients. (16)

3. Answer: C

Although the most likely cause of vitreous haemorrhage in this patient is proliferative diabetic retinopathy, an ultrasound B-scan is still needed to exclude retinal detachment due to poor fundal view (beware of patients with no previous history of proliferative diabetic retinopathy).

Patients who have had PRP treatment in the past are still at risk of developing further proliferative changes and bleeds if the glycaemic control is not optimal. For patients with dense vitreous haemorrhages, PRP can only be performed when the fundal view is clearer and therefore time is needed for the blood to settle before further treatment.

4. Answer: E

Diabetic retinopathy (DR) is classified into no DR, mild, moderate, severe and proliferative DR. Mild DR is defined as having at least 1 microaneurysm and/or dot and blot haemorrhages on fundal examination while moderate DR are characterised by the above changes along with venous beadings and cotton wool spots.

Severe DR follows the "4-2-1" rule whereby a patient has any of the following: diffuse intra-retinal haemorrhages and microaneurysms in 4 quadrants, venous beading in ≥2 quadrants, or intra-retinal microvascular abnormalities (IRMA) in ≥1 quadrant. (17)

Moderate DR is defined as anything less than severe DR according to the "4-2-1" rule but more than mild DR. Proliferative DR includes neovascularisation of the iris, optic disc and/or elsewhere in the retina and/or pre-retinal haemorrhages. A patient with moderate DR or worse should be referred to the ophthalmology services for closer follow-up.

5. Answer: B

In Valsalva retinopathy, dense or large haemorrhages (≥ 3 disc diameter) usually do not resolve spontaneously. Therefore, active intervention with Nd:YAG membranotomy is usually advocated after a short period of observation to avoid further complications such as haemosiderosis and epiretinal membrane formation. This procedure normally has a high success rate but pars plana vitrectomy sometimes may be required if the haemorrhage does not drain post-Nd:YAG membranotomy.

CASE BASED DISCUSSION: AN UNUSUAL CASE OF SUDDEN BILATERAL VISION LOSS

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DIABETIC RETINOPATHY: A REVIEW

KS Cooper, D Vaideanu-Collins

Abstract

Diabetes is an increasingly common, chronic disease affecting organs throughout the body including the retina, leading to diabetic retinopathy (DR). Damage is done via a microangiopathic process which can be slowed by gaining tight control over glucose levels, best achieved with the input of a multidisciplinary team.

DR can be classified into non-proliferative and proliferative disease, each with specific identifying features clinically observed on fundoscopy. DR can also lead to macular oedema which can be sight threatening. A screening program is in place within the UK to monitor those suffering from diabetes and ensure quick identification of disease progression.

Treatment is constantly developing and is always tailored to the needs of the individual patient. Available ocular treatment modalities will be discussed.

Keywords: *diabetes; diabetic retinopathy.*

Introduction

In 2015, 2.9 million people in the UK were living with diabetes and this is forecast to increase significantly, with 4.6 million cases expected by 2030 [1]. 700 patients are diagnosed with diabetes every day (1 patient every 2 minutes). The management of this chronic condition is complex, with many associated macro and micro vascular complications which require specialist input, such as cardiovascular problems, diabetic nephropathy and diabetic retinopathy (DR), to name just a few. A holistic approach is therefore essential in the management of diabetes, with regular reviews of glycaemic control as well as screening for the complications which frequently occur, requiring the input of a multidisciplinary team.

Prevalence of DR within the Diabetic population varies according to country and study and overall is around 40%, being more common in type 1 diabetics. DR is present in 12% of new diagnoses of diabetes, usually type 2, with incidence increasing proportionately with time.

The Wisconsin study found that 83% of patients with type 1 DM had retinopathy after 25 years of disease and 25% had macular oedema as well. The progression of retinopathy to more severe stages was shown to be closely linked to glycaemic and hypertensive control [2].

The high incidence of diabetes, coupled with high incidence of DR in these patients, makes DR a leading cause of blindness in the working age group of the UK [3]. Risk factors which affect the likelihood of developing DR and its progression are: duration of diabetes; poor glycaemic control (with HbA1C levels being a good indicator); age at diagnosis < 12, diastolic blood pressure less than or equal to 83 and waist to hip ratio [4].

Pregnancy can be associated with severe progression of DR, especially if the glycaemic control is poor in the first trimester [5]. Nephropathy and its severity is directly linked to retinopathy. Worsening nephropathy is linked with progression of DR and if renal disease is well treated, particularly in the case of transplantation, DR may improve [6].

Pathophysiology

The development and progression of DR is a microangiopathic process dependent on glucose concentrations and blood pressure, the small blood vessels of the eye being particularly susceptible to damage from hypertension, and high glucose concentrations having a direct effect on the retinal cells. There are many proposed pathways of damage to the retina in DR making the pathophysiology of DR very complex.

Damage to capillaries and cells within the retina occurs in response to increased sorbitol levels, which in turn lead to local biochemical changes. As sorbitol is broken down, excess glycation end-products accumulate which in turn leads to activation of protein kinase C. Together this leads to increased oxidative stress on vasculature as a result of free radical production [7].

Capillary damage can lead to the death of pericytes and loss of vascular smooth muscle which leads to dysfunction of the capillaries allowing leakage into retinal tissues. This closely correlates with clinical signs suggestive of retinal haemorrhage including dot and blot haemorrhages, and more advanced flame haemorrhages.

Such damage as described above can lead to areas of the retina not being adequately perfused, resulting in retinal hypoxia. The retina responds to this hypoxia by creating intraretinal microvascular abnormalities (IRMA), shunts between arterioles and venules which attempt to reperfuse hypoxic tissue. This is the neovascularization seen in the proliferative phase of diabetic retinopathy and is driven by a variety of angiogenic stimulators, most prominently VEGF. This process is a result of the imbalance between angiogenic and antiangiogenic factors and a key therapeutic target in an attempt to slow proliferative DR [8].

The magnitude of impact that tight glycaemic control can have on DR development has been shown through the Diabetes Control and Complication Trial (DCCT). The risk of development of DR was reduced by up to 76% in patients in the trial who underwent a 6.5 year period of intensive therapy with near normal glucose levels throughout. The Epidemiology of Diabetes Interventions and Complications study (EDIC), a follow up, showed that further risk of DR development, even after intensive therapy has ended, is greatly reduced for up to 10 years, a phenomenon termed as metabolic memory [9].

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Screening

The nature of DR with its gradual onset and late presentation of clinical symptoms mean that the condition can be well developed before it is diagnosed, making treatment much more challenging. For this reason, a screening program is in place within the UK and other countries around the world, looking for early signs of the disease in those diagnosed with diabetes in the hope that treatment can be started earlier, better control can be gained of the diabetes and ultimately, that blindness can be prevented.

A screening program was first implemented across the UK between 2002-2007. It is recommended that diabetic patients, type 1 and 2, receive annual screening for DR. The way in which screening is delivered to the general population has changed over the past years, with the development of telemedicine services for those living far away from national centres. Having these services available in local communities has shown improved compliance rates with screening programs resulting in decreased loss of vision from DR [10].

The ever growing burden of diabetes makes the global provision of retinal screening challenging both financially, and in regards to the number of skilled individuals required to provide the service. Automated retinal image analysis is a tool being developed, and is becoming commercially available, which reduces the number of staff required, relying on software for grading which can happen in real time, reducing delays in diagnosis [11].

Classification

Classification of DR is broadly split into background, non-proliferative and proliferative retinopathy and it is important to understand as it is closely linked to the severity of disease. Most patients living with diabetes for 20 years or more will show signs of non-proliferative DR.

Non proliferative DR has a number of identifying features ranging from micro-aneurysms and retinal haemorrhages to venous beading and retinal infarcts, more commonly known as cotton wool spots. The absence and presence of these symptoms determines the sub category of non-proliferative retinopathy (Fig 1). The above symptoms are not usually sight threatening.

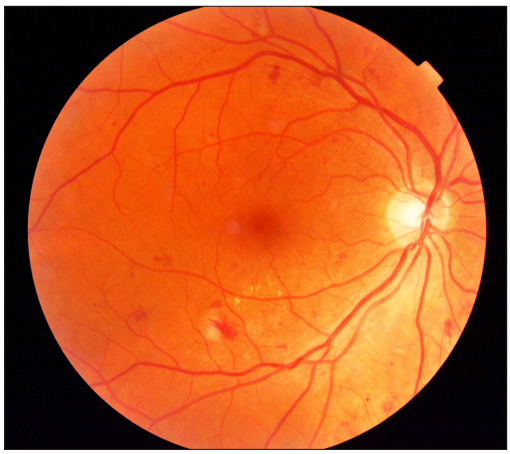

Figure 1: Pre-proliferative changes.

Proliferative DR is characterised by new vessel formation either on the disc (NVD) or elsewhere (NVE). This stages poses a much greater risk to vision as these new vessels are delicate and therefore more likely to bleed. Macular oedema is one of the main sight threatening complications of DR and it can occur in both non-proliferative and proliferative DR. Vitreous haemorrhage and retinal detachments are more commonly associated with proliferative disease [Fig 2].

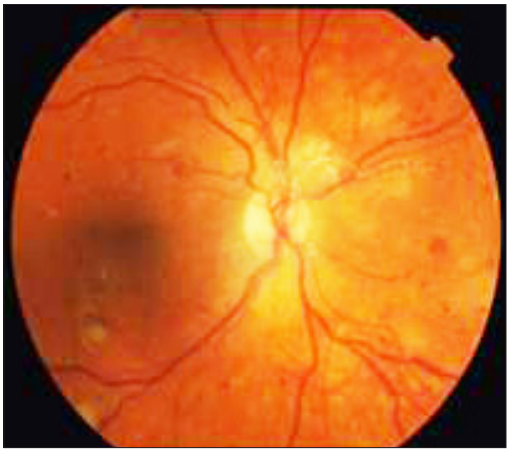

Figure 2: Proliferative changes (NVD noted in both eyes).

Macular oedema is defined as retinal thickening or hard exudates at or within a 2 disc diameter of the macular centre and it can be either focal [Fig 3] or diffuse [Fig 4] in distribution [11]. Focal oedema is often associated with circinate rings of hard exudates (lipoprotein deposits) resulting from leakage from microaneurysms. Diffuse oedema represents more extensive breakdown of the blood-retinal barrier, with leakage from both microaneurysms and retinal capillaries. Cystic changes may appear within the macula, representing focal coalescence of exudative fluid.

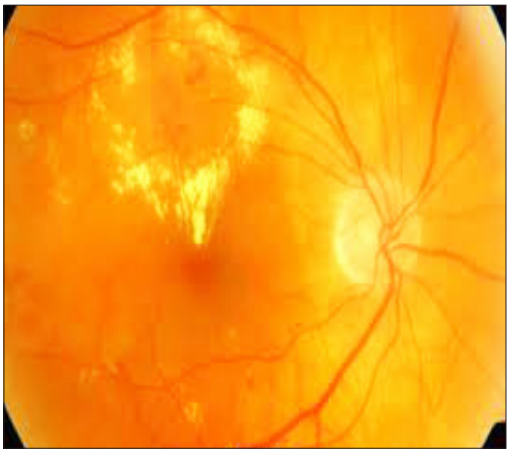

Figure 3: Focal DMO.

DIABETIC RETINOPATHY: A REVIEW

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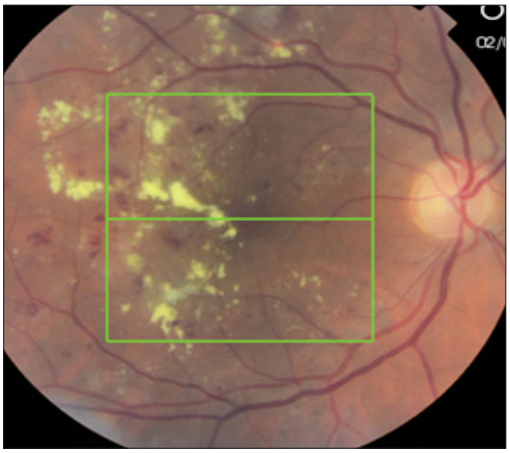

Figure 4: Diffuse DMO.

Diabetic macular oedema is most commonly classified into either being clinically significant or not. Clinically significant macular oedema (CSMO) is defined as DMO meeting at least one of the criteria presented as follows:

- *Thickening of the retina at or within 500µm of the centre of the macula.*

- *Hard exudates at or within 500µm of the centre of the macula, if associated with thickening of adjacent retina (not counting residual hard exudates remaining after disappearance of retinal thickening).*

- *Any zone(s) of retinal thickening 1 disc area or larger, any part of which is within 1 disc diameter of the centre of the macula [12].*

Diabetic macular oedema may also be classified based on optical coherence tomography (OCT) measurements, specifically, thickness of the macula, morphology of the retina, and the presence of macular traction [13].

Treatment

DR is the result of a systemic disease and therefore the most important part of the treatment is good metabolic control of diabetes. If HbA1c levels are maintained between 42-52 mmol/mol then the progression of diabetic retinopathy is substantially reduced, according to The Diabetes Control and Complications Trial [14].

However, due to the chronic nature of the disease, DR will develop in a high proportion of patients, with majority of the patients having some retinopathy after 10 years of diabetes. The most opportune time for these treatments is before any vision has been lost, since even advanced diabetic retinopathy can be present when a person has no vision complaints or problems.

Diabetic retinopathy cannot be cured but effective ocular treatments have been established that preserve vision and dramatically reduce the risk of vision loss.

Laser treatment

Retinal laser photocoagulation remains the mainstay of treatment for proliferative diabetic retinopathy and focal macular oedema [15].

The Early Treatment for Diabetic Retinopathy Study has found that laser photocoagulation for macular oedema reduces the incidence of moderate visual loss (doubling of visual angle or roughly a 2-line visual loss) from 30% to 15% over a 3-year period while the Diabetic Retinopathy Study has found that adequate scatter laser panretinal photocoagulation reduces the risk of severe visual loss by more than 50% [16, 17] [Fig 5].

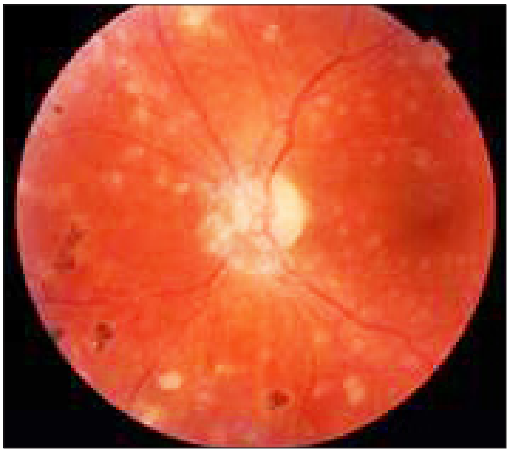

Figure 5: Fundus appearance following laser therapy.

Anti-VEGF intravitreal therapy

In the last 5 years, the treatment of diabetic maculopathy (the main reason for visual impairment in diabetic retinopathy) has been revolutionised by the introduction of anti-VEGF intravitreal injections (ranibizumab and aflibercept being the most commonly used medication in UK). However, the short lived half-life of these drugs leads to the need to be repeated with recurrence of the oedema. Therefore, deferred laser can be considered in these patients once the retinal swelling has reduced, as it may stabilise the disease and decrease the number of injections needed. A downside of grid laser can be "burn creep" with the expansion of pigment scars and consequent drop in visual acuity.

Intravitreal steroid therapy

As the pathophysiology of diabetic maculopathy is complex and inflammation is believed to play a major role, intravitreal steroids have also been used. The steroids used are in the form of intravitreal implants (Orzudex (Dexamethasone) and Iluvien (Fluocinolone acetonide)), which provides sustained release at a constant rate thus lasting much longer (4 months and 3 years respectively). However, due to the side effects profile of these steroids (especially intra ocular pressure rise), this is second line treatment.

DIABETIC RETINOPATHY: A REVIEW

KS Cooper, D Vaideanu-Collins

The Diabetic Retinopathy Clinical Research network (DRCR.net) Randomized Trial Evaluating Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema, known as the Laser-Ranibizumab-Triamcinolone for DME Study 2-year results demonstrated that ranibizumab with prompt or deferred focal/grid laser achieved superior visual acuity and optical coherence tomography (OCT) outcomes compared with focal/grid laser treatment alone. In the ranibizumab groups, approximately 50% of eyes had substantial improvement (10 or more letters) and 30% gained 15 or more letters. Intravitreal triamcinolone combined with focal/grid laser did not result in superior visual acuity outcomes compared with laser alone, but did appear to have a visual acuity benefit similar to ranibizumab in pseudophakic eyes [18].

Vitrectomy

Another surgical option used as an adjunct in the treatment for DMO is vitrectomy, besides being the main treatment for non-clearing diabetic vitreous haemorrhage and tractional diabetic retinal detachment. The removal of the vitreous is believed to reduce vascular permeability and relieve traction on the retina. Indeed, vitrectomy combined with IVTA for eyes with DMO refractory to prior anti-VEGF therapy has resulted in significant improvements in vision. DMO refractory to previous IVTA therapy has also shown good response once vitrectomy was performed before IVTA was repeated, with significant improvements in BCVA and the rate of DMO resolution reaching 77.5% [19].

As it can be seen from the above, many modalities of treatment have been developed to treat ocular complications of diabetic retinopathy, each with their own benefits and drawbacks. In addition, even more novel therapies have been developed in recent years and show very promising results. Despite the choice of therapy adopted, control of other systemic comorbidities is also important in improving outcomes of treatment.

As diabetes is a multisystem disease, it is very important that a multidisciplinary approach is taken in treating it and that communications between different specialists involved in treating the end-organ complications and general practitioner is maintained at all time for the best results.

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RECURRENT BRANCH RETINAL VEIN OCCLUSION WITH RESISTANT MACULAR OEDEMA

AF Fahem, MD Gillam, MA Reddy

Abstract

Branch retinal vein occlusion is a common retinal vascular disease. Visual impairment is determined by the extent of macular involvement usually relating to the development of macular oedema and/or macular ischemia. Treatment involves controlling the underlying systemic risk factors in addition to treating macular oedema. Ocular treatment of venous occlusion in the eye has evolved rapidly over the last decade and here; we present a case of a patient unresponsive to treatment and highlight important aspects of diagnosis and treatment.

Case history

We present the case of a 72 year old male patient referred from the diabetic eye screening service when routine screening revealed vascular tortuosity and multiple haemorrhages in the superotemporal quadrant of the right retina.

He is a type two diabetic controlled with tablets and insulin, and was noted to be hypertensive and have aortic stenosis. Additionally, he had a history of bladder cancer. He reported being a heavy smoker.

When he was first seen in our medical retina clinic in June 2012 his best corrected Snellen visual acuity was 6/7.6 in the right eye, 6/4 in the left eye. Anterior segment examination of both eyes revealed no abnormalities. Posterior segment examination of the right eye showed sectoral vascular tortuosity, multiple dot blot haemorrhages in the superotemporal quadrant and an isolated cotton wool spot, features consistent with a branch retinal vein occlusion (BRVO) (Fig 1). No features of diabetic retinopathy were noted. There were no abnormalities found in the left posterior segment. Optical Coherence Tomography (OCT) (Fig 2) and Fundus Fluorescein Angiogram (FFA) were done at that time and showed no macular oedema or neovascularisation.

The patient underwent a systemic work-up including baseline blood tests, clotting factors and a coagulation screen which were all within normal limits.

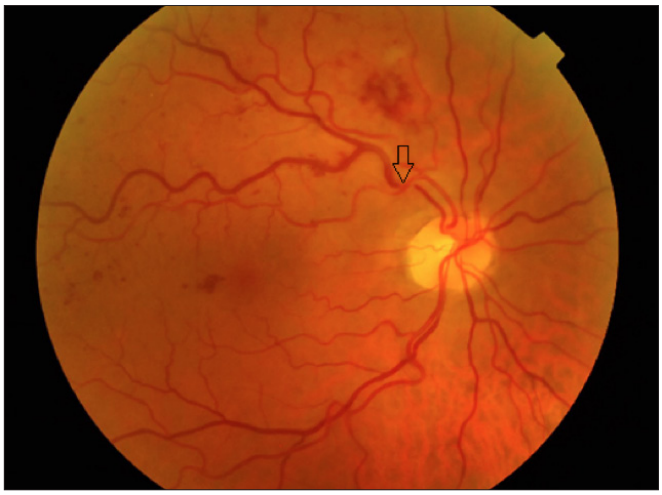

Figure 1: Right Fundus photographs showing vascular tortuosity and multiple haemorrhages in the superioteporal quadrant. Note that the site of occlusion is identified by the arteriorvenous crossing point highlighted with the arrow.

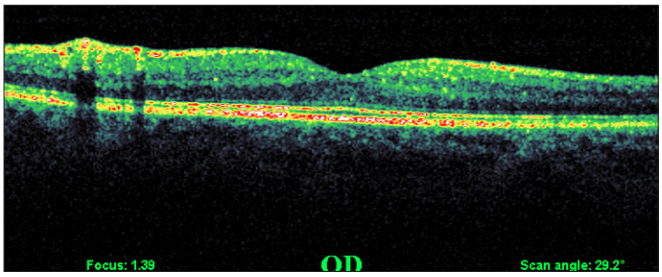

Figure 2: OCT after the first BRVO showing normal foveal contour and no macular oedema.

This patient was followed up in our clinic and his BRVO was noted to be resolving in subsequent visits with stable vision for 2 years. 2 years after his initial referral, he presented with a subacute vision loss in his right eye.

His visual acuity was profoundly reduced to counting fingers (CF) in the right eye and fundal examination showed multiple flame-shaped haemorrhages, cotton wool spots, haemorrhages involving the macula with significant macular oedema confirmed by OCT (Figure 3 and 4) compare with the normal images of the left eye (Figure 5) .

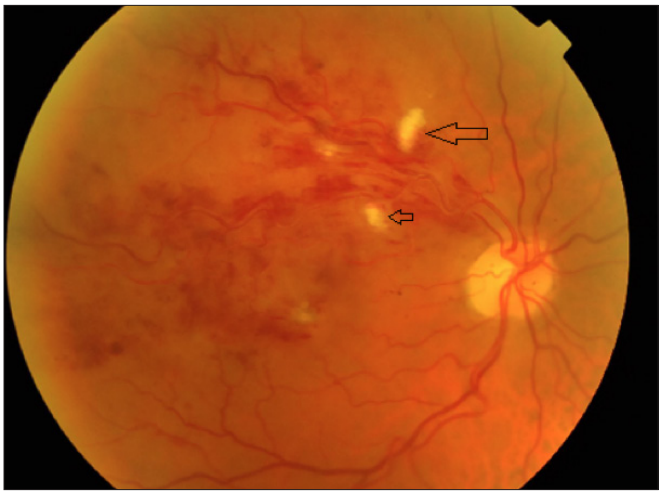

Figure 3: Right fundus photographafter the second BRVO showing more extensive involvement, flame shaped haemorrhages , multiple cotton wool spots (the two arrows) and macular involvement.

RECURRENT BRANCH RETINAL VEIN OCCLUSION WITH RESISTANT MACULAR OEDEMA

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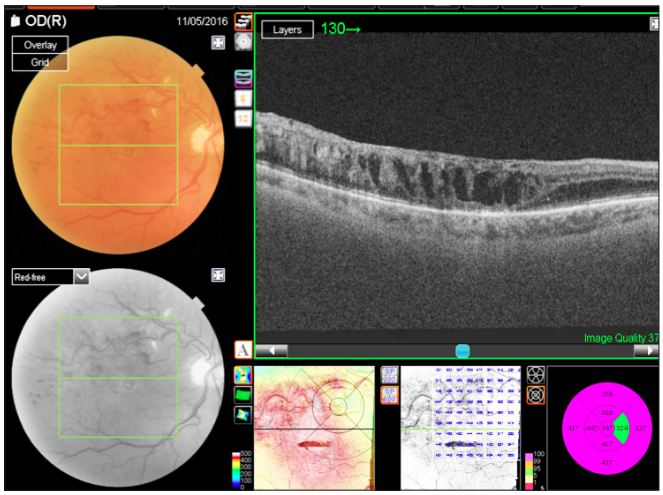

Figure 4: OCT showing multiple cystoid spaces (macular oedema) with loss of the normal foveal depression due to increased macular thickness.

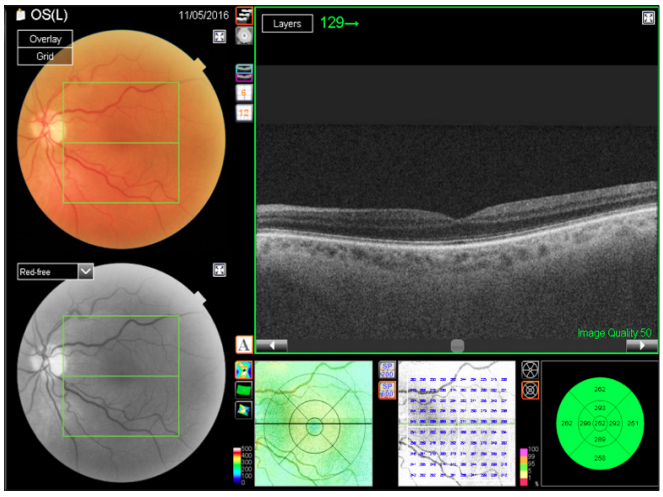

Figure 5: Normal left colour fundus photograph with normal OCT. note the normal foveal depression shown on OCT (the image on the right).

FFA was also done and showed considerable ischemic changes (Figure 6). All the area with relatively darker background to the rest of the photo represents an area of severe ischemia. This appears hypoflourescent due to "capillary drop out" (lack of capillary prefusion) caused by the occlusion. The macular area, which comprises the area between the main vascular arcades, is bisected by this area of ischaemia. This area is the part of the retina responsible for visual acuity and colour vision.

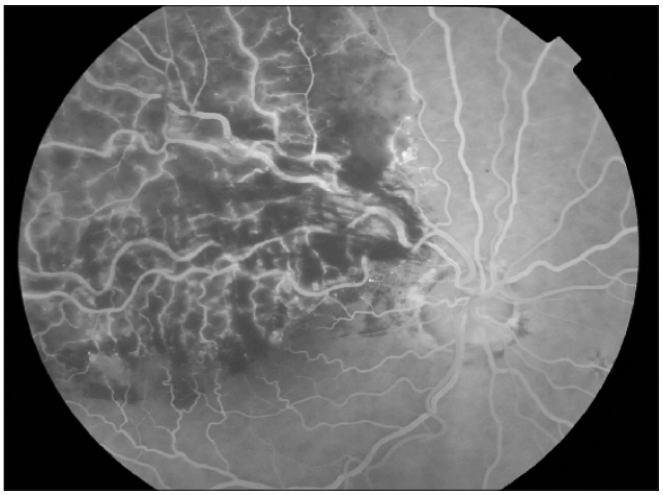

Figure 6: FFA showing extensive ischemic changes with macular involvement.

In order to treat the macular oedema, the patient received one injection of intravitreal dexamethasone. At 4 month follow up, there was no change in the extent of his macular oedema.

He then went onto receive 5 injections of an intravitreal anti-VEGF agent (ranibizumab) at monthly intervals. Unfortunately, at follow up, there was still no clinically significant improvement in his macular oedema and no improvement in visual acuity. In conjunction with the patient, a decision was made to discontinue treatment.

He is currently being monitored in our medical retina service to assess for the development of neovascularisation.

Discussion

Retinal vein occlusion is a common retinal vascular disease. It comprises central and branch retinal vein occlusion. It is second most common retinal vascular disease entity after diabetic retinopathy (1)

While central retinal vein occlusion (CRVO) is usually more severe than branch retinal vein occlusion BRVO, the latter tends to be 4-6 times more common than CRVO (2)

Vein occlusion usually occurs when the vein is being compressed by a crossing arteriole thickened due to atherosclerosis. Some regard it as sequelae to arteriovenous nipping. When the occlusion occurs in the central vein it causes central retinal vein occlusion or CRVO, or BRVO when the occlusion affecting one of the branch veins. (3)

Our patient was at high risk for the development of a branch retinal vein occlusion. He was more than 65 years old, had a history of hypertension and diabetes mellitus and was a smoker. (2)

RECURRENT BRANCH RETINAL VEIN OCCLUSION WITH RESISTANT MACULAR OEDEMA

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Our patient did not present himself to the ophthalmology service, in common with the vast majority of patients with a branch retinal vein occlusion, He was completely asymptomatic.

All patients with type 2 diabetes mellitus are screened for retinal changes related to diabetic retinopathy annually (4) and this is very helpful for picking up signs of other eye pathology. Unusually, our patient experienced a second vascular occlusion in the same area of the retina which was symptomatic. In those which are symptomatic, sudden painless drop in vision is the usual presenting feature and it correlates with the degree of macular involvement.

Fundal examination

Dilated fundal examination is essential. It usually shows the signs discussed above that characteristically only a quadrant of the posterior pole most commonly the superior-temporal one as in our case, Figure 1 & 3.

Investigations

In addition to full medical history, certain systemic and ocular investigations should be carried out routinely in all patients with BRVO.

Blood pressure, Blood glucose, lipid profile, FBC, ESR, should be done routinely in all patients (5). In our patient BP was 140/90, high HbA1C; 63 mmol/mol, normal lipid profile. Other blood tests where within normal at the time of presentation.

Glaucoma and ocular hypertension (intraocular pressure (IOP)>21mmHg) are important risk factors for developing vein occlusions (2). Therefore, IOP should always be assessed. In our patient, his IOPs were within normal and with no history of glaucoma.

Ocular investigations include colour fundus photographs for monitoring and future comparison, OCT for to assess for the presence of macular oedema and FFA to look for ischemic changes as well as neovascularisation.

Macular oedema and neovascularisation are the most important vision threatening complications encountered in retinal vein occlusion.

The ischemic retinal areas of BRVO release what is known as vascular endothelial factor (VEGF) that can promote angiogenesis and new vessel formation. VEGF also disrupts the inner blood retinal barrier resulting in leaky retinal capillaries and hence formation of macular oedema (6).

Treatment

Whilst our patient received no treatment from an ophthalmic perspective between the first and second vascular event, he did receive the mainstay of management following a BRVO, to treat and/or control the underlying cause as much as possible. Tight control of serum lipids, blood pressure and blood sugar have all been monitored and close follow up with his GP and cardiologist was provided.

However he continues to smoke 40 cigarettes a day. Branch retinal vein occlusions which do not affect the central vision are not treated from an ophthalmology perspective specifically as they are generally relatively asymptomatic and often at least partially resolve.

Due to the development of macular oedema in the second BRVO, our patient was treated with intravitreal dexamethasone. (7) due to its potent anti-inflammatory effects, it helps in reducing capillary permeability, stabilizing the endothelial cells tight junctions and reducing VEGF secretion (8).

As this did not provide any improvement in macular oedema or visual acuity, an anti VEGF agent, ranibizumab were used (9). It acts by inhibit VEGF synthesis responsible for increased capillary permeability and macular oedema (6). Unfortunately macular oedema was still refractory to treatment and vision failed to improve.

Present day treatment of macular oedema secondary to BRVO comprises different modalities; the widely used options are intravitreal injections of anti-VEGF agents or steroids. Macular grid laser is another treatment option, although it has been largely superseded by intravitreal injections. All of these treatments have been proven to have genuine effects on reducing the macular oedema and improving vision in many randomised multi-centred clinical trials (7, 9, 10)

This case is unusual in that our patient had distinct branch retinal vein occlusions in the same quadrant of the retina in the same eye. While the first BRVO episode has passed smoothly without noticeable impact on vision, the second attack was more severe, visual acuity dropped from 6/7.6 Snellen to counting finger with marked fundus involvement in terms of florid vascular tortuosity, flame shape haemorrhages and significant macular oedema.

RECURRENT BRANCH RETINAL VEIN OCCLUSION WITH RESISTANT MACULAR OEDEMA

AF Fahem, MD Gillam, MA Reddy

It is unusual for BRVO to cause such significant drop in vision. However, the fact that it has affected an area of previous vascular insult together with the multiple risk factors the patient already has had and the extensive macular ischemia in the second occlusion, might explain both the recurrence as well as the severity of the second attack.

Neovascularisation is a major late complication especially in ischaemic BRVO which can result in vitreous haemorrhage. Its incidence ranges from 36%-66% depending on severity of ischaemia. Therefore, continuing follow up for 24 months at 3-4 months interval is recommended to look for any neovascularization and treat it promptly with sectoral laser photocoagulation applied to the ischaemic retinal quadrants (5, 11, 12).

Whilst BRVO's are generally managed by ophthalmologists, it is important for the general physician to be able to identify such pathology as it can be an important mediator of more extensive cardiovascular or haematological disease. These patients will also require prompt referral to an ophthalmology service. General physicians also play a vital role in the treatment and control of many of the conditions which predispose patients to developing a branch retinal vein occlusion.

MCQs

1. Risk factors for BRVO include all of the followings except:

a. High IOP

b. Smoking

c. Hypertension

d. Beta blockers

e. Diabetes mellitus

2. The usual presentation for patient with acute BRVO is

a. Sudden painful reduction in vision

b. Sudden painless reduction in vision

c. Painful red eye with no vision impairment

d. Gradual painless reduction in vision

3. Fundal examination findings in patient with BRVO includes all of the following except

a. Cotton wool spots

b. Flame shape haemorrhage

c. Macular drusen

d. Vascular tortuosity

e. Macular oedema

4. Routine investigations to all patients with BRVO include all the following except

a. FBC

b. Blood glucose

c. Lipid profile

d. ESR

e. Protein c and S levels

5. Treatment of macular oedema in BRVO includes all of the followings except

a. Intravitreal anti-VEGF

b. Intravitreal steroids

c. Macular grid laser

d. Oral acetazolamide

RECURRENT BRANCH RETINAL VEIN OCCLUSION WITH RESISTANT MACULAR OEDEMA

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Answers

1 - D

All other factors are associated with BRVO. B-blockers have no such association.

2 - B

As with any vascular insult the onset is usually sudden and painless. A) characteristic of GCA, optic neuritis and acute angle closure glaucoma. C) can occur in conjunctivitis,scleritis and some cases of anterior uveitis

3 - C

Macular drusen is usually seen in AMD. All other features can be seen in BRVO.

4 - E

Only in special cases of vein occlusion like young onset, suspicion of hereditary prothromobotic conditions

5 - D

Oral acetazolamide can be used in macular oedema secondary to other causes especially in retinal dystrophies but with controversy. All other options can be used in BRVO related macular oedema.

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AN INTRODUCTION TO THE MANAGEMENT OF COMMON EYELID LESIONS

SR Dawson, D Cheung, S Aggarwal

Abstract

Eyelid lesions commonly present in a variety of ways to both primary and secondary care. Many lesions are non-cancerous growths which can be treated conservatively and observed. However a significant number of malignant eyelid lesions also present, requiring onward referral to secondary care for management. The most common malignant lesion occurring around the eyelids is a basal cell carcinoma.

Much less common but potentially fatal periocular malignant lesions include squamous cell carcinoma, sebaceous gland carcinoma and malignant melanoma. Unfortunately a lack of suspicion by primary care clinicians about these lesions can occasionally lead to their misdiagnosis, consequent late referral and compromised prognosis for the patient.

Introduction

When a patient presents with an eyelid lesion, a systematic history should be taken and a focused examination performed, particularly looking for features suggestive of malignancy. Studies have shown 5% to 10% of all skin cancers involve the eyelids. (1) It is important to ascertain if the lesion is progressively enlarging and assess for any risk factors for malignancy such as high levels of sun exposure, previous skin cancers or immunosuppression.

Whilst examining the lesion: site, size, shape and surface features such as crusting or bleeding should be noted. Important signs for malignant neoplasia include telangiectasia and madarosis (eyelash loss) commonly seen in basal cell carcinomas (BCC'S), caused by local invasion of the lash follicles. Palpating the lesion to ascertain mobility and tenderness can also aid diagnosis.

Palpation can also sometimes give clues as to where the lesion is arising e.g. from within the tarsal plate (chalazion) or from within the skin (epithelial cyst). Although an ophthalmologist has the advantage of a slit lamp microscope for detailed examination, primary care clinicians can glean a great deal of information just with the naked eye and further information still with simple magnifiers or using a direct ophthalmoscope.

History	*Examination*
• Duration of symptoms: when did the lesion first appear? • Rate of growth. (Very rapid suggests infective or inflammatory aetiology. Gradually progressing over 2-3 months may be a sign of malignancy). • Previous skin cancers • History of excessive sun exposure and skin fairness (risk factors for melanoma, SCC and BCC). • Immunosuppression: history of renal transplant or HIV? (risk factors for SCC and BCC).	• Site/Size/Shape • Surface features e.g crusting/bleeding/ulceration/ madarosis (eyelash loss)/ telangiectasia/ erythema/ pigmentation/ translucency • Tender to touch. (Often acute and associated with infection). • Eye movements to assess for diplopia (presence could indicate invasion of lesion into the orbit) • Palpate for regional lymphadenopathy.

Figure 1: Important features to elicit from history and examination.

Non-Malignant lesions

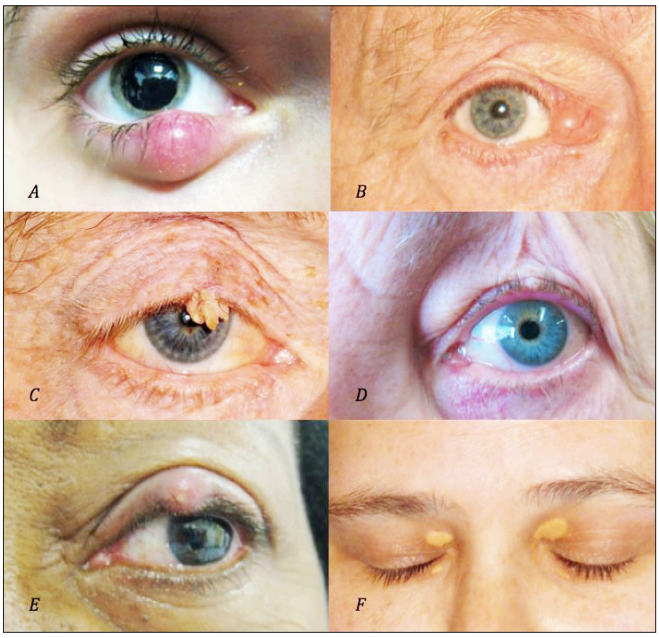

Figure 2: Non-malignant Lid Lesions. A: Chalazion. B: Cyst of moll. C: Viral papilloma. D: Cyst of Zeiss. E: Stye. F: Xanthelasma.

Chalazia

Clinical features

Chalazia are caused by a blockage of the meibomian glands and can involve either the upper and lower lids. They are erythematous and can be tender to touch.

Management

Chalazia can be treated conservatively or drained via a minor procedure if persistent or symptomatic. The patient should be advised to use daily warm compresses over the lesion aiming to relieve the blockage. The authors recommend the use of microwaveable heat retaining wheat germ containing bags over more traditional methods. (2)

If chalazia persist or are recurrent in the same location, clinicians should be suspicious of sebaceous cell carcinoma (SGC) and therefore a referral to their local ophthalmology department for further investigation is recommended.

AN INTRODUCTION TO THE MANAGEMENT OF COMMON EYELID LESIONS

SR Dawson, D Cheung, S Aggarwal

Viral Papilloma

Clinical features

Viral papillomata can occur anywhere on the body. These slow growing, non-pigmented, non-tender lesions are often polypoid and can grow large enough to become a functional and cosmetic nuisance.

Management

If asymptomatic the lesion can be left alone and patients often report lesions dropping off spontaneously. If symptomatic they can be removed via a minor procedure. Prior to their removal, the authors would recommend photography of all suspected 'viral papillomata' to record the appearance and location.

Some hyperkeratotic, polypoid lesions with surface crusting labeled as 'probable viral papillomata' should be treated with suspicion and sent for histological analysis for diagnosis confirmation. Although the vast majority are confirmed to be viral papillomata, a very small proportion of these so called 'keratin-horns' represent premalignant and even malignant lesions such as actinic keratosis or squamous cell carcinoma's (SCC's).

Cyst of Moll and Cyst of Zeiss

Clinical features

Cysts of Moll are caused by obstructions of the modified sweat glands of Moll and appear translucent. Cysts of Zeiss are caused by blockages of the modified oil producing glands of Zeiss and are commonly creamy white. They are both located in the surface skin epithelium commonly in or around the eyelash line.

Management

Small cysts of Moll and Zeiss may be left alone. Their removal or drainage can be performed if they represent a cosmetic or function problem. However, care must be taken whilst removing them to avoid cicatricial distortion of the eyelash line and subsequent inturning of the eyelashes. Cystic BCCs can occasionally be misdiagnosed for translucent cysts of Moll.

Referral to ophthalmology for slit lamp examination and diagnostic incisional biopsy is therefore recommended if there is any suspicion of malignancy. Sinister signs to look out for include telangiectasia and eyelash loss (madarosis).

Xanthelasma

Clinical features

Xanthelasma consist of fatty deposits in the dermis causing yellowish plaques. They are often bilateral and can be associated with raised serum cholesterol.

Management

Patients with xanthelasma should have their lipid profile checked by their GP. Surgical excision and argon laser can be used to improve the cosmetic appearance. Although cryotherapy and trichloroacetic acid peels have been described, they can cause superficial skin depigmentation and are not particularly effective for thicker lesions.

External Hordeolum (Stye)

Clinical features

Often confused with chalazia, a stye is an acute abscesses caused by a blockage in the eyelash follicles. They are often tender and erythematous. Management: warm compresses can help to relieve symptoms. If associated with pre-septal cellulitis, oral antibiotics may be required (commonly oral Flucloxacillin).

Malignant lesions

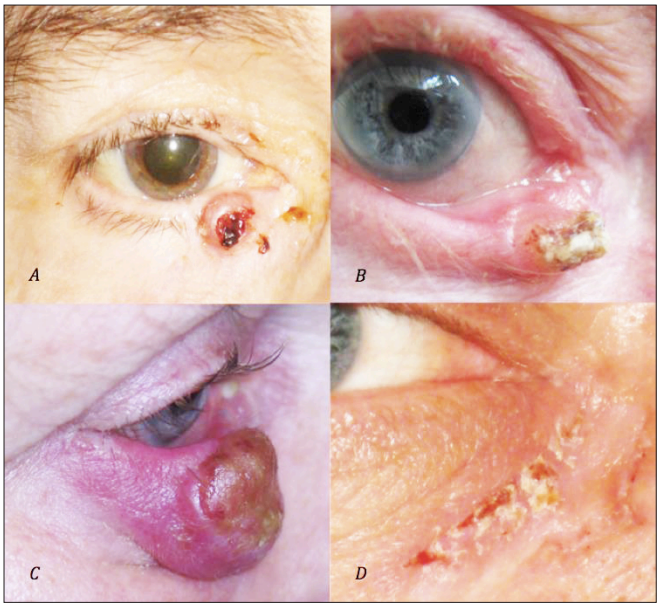

Figure 3: Malignant lid lesions. A: Basal cell carcinoma. B: Squamous cell carcinoma. C: Sebaceous gland carcinoma. D: Morphoeic basal cell carcinoma.

AN INTRODUCTION TO THE MANAGEMENT OF COMMON EYELID LESIONS

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Basal Cell Carcinoma (BCC)

Clinical features

BCC is the most common eyelid tumour, accounting for 90% of all cases. (3) They are slow growing, rarely metastasise and more commonly affect the lower lid and outer canthus. BCC lesions affecting the inner canthus are particularly dangerous due to their predilection for intraorbital invasion. The clinical subtypes commonly found on eyelids include (4):

- *Noduloulcerative BCC (rodent ulcer): these present as a firm nodule with typical rolled pearly edges, fine telangiectasia and surface ulceration.*

- *Sclerosing BCC: these have minimal surface changes or scar like plaques which overlie extensive infiltration.*

- *Superficial: erythematous, scaly plaques.*

- *Other less common subtypes include; micronodular, pigmented and morphoeic basal cell carcinoma.*

Risk factors

Ultraviolet light exposure, skin fairness and increasing age have been shown to increase the risk of developing BCC's. (3)

Management

The British Association of Dermatologists classify periocular BCCs as high-risk skin neoplasms for which prompt referral is recommended. The gold standard treatment for periocular BCC is surgery. Oculoplastic surgeons have an important role in providing curative surgical excision with reconstruction after histological confirmation of clearance of the lesion whilst respecting the ocular surface. Other non-curative treatments include cryotherapy, topical imiquimod 5% cream, topical chemotherapy with 5-Fluorouracil, photodynamic therapy and Vismodegib. (4)

Squamous Cell Carcinoma (SCC)

Clinical features

SCC's are less common (accounting for 5-10% of eyelid malignancies) but more aggressive than BCC's and tend to metastasise to regional lymph nodes. Like BCCs, the most common location is the lower eyelids due to increased sun exposure in this area. (5)

Subtypes include

- *Nodular type: typically have irregular margins and are hyperkeratotic.*

- *Ulcerating: erythematous base, well defined, indurated and slightly everted borders.*

- *Cutaneous horn*

- *Bowen's disease (SCC in situ; there is no invasion through the epidermal basement membrane. A small percentage can progress and become invasive SCC's.)*

Risk factors

Fair skin, prolonged sun exposure, exposure to arsenic, hydrocarbons and radiation have all shown to increase the risk of SCC's. (5) Immunocompromised patients such as acquired immune deficiency syndrome (AIDS) sufferers or those post renal transplant have a higher chance of developing the condition. (6) Management: both wide local excision by Moh's micrographic technique and excisional biopsy with histological confirmation of complete excision, offer the best chances of complete cure.

If the lesion has spread to the orbit, orbital exenteration may be indicated. Other therapeutic options if surgery is not possible include cryotherapy, imiquimod, photodynamic therapy, 5-Fluorouracil and mitomycin, although these are usually either used as an adjunct to surgery or in a palliative setting.

AN INTRODUCTION TO THE MANAGEMENT OF COMMON EYELID LESIONS

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Malignant Melanoma

Clinical features

Malignant melanoma rarely affects the eyelids (they account for <1% of all eyelid tumours), however they frequently metastasise and are therefore associated with high mortality. (4,5) year survival is only 10% in those who present with metastases, therefore early diagnosis is critical. (7) Melanomas are usually pigmented but it is important to remember rare amelanocytic types exist. The acronym ABCDEF can be used to assess the important features suggestive of malignancy. (7)

A - Asymmetry

Common moles are usually round and symmetrical. Asymmetry of a lesion should raise suspicion of melanoma.

B - Border

Melanomas often have irregular edges, which may be uneven.

C - Colour Variations

Moles are usually uniform in colour. Look for any difference in colour within the same lesion.

D - Diameter

Lesions which measure >6mm in diameter should raise suspicion of melanoma.

E - Evolving

Any change in size or colour of the lesion.

F - "Funny looking"

Melanomas can appear dissimilar to other pigmented lesions on the body. Ensure thorough examination of the patient, looking for other lesions to compare.

Sub-types include

- Lentigo maligna: *these are initially flat and spread horizontally. They become elevated as they infiltrate into the deeper layers of skin.*

- Superficial spreading: *smaller, less well-defined pigmented lesions, which can have elevated areas and nodules.*

- Nodular type: *these lesions are pigmented, have irregular borders, are rapidly growing and are associated with surface features such as ulceration and bleeding. (4)*

Risk factors

Increasing age, sun exposure and fair skinned individuals.

Management

The seven point check list (figure 4) can be a helpful guide when making a decision whether or not to refer, although oculoplastic surgeons have a lower threshold for reviewing and biopsying any pigmented lesion. Treatment is via local excision if possible; although there is debate amongst clinicians as to what the recommended margins for excision should be. Oculoplastic surgeons would usually opt for narrower margins than those traditionally recommended by the British Association of Dermatology. (8, 9, 10)

Malignant melanoma 7-point checklist [7]

Major features

- Change in size
- Irregular shape
- Irregular colour

Minor features

- Largest diameter 7 mm or more
- Inflammation
- Oozing- including crusting or bleeding
- Change in sensation (?itchy)

2 points are scored for any major features and 1 point for any minor features. Lesions scoring ≥3 or a high index of suspicion with lower score require prompt referral. Other lesions can be monitored regularly to assess for change.

Figure 4: Seven point checklist for suspected malignant melanoma.

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Sebaceous Gland Carcinoma

Clinical features

SGCs are rare (accounting for 1-5.5% of all eyelids tumours) and most frequently affect the upper lids. (11) There are two main types; nodular and spreading. Nodular presents with a firm nodule often mistaken for a chalazion. The spreading type often resembles a chronic conjunctivitis and involves diffuse infiltration of the lids and conjunctiva. (12)

SGCs arise from the meibomian glands or less commonly from the glands of Zeiss or sebaceous glands of caruncle. They carry significant mortality (10% overall but up to 67% 5 year mortality if extra-regional spread) due to difficulties in diagnosis and subsequent delayed treatment.

Risk factors

SGCs are more common in females and the elderly population and has been associated with Muir-Torre syndrome (a rare autosomal dominant condition predisposing to internal and cutaneous malignancies). (4)

Management

Outcomes are highly dependent on the degree of spread at the time of diagnosis. It is therefore imperative to have a high index of suspicion when seeing patients with recurrent or non-healing chalazion or patients with unilateral blepharitis.

Such patients should be urgently referred to their local hospital eye service where the diagnosis can be confirmed with full thickness biopsy. Following confirmation, wide local excision is performed with margin control. SGC can metastasise locally via pagetoid spread to the ocular surface and therefore conjunctiva mapping biopsies are also performed. Depending on the extent of the lesion, regional lymph node clearance and exenteration are options to be considered. (4)

Conclusion

When assessing patients with eyelid lesions it is important to be able to recognise the signs that could indicate malignancy and refer appropriately.

Red flags for such lesions include:

- *Ulcerating or bleeding lesion*
- *Progressively enlarging over 3-4 months*
- *Loss of lashes (madarosis)*
- *Distortion of lid architecture*
- *Unilateral blepharitis (13)*
- *Recurrent 'chalazion' in the same location*

Any lesions with these findings need to be referred urgently. Patients with non-malignant lesions can usually be managed conservatively and observed. However, if the lesions become symptomatic or affect the patient's vision, a referral for further assessment and possible removal should be considered.

Increasingly, management decisions of non-cancerous periocular lesions are influenced by local clinical commissioning groups CCG policies on 'aesthetic and limited clinical value' procedures. Regrettably oculoplastic colleagues have reported cases of dangerous periocular malignancies being referred late after initially being misdiagnosed as benign cysts. If there is any diagnostic doubt, the authors recommend referral to a local ophthalmology department where slit lamp examination and biopsy can be performed.

MCQ's

1) All are features of a basal cell carcinoma except:

a) Slow growing

b) Telangectasia present on surface

c) Pearly edge

d) Commonly metastasise to the liver

e) Central ulcer

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2) Which of the following statements regarding malignant melanomas is untrue?

a) Commonly metastasise

b) Management involves local excision

c) Associated with excessive sun exposure

d) Subtypes include; lentigo maligna and nodular

e) Survival rate is mostly related to surface area of lesion

3) Which of the following statements are true regarding chalazia?

a) Treatment is always by incision and curettage

b) Risk factors include excessive sun exposure

c) Very rarely respond well to warm compresses

d) Recurrent, non healing chalazia should be referred for further investigation

e) Patients with blepharitis are less likely to develop chalazia

4) Which of the following are red flags and therefore prompt urgent referral to secondary care for further investigation?

a) Unilateral blepharitis

b) Madarosis (loss of lashes)

c) Rapidly progressing lesion

d) Lesion with surface crusting

e) All of the above

5) Which of the following has not been shown to be a risk factor for developing SCC?

a) Excessive sun exposure

b) Smoking

c) Type 2 Diabetes

d) Previous renal transplant

e) Exposure to industrial carcinogens

Answers

1) D

Classic features of a BCC include pearly, rolled edge with central ulcer, which can often bleed. Telangectasia is often present and there can be loss of lashes. BCC's very rarely metastasise.

2) E

Survival rates are related to the depth of lesion at presentation. Lesions ≤0.76mm thick have a 95% survival rate at 5 years compared to those ≥4mm which have a 45% survival rate. (7)

3) D

All non-healing, recurrent chalazia should be referred to an ophthalmologist promptly for further investigation. Chalazia often respond well to warm compresses and only require incision and curettage if persistent or symptomatic. Blepharitis and rosacea both increase the risk of developing chalazia. (6)

4) E

All options are red flags and could indicate malignancy. Urgent referral to secondary care is advised if lesions feature any of these signs.

5) C

Diabetes has not been shown to be a risk factor for developing SCC. Other risk factors for SCC include: immunosuppression (e.g AID's sufferers), X-ray exposure and the wart virus. (7)

AN INTRODUCTION TO THE MANAGEMENT OF COMMON EYELID LESIONS

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HYPOTONY & CHOROIDAL FOLDS ASSOCIATED WITH VENLAFAXINE MEDICATION

SM Giulvezan, S Ugradar, N Davies

Abstract

We report a case of hypotony and posterior segment changes secondary to systemic psychotropic medication.

Ocular toxicity secondary to systemic medications varies in severity from asymptomatic to irreversible damage despite medical or surgical treatment. The eye is the second most likely organ to suffer from drug toxicity after the liver (1) and any effects that drugs may have on the eye need to be highlighted early to potentially prevent progression of disease.

Venlafaxine is a commonly used serotonin-noradrenaline reuptake inhibitor (SNRI) used in depressive and anxiety disorders. Patients are often on this drug long term and significant ocular side effects are not known to be very common. The following case however leads the authors to believe that an increased dose of venlafaxine led to hypotony and chroidal folds with induced hypermetropia.

Case History

A 45 year old man with no significant past ophthalmic history presented with unilateral blurred vision in his left eye. His past medical history included an anxiety disorder for which he had been on venlafaxine for 10 months. 6 weeks prior to this presentation however his dose was increased from 75mg to 150mg.

He was referred to ophthalmology following his complaint of blurred vision. On initial examination visual acuities were 6/5 in the right eye and 6/9 in the left eye. Initial intraocular pressures (IOP) were 10mmHg on the right and 8 mmHg on the left.

Auto refraction showed emmetropia in the right eye and +1.75 dioptres of hypermetropia on the left. The visual acuity in his left eye improved to 6/5 with the refractive error corrected. The refractive error was felt to be due to a shortening of axial length because of hypotony. Biometry was performed and confirmed this was the case with axial length of 22.89mm on the right and 22.49mm on the left.

A diagnosis of hypotony with subsequent choroidal folds and reduced axial length was made, most likely related to venlafaxine.

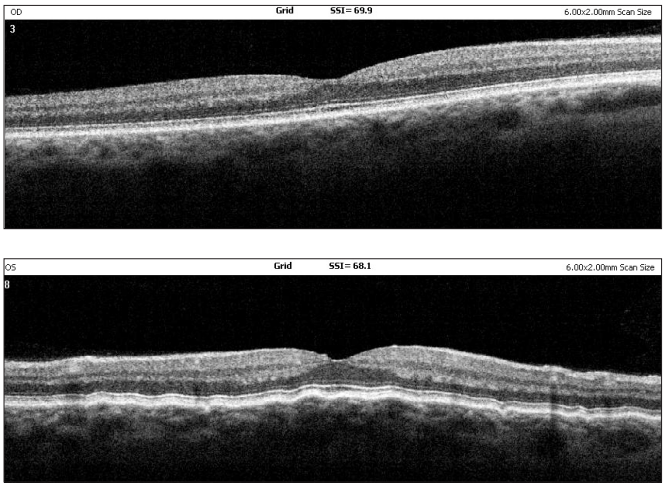

Figure 1: Shows OCT scans of the left and right eyes, centred on the fovea. The right scan shows normal neurosensory retina, RPE and normal choroid. The scan of the left eye shows the choroidal folds and a slight raising of the fovea.

A clinical diagnosis was made at this stage and there were 2 aspects to the management plan.

1. Rule out other causes of choroidal folds

2. Discuss with psychiatrist to reduce the dose of venlafaxine

Investigations

- **Blood tests - FBC, U & Es, inflammatory markers, hepatitis screening, thyroid screening, autoimmune screening**

- **Imaging - MR Head and Orbit**

The results of the investigations were all normal. The psychiatrist advised the patient to reduce the dose of venflaxine to 75mg once per day and the patient was reviewed in ophthalmology clinic 8 weeks later.

At the follow up visit, his vision had improved (6/5), intra ocular pressures measured 11mmHg bilaterally. The choroidal folds remained the same and axial length was unchanged.

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Discussion

Venlafaxine is the first nontricyclic serotonin/norepinephrine reuptake inhibitor. It is used in the treatment of depression, generalized anxiety, social anxiety, panic disorder, attention deficit disorder. Venlafaxine has an overall side effect and safety profile that is comparable to the "selective" serotonin reuptake inhibitor (SSRI) antidepressants, sharing the same serotonergic adverse effects, while in addition provoking noradrenergic adverse effects, in particular cardiovascular such as dose-dependent blood pressure elevation, a risk of QT interval prolongation, which can lead to torsades de pointes, an unusual and potentially fatal type of ventricular tachycardia.

Adverse events pertaining to the digestive (nausea, dry mouth), nervous (dizziness, somnolence, insomnia) and urogenital (abnormal ejaculation) systems as well as sweating were the most frequently reported adverse events. (2,3,4,5)

Reported adverse effects on the eye are mydriasis which can trigger an attack of acute angle-closure glaucoma (ACG) and abnormal vision. The action of serotonin at 5-HT2A and 5-HT2c receptors located in the iris-ciliary body complex leads to an increase in IOP, because the activated receptors produce an increase in ciliary body flow and increase in aqueous humour production. Opposing the agonist action of serotonin on 5-HT1A receptors leads to a decrease IOP, this occurs through inhibition of adenylate cyclase in the ciliary body and a subsequent decreased production of aqueous humour. (6,7)

Clinically, chorioretinal folds appear as alternating yellow and dark bands, most frequently involving the posterior pole. (8,9) Chorioretinal folds are usually curvilinear and oriented more or less parallel to one another, and also can be circular or radial. Patients with chorioretinal folds may be asymptomatic, and in this case no treatment needs to be applied, or they may present with metamorphopsia or hyperopia, and in this case, the management depends on the underlying etiology.

The causes of choriodal folds can be remembered using the mnemonic: "T.H.I.N. R.P.E.".

- Tumors. Choroidal tumors, such as melanoma and metastasis from sites such as breast and lung, may produce chorioretinal folds. Other less common lesions such as melanocytoma, choroidal hemangioma and choroidal osteoma may induce similar findings. (8)

- Hypotony. Hypotony caused by wound leaks, overfiltration following glaucoma surgery and a cyclodialysis cleft can produce a characteristic maculopathy with folding of the choroid, RPE and retina. (10)

- Inflammation. Thickening and inflammation of the sclera may result in chorioretinal folds. This can occur in posterior scleritis and a variety of other disorders. These include orbital inflammatory pseudotumor, thyroid eye disease, autoimmune connective tissue diseases such as rheumatoid arthritis, and vasculitides such as Wegener's granulomatosis and polyarteritis nodosa. (8)

- Idiopathic. When no pathologic condition can be found in association with chorioretinal folds, they are considered to be idiopathic. These patients are often male and present with acquired hyperopia and normal or near normal visual acuity. (11)

- Neovascular Membrane. A choroidal neovascular membrane associated with age-related macular degeneration may contract spontaneously or following laser photocoagulation, resulting in focal shrinkage of the choroid, thereby producing chorioretinal folds. (12)

- Retrobulbar Mass. Both benign and malignant orbital masses may indent the globe and cause scleral edema and congestion of the choroidal vasculature, resulting in chorioretinal folds. The differential diagnosis of orbital tumors is broad and includes cavernous hemangioma, lymphangioma, hemangiopericytoma, glioma, meningioma, rhabdomyosarcoma, lymphoma, fibrous histiocytoma, epithelial tumors of the lacrimal gland, neuroblastoma, and metastatic tumors. (8)

- Papilloedema. Increased intracranial pressure from a variety of etiologies including intracranial tumors, pseudotumor cerebri, benign intracranial hypertension and dural arteriovenous malformations can result in papilledema associated with chorioretinal folds. (13)

- Extraocular Hardware. A scleral buckle used for the treatment of rhegmatogenous retinal detachment may result in scleral thickening in the vicinity of the buckle, occasionally producing chorioretinal folds near the posterior slope of the buckle. (8)

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After excluding other causes, the most likely diagnosis in this patient is hypotony and choroidal folds related to venaflaxine. This effect on intraocular pressure appears to be dose-dependent as evidenced by the equalisation of the intraocular pressures and improved visual acuity in the affected eye at the follow up visit.

The anatomical changes of the choroidal folds however remained. It is not clear why the presentation was with unilateral rather than bilateral changes. We postulate that there are subtle differences between the eyes in the rate of aqueous production and in outflow facility that resulted in a lower IOP on the left than the right. Further follow up is planned to reassess after a longer time period on the lower dose.

This case is the first report of hypotony and choroidal folds with induced hypermetropia in a patient taking the higher dose of venlafaxine.

Test yourself

1. Which of the following is most likely to produce choroidal folds:

a. Dysthyroid eye disease

b. Hypermetropia

c. Retinal detachment

d. Traumatic globe injury

e. Wet macula degeneration

2. Secondary Angle Closure Glaucoma does not occur in:

a. Pseudoexfolation

b. Iris neovascularization secondary to retinal vein occlusion

c. High myopia

d. Topiramate medication

e. body melanoma

3. Pupil dilation can occur as a side effect of systemic treatment with:

a. Beta blockers

b. Chlorpromazine

c. Morphine

d. Omeprazole

e. Tamsulosin

4. In ophthalmic history taking and examination which of the following is true?

a. Blurred near vision implies myopia

b. A pinhole will improve acuity in uncorrected hypermetropia

c. Visual acuity can only be tested at 6 meters

d. Painless loss of vision in one eye can often imply optic neuritis

e. Loss of colour vision suggests a macula problem

5. Investigation: Which of the following is true?

a. MRI scan is the best technique for imaging orbital bones

b. Optical coherence tomography uses ionizing radiation

c. Biometry is used to measure axial length before cataract surgery

d. Glasses can be prescribed after autorefraction

e. Thyroid hormone levels are always raised in autoimmune thyroid disease

Right answers

1. In hypermetropia the axial length is reduced and is the most common cause of choroidal folds.

Dysthyroid eye disease is not very common. Retinal detachment involves retinal folds rather than choroidal folds. Trauma causes commotio retinae or choroid rupture. In wet macula degeneration choroidal folds are not a feature.

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2. Glaucoma is an optic neuropathy and can cause irreversible blindness.

Angle closure can occur as a primary problem in small or short eyes. Secondary causes of angle closure include those from lax zonules (PXF), a 'posterior pushing mechanism' (topiramate or melanoma) or an 'anterior pulling mechanism' (iris neovascularisation). Patients with high myopia have wide angles which will not close and are more predisposed to primary open angle glaucoma.

3. Chlorpromazine is an antipsychotic.

It can cause mydriasis because of its anticholinergic effect. Chlorpromazine should be used with caution in patients with glaucoma and small eyes. Beta blockers and omeprazole do not affect pupil size, opiates cause constricted pupils and tamsulosin affects the dilator muscle which can cause problems during cataract surgery, but does not typically affect the size of the pupil.

4. Myopia gives sharp vision near the eye and blurred vision in the distance.

A pinhole will improve vision in all refractive errors. Visual acuity can be tested at any appropriate distance as long as the chart is calibrated for that distance. Loss of vision in optic neuritis is typically painful especially on eye movement. Macula problems lead to reduced acuity and difficulty reading and also distortion of objects in the central vision. Colour vision changes are more often noted in optic nerve disease.

5. The best imaging technique for the bony orbit is a CT scan.

OCT uses infrared light to image the retina and is therefore safe, non-invasive and does not use ionising radiation. Ocular Biometry is used to take measurements of the eye prior to cataract surgery. The corneal curvature and depth of the anterior chamber are measured as well as the axial length. These data are used in various equations to calculate the strength of the required lens implant. Autorefraction measures refractive error in a patient but is not completely accurate; after this a subjective refraction is performed, refining the intial measurements to obtain the best spectacle prescription for the person. Dysthryoid eye disease is an autoimmune disease and can occur in euthyroid, hyperthrooid or hypothyroid states.

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DIABETIC RETINOPATHY: THE IMPORTANCE OF SCREENING

MS D'souza, Y D'Souza

Abstract

Diabetic retinopathy is a known complication of diabetes. The consequences can be life-changing with over a thousand new cases of blindness in the UK per year due to diabetic retinopathy. The UK has therefore introduced national screening programmes to detect early stages of retinopathy which can be managed appropriately thereby preventing further deterioration of visual acuity.

This case exemplifies what may happen without timely screening and explores the criteria required for an effective screening programme in the context of diabetic retinopathy. Available treatment options are also briefly discussed.

Case History

Mr X, a 49 year old man with type 2 diabetes, was referred from casualty with reduced vision. He takes metformin for his diabetes and has no known drug allergies. He was unsure of his last HbA1c and had not attended diabetic screening services in the UK as he was living overseas for two years.

On examination his visual acuity was 6/24 in the right eye and 6/48 in the left eye. Both fundi looked ischaemic with multiple haemorrhages. New vessels were visible clinically and fluorescein angiography of both optic discs confirmed the diagnosis of bilateral proliferative diabetic retinopathy (Figure 1 a-d). Optical coherence tomography (OCT) revealed bilateral macular oedema with retinal thickening involving the centre of the macula (Figure 1 e, f).

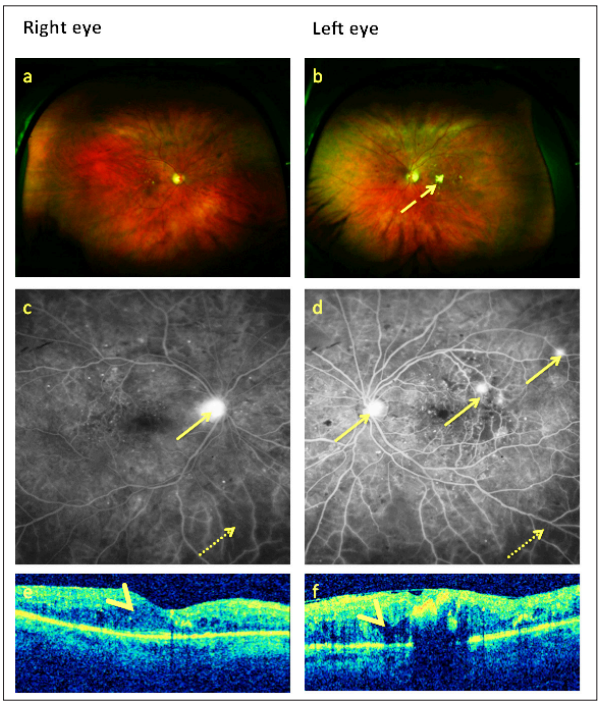

Figure 1: Figure showing colour images (a,b), fluorescein angiography (FFA) (c,d) and optical coherence tomography (OCT) images (e,f) of the right and left eye. Dashed arrow denotes exudative plaque at the left macula, arrow indicates new vessels, dotted arrow points to areas of ischemia and arrow head to fluid in the retina on OCT.

Bilateral panretinal photocoagulation was commenced immediately. Mr X was also scheduled to receive bilateral intravitreal anti-VEGF injections. The prognosis is guarded due to a dense pre-existing plaque of exudates at the left fovea. A second session of bilateral pan-retinal photocoagulation is planned.

Discussion

Diabetic retinopathy

Diabetic retinopathy affects the retinal microvasculature in patients with poorly controlled diabetes (1). The pathological process is triggered by hyperglycaemia which causes endothelial damage (1). Endothelial cells consequently release cytokines resulting in increased vascular permeability. Microaneurysms form leading to capillary occlusion and consequent hypoxia and ischaemia. This stimulates the formation of new blood vessels that are prone to bleeding and rupture. These new vessels may predispose to retinal detachment as the vitreous gel condenses and contracts following haemorrhage from the new vessels and resultant fibrosis (2). If the macula is involved there is consequent loss of central vision (1).

Diabetic retinopathy may progress from no retinopathy through to non-proliferative, proliferative and then advanced retinopathy (2,3). Signs of non-proliferative retinopathy include microaneurysms, haemorrhages, hard exudates, cotton wool spots, venous beading and intra-retinal microvascular abnormalities. When new blood vessels form, this is known as proliferative retinopathy.

If this process occurs in the macula, the centre of the posterior pole of the eye which is responsible for best visual acuity, the disease is known as diabetic maculopathy(3). Diabetic maculopathy may be classified into the following: focal, diffuse, ischaemic or mixed.

Ocular complications are also associated with diabetic eye disease including retinal detachment, cataract, optic neuropathy, glaucoma and rglaucoma, retinal vein occlusion and/ or optic disc swelling (2).

Screening

National screening programmes for diabetic retinopathy were introduced in the UK in 2002 (2). The National Institute of Clinical Excellence (NICE) recommended that type two diabetics should be screened at the time of diagnosis and annually thereafter (4). Screening is a tool used to identify potential disease in patients who would benefit from treatment. To ensure effectiveness of a screening programme, the Wilson and Junger criteria should be met (Figure 2) (5).

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Wilson and Junger criteria for screening

1. The condition should be an important health problem
2. The natural history of the condition should be understood
3. There should be a recognisable latent or early symptomatic stage
4. There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific.
5. There should be an accepted treatment recognised for the disease
6. Treatment should be more effective if started early
7. There should be a policy on who should be treated
8. Diagnosis and treatment should be cost-effective
9. Case-finding should be a continuous process

Figure 2: Screening criteria (2)

Diabetic retinopathy is a chronic progressive and potentially-sight threatening disease affecting roughly a third of all diabetics (6). With 422 million adults living with diabetes worldwide, diabetic retinopathy is an important health problem (6). Once the leading cause of blindness, it is estimated that diabetic retinopathy causes 1,280 new cases of blindness per year in England (7).

The condition progressively worsens if untreated due to retinopathy and/or maculopathy, however this damage can be easily seen on fundoscopy before loss of vision. Early identification and treatment of diabetic eye disease results in better outcomes and a lower incidence of vision loss (2).

The treatment for diabetic retinopathy includes panretinal photocoagulation (PRP) as this patient received. This involves laser photocoagulation which burns the peripheral retina thereby preventing the formation of new blood vessels and causing regression of new vessels (3). This can cause transient worsening of central vision, but the abnormal vessels regress approximately eight weeks post procedure (3). The Early Treatment Diabetic Retinopathy Study (ETDRS) found that risk of severe visual loss within two years of PRP reduced from 38% to 19% in patients with high-risk proliferative diabetic retinopathy (9). Based on these results, Mr X may have considerable benefit from PRP therapy.

Macula laser is used to treat non-centre involving maculopathy. Newer treatments for diabetic maculopathy include antibodies to vascular endothelial growth factor (VEGF)2. VEGF is responsible for stimulating angiogenesis; therefore VEGF inhibition prevents growth of new vessels. Various trials have shown the efficacy of of anti VEGF agents such as ranibizumab and aflibercept compared to traditional laser therapy (10-12).

There are some drawbacks to screening including patient anxiety and potential over diagnosis. Increased patient complacency may result in missed diagnoses and finally screening for diabetic retinopathy is associated with great costs outwith the increased number of expensive injections required following better detection of diabetic eye disease.

Despite the high cost associated with screening, numerous studies have demonstrated its cost effectiveness (13-15). This is due to the financial burden of managing complications resulting from worse disease. In addition, visual loss is an important cause of disability in the working aged population. The impact of this has been estimated at 11,300 disability adjusted life years (DALYs) lost per year in the UK due to disability associated with partial sight and blindness resulting from diabetic retinopathy (16).

In addition, diabetic retinopathy has a negative impact on quality of life, which can be drastically improved with early diagnosis and treatment due to screening (2). This case exemplifies what happens when people are not screened and present to ophthalmology services with relatively advanced disease.

Prevention

Lifestyle modifications such as weight loss, increased exercise and dietary modification can prevent progression from impaired glucose tolerance test to diabetes (17). If prevented it will not only prevent diabetic retinopathy but other complications of diabetes such as neuropathy and nephropathy.

This case highlights the importance of health promotion, diabetes screening and prompt early treatment which will aid prevention, early detection and reduce the incidence of blindness in the population in a cost-effective way.

Multiple Choice Questions

Q1: Features of non proliferative diabetic retinopathy do not include

a) Hemorrhages
b) Venous beading
c) Intra retinal microvascular abnormalities
d) New vessels
e) Microaneurysms

Q2: Treatment options for diabetic maculopathy include

a) Oral Rifampicin
b) Intravenous steroids
c) Intravitreal anti-VEGF drugs
d) Warfarin
e) Oral Pioglitazone

Q3: Investigations for diabetic eye disease include

a) Fundus fluorescein angiography
b) ECG
c) ECHO
d) Carotid Doppler
e) Ultrasound

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Q4: which of the following is not a criteria for a good screening programme

a) There should be a recognisable latent or early symptomatic stage.
b) There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific.
c) There is no accepted treatment recognised for the disease.
d) Treatment should be more effective if started early.
e) Diagnosis and treatment should be cost-effective.

Q5: Drawbacks of screening are

a) Anxiety
b) False positives
c) False negatives
d) Cost
e) Burden of disease

Answers

1. d
2. c
3. a
4. c
5. e

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A STEP-BY-STEP APPROACH TO PTOSIS FOR THE FOUNDATION DOCTOR

E Saxby, CF Ferreira, J Foulds

Abstract

Ptosis is the medical name for drooping of the upper eyelid. It is frequently seen but rarely acted on by clinicians. Three muscles primarily perform retraction (elevation) of the upper eyelid, these are levator palpebrae superioris (LPS), Muller's muscle and frontalis. LPS, supplied by the third cranial nerve/oculomotor nerve, is a skeletal muscle that performs the majority of eyelid retraction. It is controlled by cranial nerve III, the oculomotor nerve. Interruption or damage to any of the three muscles, or the nerves supplying these muscles, can cause drooping of the upper eyelid.

Ptosis is usually not the primary reason that a patient is referred to hospital, it is more commonly an incidental finding or part of a larger clinical picture. The causes can be generally categorized as either neurogenic, myogenic, disorders of the neuromuscular junction, mechanical or aponeurotic. Within these subgroups, the underlying reason for the upper lid descent may be congenital or acquired, and maybe benign or malignant.

This review provides junior doctors with a step-by-step approach to the patient with ptosis. By ensuring an accurate history and examination have been performed and that potential differential diagnoses are understood, no life threatening conditions should be missed.

Introduction

Ptosis is the medical name for drooping of the upper eyelid, which can happen in one or both eyes (1). It is often regarded as primarily a cosmetic issue, however ptosis can cause visual impairment and may be a sign of underlying systemic disease (2).

Ptosis is rarely the primary reason that a patient is referred to hospital. It is more commonly an incidental finding or part of a larger clinical picture. The diagnosis is often made by junior doctors when clerking or reviewing patients.

In this review, we will take you through a straightforward approach to diagnose, investigate and manage patients with ptosis, so that no important pathology is missed.

Eye Lid Anatomy

There are 2 muscles that are primarily responsible for eyelid retraction. These are levator palpebrae superioris (LPS) and Muller's muscle.

LPS is a skeletal muscle that performs the majority of the eyelid retraction. It has its origins at the lesser wing of the sphenoid bone. When traversing the orbit it broadens and becomes a fibrous aponeurosis that inserts into the tarsal plate. Where this aponeurosis attaches to the skin and orbicularis muscle, the upper eyelid crease is formed (2). LPS is controlled by cranial nerve III, the oculomotor nerve. The nerve has its origins in the mid brain. From there it travels through the interpeduncular cistern to the cavernous sinus, before reaching the orbital apex and entering the orbit via the superior orbital fissure (3).

Along with innervating LPS, the oculomotor nerve also supplies the majority of the extraocular muscles. The nerve has superficial parasympathetic fibers running within it, which are responsible for innervating the sphincter pupillae muscles involved in pupillary constriction and accommodation.

Muller's muscle is a smooth muscle that originates on the underside of LPS and attaches to the superior tarsal plate of the upper lid. The muscle is innervated by the sympathetic nervous system. Postganglionic sympathetic fibers originate in the superior cervical ganglion and travel via the internal carotid plexus where branches communicate with the oculomotor nerve as it passes through the cavernous sinus. The sympathetic fibers enter inferior aspect of Muller's muscle (4).

The muscle 'frontalis' lifts the brow and is a minor contributor to upper lid retraction, for this reason it is known as a secondary retractor. Frontalis is supplied by cranial nerve VII, the facial nerve.

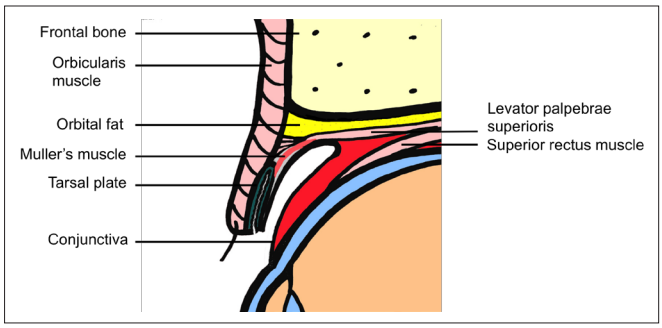

Figure 1: A cross section view through an upper lid.

Take a history

Before beginning your examination of the patient, it is imperative to take an accurate and comprehensive history.

- **When was the ptosis first noticed?**
- **Was the onset gradual or sudden?**
- **Is there anything that makes it better or worse?**
- **Does it change during the course of a day?**
- **Do they have any other symptoms? Headaches? Fatigue? Lethargy?**

A thorough systems review is vital and may reveal other symptoms that aid you in formulating a diagnosis.

Ask the patient for any old photographs of themselves. These can be very valuable as they may identify whether the ptosis was present 10 days ago, or 10 years ago.

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Examination

Begin by standing back from the patient. Take time to look at how they are holding themselves. Is there any facial asymmetry? Are they tilting their head back to reduce the visual impact of ptosis? Are there any signs of muscle weakness or limited expression?

Then begin by performing a full clinical examination including neurological and cranial nerve examination. It is particularly important to focus on the pupillary reactions, extraocular muscle movements and facial sensation. Impairment of these functions could suggest serious underlying neurological condition.

It is then important to assess whether the patient has true ptosis or 'pseudoptosis'. The appearance of pseudoptosis may be caused by conditions such as blepharospasm or dermatochalasis (excess skin on the upper lid). There are several important measurements that can aid your examination and help you come to a diagnosis.

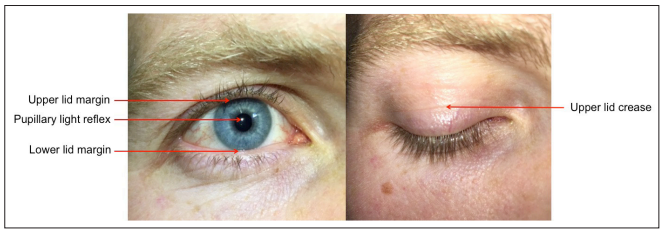

Figure 2: Surface anatomy for ptosis measurements.

LPS Function

Place your thumb on the patient's brow to isolate LPS and removes the effects of the frontalis muscle. Ask the patient to look downwards and place a ruler at the upper lid margin (the lash line). Then ask the patient to look upwards and measure the new position of the upper lid margin. The distance between the two positions indicates the LPS function. Normal range is between 13-17mm.

Lid Crease Height

With the patient in down gaze, measure the distance from the upper lid margin to the lid crease. As mentioned above, the lid crease is the site of insertion of LPS aponeurosis to the overlying orbicularis and skin. Normal lid crease height should be between 6-8mm in males and slightly higher in females at 8-10mm.

Marginal Reflex Distance and Palpebral fissure height

Ask the patient to focus, with both eyes, on a focal light source. You should then be able to see the pupillary light reflex in both eyes. Measure the distance from the pupillary light reflex to the upper lid margin. This distance is called marginal reflex distance one (MRD1). Then measure from the pupillary light reflex to the lower lid margin. This distance is called marginal reflex distance two (MRD2). MRD1 is normally 4-5mm and MRD2 is normally 5mm. The distance between upper and lower lid margins is known as the palpebral fissure (PF). MRD1 + MRD2 = PF (5). Once the history and examination is complete, you should already have an idea what is causing the patient's symptoms. Now it is time to think about what can cause ptosis.

What are the causes of ptosis?

Ptosis may be present from birth (congenital) or may present later in life (acquired). The underlying cause may be benign and harmless or it could be life threatening. For this reason it is important all serious pathology is ruled out.

In this review, I will be focusing on acquired ptosis, which can be broken down into 5 subgroups. These include myogenic, neurogenic, disorders of the neuromuscular junction, aponeurotic or mechanical (6).

Myogenic Ptosis

Dysfunction of the levator muscle inhibits the eyelid from rising into the proper position. Of particular importance in this group are the conditions Myotonic Dystrophy and Chronic Progressive External Ophthalmoplegia (CPEO).

Myotonic dystrophy is a hereditary disease with autosomal dominance. The disease affects roughly 9500 individuals in the UK and is characterized by muscle weakness and myotonia (7). Myotonic dystrophy type 1 is caused by mutations in the DMPK gene, while type 2 results from mutations in the CNBP gene (8). Patients generally present with bilateral ptosis and limited facial expression, however there are many other systemic effects of the disease such as cataracts, frontal balding and heart block.

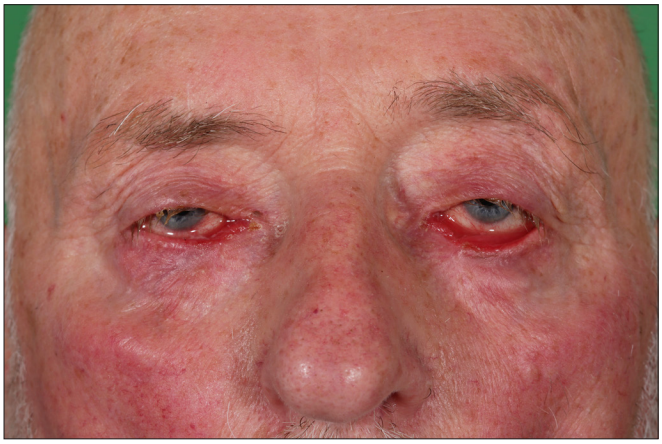

Figure 3: A patient with myotonic dystrophy exhibits bilateral ptosis, note also the bilateral lower lid ectropion.

CPEO is a disorder characterized by slowly progressive paralysis of extraocular muscles. Patients usually experience bilateral, symmetrical, progressive ptosis follow by ophthalmoparesis (weakness or paralysis of one or more extraocular muscles) months to years later (9). CPEO is a mitochondrial myopathy and therefore displays a mitochondrial mode of inheritance.

Extrinsic eye muscles contain a larger volume of mitochondria than any other muscle group and this explains their preferential involvement in mitochondrial myopathies. A diagnosis can be confirmed by performing a muscle biopsy. When the biopsy is treated with a red dye that stains mitochondria, the muscles affected by the condition show ragged red fibers, indicating excessive mitochondria. CPEO typically affects individuals in their 30's and the condition usually presents with mild symptoms and progresses slowly.

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Neurogenic Ptosis

Dysfunction or damage to the third cranial nerve, the sympathetic nervous system or the central nervous system can result in neurogenic ptosis. There may be a serious, life threatening condition underlying this form of ptosis, so it is an important diagnosis not to miss. Included within causes of neurogenic ptosis are third cranial nerve palsy and Horner's syndrome.

As mentioned earlier, cranial nerve III, the oculomotor nerve supplies all the muscles of extraocular movement other than the lateral rectus and the superior oblique, which are supplied by cranial nerve VI and IV respectively. The oculomotor nerve also supplies LPS and is therefore crucial for eyelid elevation.

Dysfunction of the nerve can result from ischaemia, infection, compression, trauma and demyelinating disease, such as multiple sclerosis. A third nerve palsy results in a 'down and out eye' with ptosis and possible pupil dilatation. The eye has a 'down and out' appearance, as it is only the lateral rectus and superior oblique muscles that are functioning. The ptosis is caused due to loss of action of LPS.

A patient with suspected third nerve palsy and a dilated or 'blown' pupil suggests a compressive cause. Any compressive lesion is likely to affect the parasympathetic fibers that run superficially along the oculomotor nerve, causing disruption to the innervation of the sphincter pupillae muscle. The sphincter pupillae is a circular muscle within the iris, responsible for pupil constriction and without this muscle functioning the pupil will dilate.

Aneurysms of the posterior communicating artery, basilar artery and superior cerebellar artery tend to cause an isolated third nerve palsy, as can any other compressive intracranial lesion (10) . For this reason a patient with ptosis, a down and out eye and a dilated pupil is a medical emergency. A pupil sparing third nerve palsy is commonly due to ischaemic injury within the nerve. This is most often caused by diabetes or hypertension.

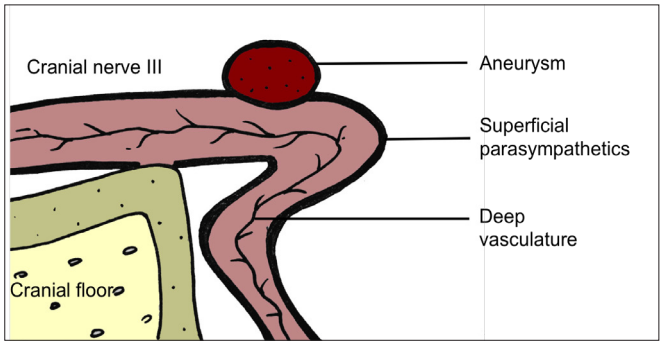

Figure 4: A compressive aneurysm causing impairment of the parasympathetic fibers, resulting in a third nerve palsy with a dilated pupil.

Horner's syndrome refers a triad of clinical findings, namely, ipsilateral ptosis, pupillary miosis and facial anhidrosis. This constellation of signs results from interruption of the sympathetic innervation to the eye and ocular adnexa (11).

Horner's Syndrome may develop from any lesions that affect the sympathetic pathway. It can be congenital, acquired or purely hereditary. The interruption of the sympathetic chain may occur centrally (between the hypothalamus & the fibers point of exit from the spinal cord, C8-T2) or peripherally (in the cervical sympathetic chain, at the superior cervical ganglion, or along the carotid artery)(12). The causes of Horner's syndrome may be classified into first, second and third order neuron lesions.

First order neuron lesions that can give rise to the syndrome include, trauma, infection e.g. meningitis, skull base tumours and demyelinating disease. Second order neuron lesions giving rise to the syndrome include the following, Pancoast tumour, cervical rib, aneurysm or dissection of the descending aorta and lymphadenopathy. Third order neuron lesions giving rise to the syndrome include internal carotid artery dissection, carotid cavernous fistula, migraines and herpes zoster infections. This is not a comprehensive list of all causes of Horner's Syndrome, however it highlights the potential life threatening pathologies that may be underlying.

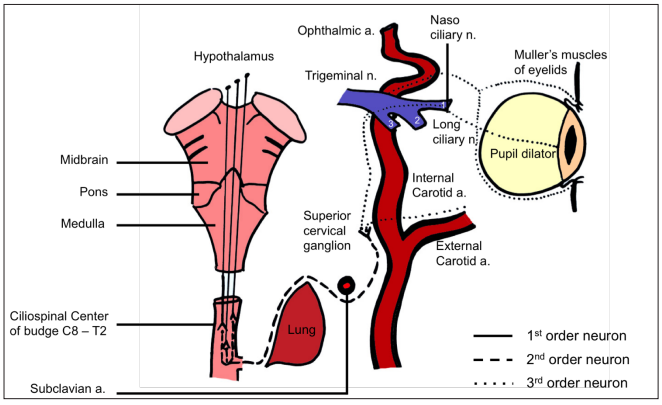

Figure 5: The sympathetic innervation of the eye and ocular adnexa.

Horner's Syndrome will produce a different pattern of ptosis from a third nerve palsy. As the sympathetic chain innervates the Muller's muscle and not LPS, the patient with Horner's syndrome should only experience mild or partial ptosis. Due to the disruption of the sympathetic pathway, a patient with Horner's syndrome would be expected to suffer from a constricted pupil as the smooth muscle of the iris dilator will not be functioning but the sphincter pupillae muscles will be unheeded.

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Figure 6: A patient with right-sided Horner's Syndrome. Horner's syndrome comprises the triad of partial ptosis, miosis and facial anhidrosis.

Patients with facial nerve palsy involving the frontalis muscle do not experience blepharoptosis. The frontalis muscle only acts as a secondary retractor and is used as a compensatory mechanism by patients with aponeurotic ptosis to provide some slight lid elevation.

Disorders of the neuromuscular junction causing ptosis

This category alludes specifically to the condition of Myasthenia Gravis. Myasthenia Gravis is an autoimmune disease of the neuromuscular junction in which circulating antibodies cause fluctuant skeletal muscle weakness. The pathophysiology of myasthenia gravis is a reduced number of acetylcholine receptors at the postsynaptic muscle due to anti-acetylcholine receptor antibodies (13). In 85% of patients with myasthenia, the initial symptoms were unilateral ptosis, bilateral ptosis or diplopia (14).

To identify myasthenic ptosis, an important finding is that the ptosis is variable, often becoming more significant as the day progresses or with fatigue. At the bedside one can elicit key physical findings, including muscle fatigability on prolonged upgaze and an overshoot of the eyelid height when asking the patient to raise their eyes from down gaze to the primary position (15). Cooling the affected eyelid with an icepack for 2 minutes may also result in temporary reversal of ptosis (16). To confirm diagnosis autoantibody testing is required.

Aponeurotic Ptosis

Aponeurotic ptosis is by far the commonest cause of the ptosis. The underlying pathogenesis is dehiscence or lengthening of the levator aponeurosis connection to the tarsal plate. This is the connection that is responsible for the formation of the upper lid crease, so in these patients the crease is often absent or elevated. Aponeurotic ptosis occurs more commonly in the elderly and it is the most common cause of ptosis in these populations (17).

Mechanical Ptosis

Mechanical ptosis should be an easy diagnosis to make. It is commonly caused by an increase in weight of the upper lid but can also be due to scarring following previous surgery or trauma. An increase in weight of the upper lid may be due to excess skin, tumours, inflammation or cysts.

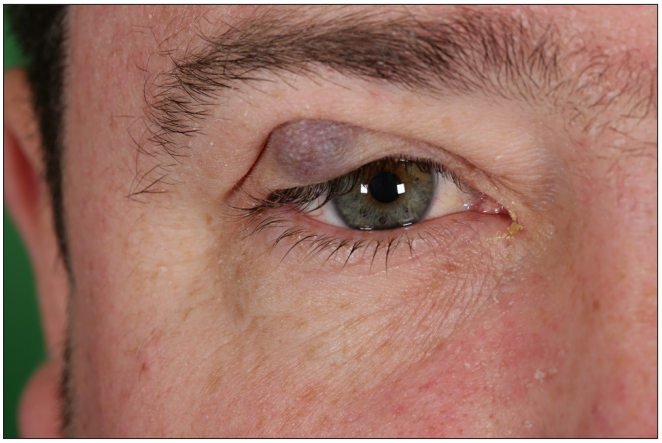

Figure 6: A pretarsal haemangioma causing excess weight on the upper lid and inducing ptosis.

How should I manage my patient?

Management of any patient with ptosis is going to be case dependent. After you take an accurate history and perform a thorough examination, you should be able to direct your line of investigation. It is important to be able to differentiate the causes of ptosis that are innocent or benign and the causes of ptosis that may be life threatening.

- *If the patient is elderly, the onset of ptosis has been gradual and on examination they have a high upper lid crease, then aponeurtotic ptosis is the most likely diagnosis and no urgent action is warranted.*

- *If the patient has a sudden onset of unilateral ptosis with ophthalmoplegia then a diagnosis of third nerve palsy must be considered, particularly if there is pupil involvement. When the diagnosis of a third nerve palsy is possible, urgent scanning with contrast must be considered to identify aneurysms or any other intracranial lesions.*

- *If the patient has a sudden onset of ptosis with miosis and anhidrosis, with a background of shortness of breath or respiratory symptoms, one must worry about a Pancoast tumour. Suspicion of a Pancoast tumour warrants discussion with respiratory medics and appropriate imaging of the chest. A sudden onset of ptosis with miosis and a background of systemic hypertension is suggestive of a carotid dissection causing Horner's syndrome. Facial anhidrosis may not be present in this case as it is often not noticeable in postganglionic lesions.*

A STEP-BY-STEP APPROACH TO PTOSIS FOR THE FOUNDATION DOCTOR

E Saxby, CF Ferreira, J Foulds

· *If the patient is within their third or fourth decade of life and they report gradual ptosis along with ophthalmoplegia and symptoms of myotonia e.g. myotonic handshake, then one must suspect myotonic dystrophy. These patients will benefit from a prompt referral to a neurologist and as they often suffer from cardiac abnormalities, a cardiologist referral may be warranted. Clinicians must think about referral to a neurologist and/or ophthalmologist in any case of acute ptosis. It is also recommended to refer any patients that are bothered by chronic ptosis to an ophthalmologist, as surgery is often very successful.*

Conclusion

Whether ptosis is a patients presenting symptom or not, it is an important clinical finding, that must be addressed. It may be congenital or acquired. It may be benign or related to serious underlying pathology. By following this step-by-step approach, foundation doctors should be confident that they would be able to accurately diagnosis, investigate and manage patients with ptosis.

MCQ's

1: Which three muscles are responsible for upper lid retraction?

1. Levator palpebrae superioris, Muller's muscle and orbicularis

2. Levator palpebrae superioris, Muller's muscle and frontalis

3. Levator palpebrae superioris, orbicularis and frontalis

4. Levator palpebrae superioris, orbicularis and temporalis

5. Orbicularis, frontalis and Muller's muscle

2: Which cranial nerve supplies the muscle, Levator Palpebrae Superioris?

1. Abducens Nerve

2. Facial Nerve

3. Trigeminal Nerve

4. Occulomotor Nerve

5. Trochlear Nerve

3: Which of the below are a form of Neurogenic ptosis?

1. Dermatochalasis

2. Horner's Syndrome

3. Myotonic Dystrophic

4. Aponeurosis

5. Upper lid chalazion

4: A patient presents with right-sided ptosis, pupillary miosis and facial anhidrosis. They also report worsening shortness of breath and have a 20-pack year smoking history. What is your number one differential diagnosis for this patient?

1. Myasthenia Gravis

2. Apical lung tumour

3. Myotonic dystrophy

4. Posterior communicating artery aneurysm

5. Recent trauma

5: You see a patient on the ward who complains of ptosis that gets worse as the day progresses. You notice this patient has a positive Cogan's twitch sign and that his ptosis improves with an ice pack. You are concerned they may have undiagnosed myasthenia gravis. Which of the below blood tests is most helpful in confirming this diagnosis?

1. CRP

2. Anti-acetylcholinesterase antibodies

3. Serum ACE

4. Anti Ro antibodies

5. VDRL test

A STEP-BY-STEP APPROACH TO PTOSIS FOR THE FOUNDATION DOCTOR

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Answer

Answer 1

The three muscles responsible for upper lid retraction are Levator palpebrae superioris, Muller's muscle and orbicularis. Levator palpebrae superioris is a skeletal muscle that provides the majority of retraction.

Answer 2

The occulomotor nerve, or third cranial nerve, supplies Levator Superioris. This is why patients with a third cranial nerve palsy present may suffer from ptosis.

Answer 3

Horner's syndrome is a form of neurogenic ptosis. Dermatochalsis is a condition whereby the patient has excess upper lid skin and is classified as a pseudoptosis. Myotonic dystrophy is a form of myogenic ptosis. Aponeurosis classically happens in elderly patients with no underlying pathology and an upper lid chalazion can cause mechanical ptosis.

Answer 4

This patient seems to be suffering form Horner's syndrome with the classic triad of ptosis, miosis and anhidrosis. In a smoker with history of shortness of breath, you need to rule out an apical lung tumour causing compression of the sympathetic chain.

Answer 5

Cogan's twitch sign, progress muscle fatigue and improvement with an ice pack are all suggestive of myasthenia gravis. Anti-acetylcholinesterase antibodies will allow you to confirm this diagnosis.

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CASE BASED DISCUSSION: COMPLICATED PNEUMONIA IN CHILDREN

L Selby, RR Russell

Abstract

Complications of community acquired pneumonia in children including empyema and pleural infection are increasing (1). Necrotising pneumonia may lead to development of a broncho-pleural fistula (2). Treatment options are varied, from a conservative approach to drain insertion, video-assisted thoracoscopic surgery, thoracotomy and decortication.

This case highlights:

- *Variable presentation of pneumonia in children.*
- *Complications of pneumonia - parapneumonic effusion (pleural fluid collection in association with underlying pneumonia 3), empyema and necrotising infection.*
- *Approaches to management.*

Case history

A 4-year old boy was admitted with a one week history of coryza, fevers up to 40°C, 3 days of intermittent abdominal pain, poor oral intake and a 12 hour history of difficulty breathing.

On arrival he was short of breath with a respiratory rate of 40 per minute, heart rate of 120 beats per minute and oxygen saturations of 91% in air. His temperature was 39.2°C.

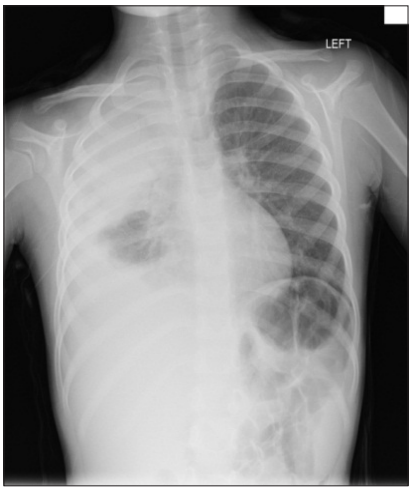

Figure 1: Initial chest x-ray.

Initial chest x-ray (CXR) (Figure 1) showed a near complete white out of his right hemi-thorax, but no midline shift. Other investigations included white blood cell count of 25x109/L (neutrophils 16x10^9/L) and CRP of 275. A diagnosis of pneumonia and effusion was made, and intravenous ceftriaxone was commenced along with oral azithromycin.

Ultrasound scan of the chest revealed a large amount of fluid confirming a parapneumonic effusion with underlying consolidated lung. He was taken to theatre and an intercostal drain inserted (Figure 2). Pleural aspirate showed pus cells, but no organisms on microscopy. Cytology showed mixed inflammatory cells in keeping with infection; no malignant cells were seen.

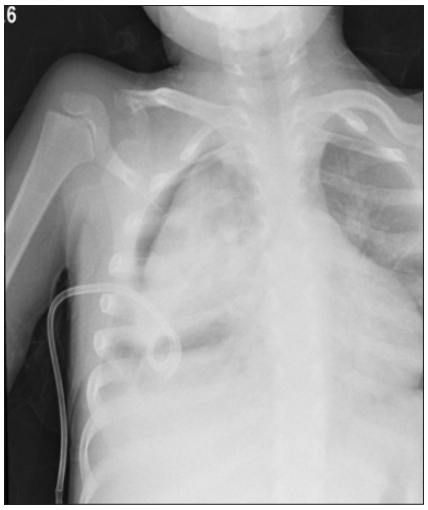

Figure 2: CXR after initial chest drain insertion.
A small rim of air is visible in the right upper zone.

The chest drain remained in-situ for 48 hours and his fevers began to settle, breathlessness reduced and his appetite improved. The chest drain was removed, and as he remained clinically stable he was discharged home with 2 weeks oral co-amoxiclav.

Twelve hours later he re-presented with back pain and difficulty breathing. Repeat CXR revealed a large right sided pneumothorax (Figure 3) with mediastinal shift.

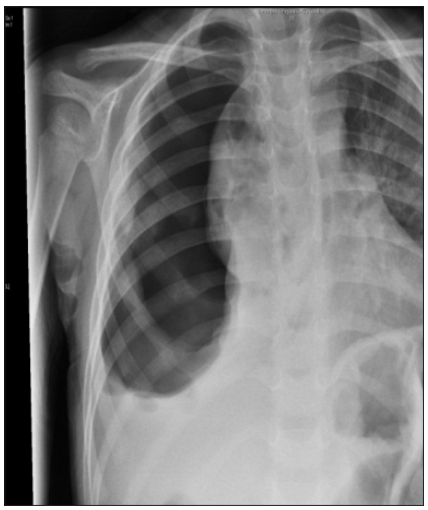

Figure 3: CXR on re-presentation.

A further chest drain was inserted but there was a recurrence of high fevers and intravenous clindamycin was added to ceftriaxone.

CASE BASED DISCUSSION: COMPLICATED PNEUMONIA IN CHILDREN

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A CT scan of the chest (figure 4) was performed the following day to determine the cause of the pneumothorax and showed a right-sided empyema, hydropneumothorax and upper lobe cavitating pneumonia with broncho-pleural fistula (arrow) explaining the air leak and development of the pneumothorax.

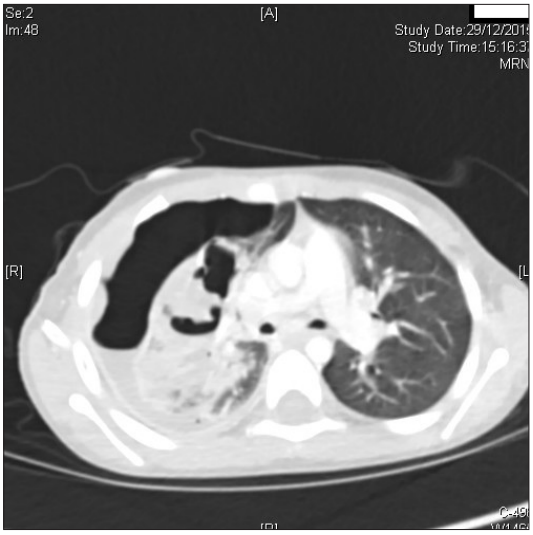

Figure 4: CT scan revealing broncho-pleural fistula.

Following insertion of a third drain there was clinical improvement with reduction in fevers and improvement in inflammatory markers. Both chest drains were removed 5 days later and CXR afterwards showed a small persisting air leak. Clinically he remained stable and intravenous antibiotics were continued. However, 3 days later, CXR was repeated (figure 5) showing re-accumulation of air with mediastinal shift.

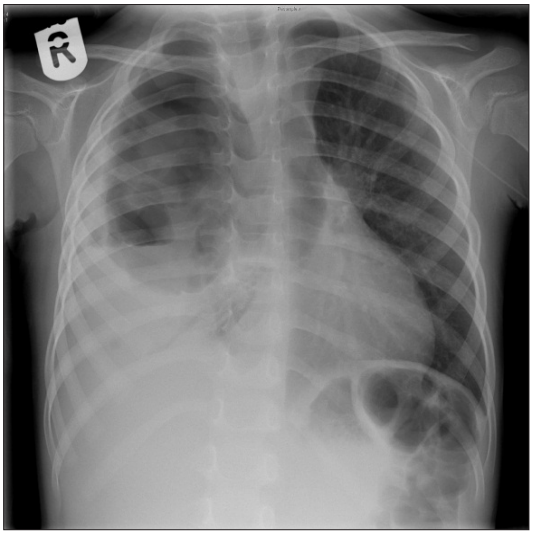

Figure 5: CXR following removal of two chest drains.

He was discussed with the paediatric surgeons and on day 26 of admission a right thoracotomy performed, the broncho-pleural fistula over-sewn and necrotic lung removed. A further chest drain was inserted to drain air post-operatively. On day 37 the chest drain was successfully removed (figure 6) and he was discharged home 24 hours later. CXR 4 months later has now normalised.

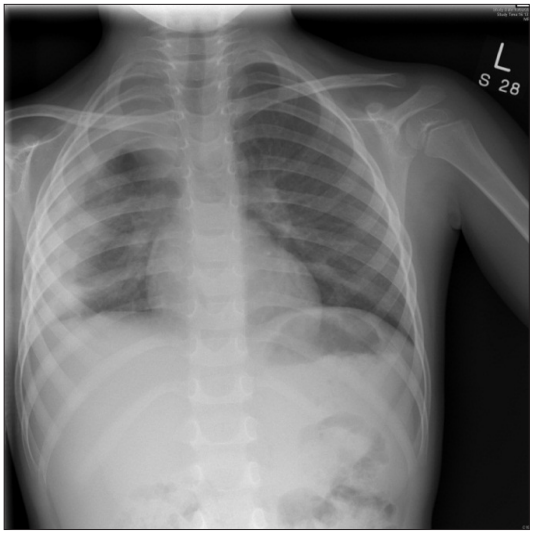

Figure 6: Post-operative CXR.

Discussion

Community acquired pneumonia is defined as 'signs or symptoms of pneumonia in a previously healthy child due to infection acquired outside hospital' (4). Presentation in children is variable; symptoms include fever, tachypnoea, or abdominal pain (3) as with this case, where the child presented with respiratory distress and hypoxia. He was admitted and a CXR performed. Intravenous antibiotics were started because he was unable to tolerate oral fluids as per British Thoracic Society guidance (3). Recommended intravenous antibiotics for severe pneumonia include penicillins and cephalosporins (3). Azithromycin is added to cover mycoplasma infection (more common in children >5 years).

Initial CXR showed a 'white out' hemithorax and it was difficult to determine if this was effusion or consolidation. Ultrasound is the best way to estimate volume of fluid in the pleural space (4), and can also easily demonstrate lung consolidation. In this case, ultrasound revealed a large parapneumonic effusion.

CASE BASED DISCUSSION: COMPLICATED PNEUMONIA IN CHILDREN

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British Thoracic Society guidelines suggest when effusion is present with persistent fever the pleural space should be drained. Enlarging effusions causing respiratory compromise should not be managed with antibiotics alone (3). However, it is possible initial manipulation of the pleural space to insert the first chest drain caused lung injury leading to development of broncho-pleural fistula, and air got into the chest through the drain itself.

Parapneumonic effusions can be managed with long courses of intravenous antibiotics, however this may prolong hospital stay and given the large effusion in this case, the decision was made to insert a drain. Examination of the pleural fluid for malignant cells is important as lymphoma may present in this way.

Following the CT scan and presence of persistent pleural fluid, we could have considered video-assisted thoracoscopic surgery or thoracotomy and decortication (excision of pleural rind with evacuation of pyogenic material). British Thoracic Society guidelines suggest failure of chest drains with antibiotics should prompt early discussion with surgeons (3). However, the collection of fluid appeared simple on ultrasound (a single pocket of fluid), so the decision was made to insert a further drain. With persistent air leak found on CXR and mediastinal shift, surgery finally took place.

It can be difficult deciding when to intervene surgically in cases like this with complicated pneumonia. There are no evidence based criteria to guide this decision (3). Early involvement of surgeons is encouraged and does not mean surgery is inevitable. It is hard to predict who will need surgery as many patients settle. Although broncho-pleural fistula is a suggested indication for surgery, a balance must be struck between treating a persisting radiological abnormality in a child who is improving against invasive surgery.

Best of 5

1: What is the best approach to the initial treatment of community acquired pneumonia in children?

a. Admit to hospital for CXR and administration of intravenous antibiotics.

b. Admit to hospital for CXR and administration of oral antibiotics.

c. Admit to hospital for CXR, administration of oxygen and intravenous antibiotics.

d. Commence oral antibiotics with clinical review in 48 hours to assess response.

e. Wait 7 days for persisting fevers (as the illness is likely to be viral) then start oral antibiotics.

2: Choose the best imaging in children with community acquired pneumonia:

a. CXR, ultrasound and CT chest.

b. CXR and ultrasound.

c. CXR and review if further imaging is required.

d. No imaging unless the child is admitted to hospital.

e. CT chest alone.

3: What is the best approach to antibiotic treatment for children with CAP?

a. Oral antibiotics unless the child is unable to tolerate oral fluids.

b. Intravenous antibiotics alone.

c. Intravenous antibiotics and oral antibiotics.

d. Intravenous antibiotics until the point of discharge home.

e. Intravenous antibiotics and anti-viral drugs.

4: In regards to imaging in children after discharge from hospital with complicated pneumonia:

a. CXR should continue to be repeated for the next 12 months.

b. CXR is only indicated if there are clinical signs.

c. CXR should be repeated every 6 weeks.

d. Annual CXR is recommended.

e. CXR should be repeated in outpatient follow up until it has normalised.

CASE BASED DISCUSSION: COMPLICATED PNEUMONIA IN CHILDREN

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5: With regards to surgical treatment of complicated pneumonia in children:

a. Early surgical intervention is the best option.

b. Early discussion with surgeons is encouraged.

c. Conservative management remains the mainstay of care.

d. There is strict UK guidance on when children are referred for surgery.

e. Guidance and protocol is the same as with adults.

Answers

1. Answer: D

Children with oxygen saturations of <92% who cannot tolerate oral fluids with persisting fevers should be admitted to hospital. For those in the community, children with a clear clinical diagnosis of pneumonia should receive antibiotics but should be reassessed if there is no clinical improvement. Children admitted to hospital should have a CXR performed. Intravenous antibiotics should be used in children unable to tolerate oral fluids and should be rationalised with clinical improvement.

2. Answer: D

Children admitted to hospital should have an initial CXR. If there is opacity and suspicion of pleural effusion this should be further evaluated with ultrasound. CT scans should not be performed routinely, however can be useful when discussing surgical options or looking for complications of pneumonia.

3. Answer: A

When a child is able to tolerate oral fluids, oral antibiotics are given. Amoxicillin is effective against the majority of organisms causing CAP and well tolerated. Macrolide antibiotics can be added if there is little initial response. Intravenous antibiotics are reserved for children with severe pneumonia and should be stopped when there are signs of clinical improvement.

Bacterial and viral pneumonia cannot easily be distinguished from one another therefore antibiotics should be started, but there is no recommendation for use of anti-viral treatment. Duration of therapy depends on clinical response; for complicated pneumonia up to 4 weeks of therapy is recommended but discussions with microbiology maybe required.

4. Answer: E

Children admitted to hospital with complicated pneumonia should be followed up as outpatients. CXRs should be performed until they normalise and this timeframe will be variable and depend on the complexity of pneumonia and effusion.

5. Answer: B

There is no consensus with regards to medical versus surgical management for empyema, however failure to respond to initial chest drain and antibiotics should prompt discussion with surgeons. Adult guidelines suggest failure to resolve in 7 days should have a surgical opinion and this could be applied to children; however it will vary case by case.

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A CASE OF A BABY MULTIPLE CONGENITAL LUMPS

GAA Burke, L Uzunova

Abstract

We present a case of a baby with three separate congenital lumps of differing pathology, one of which was a very rare tumour - infantile fibrosarcoma. The diagnostic challenge of this complex presentation is discussed with an emphasis on the clinical decision making and communication required to make the diagnosis and to manage this child.

Case presentation

A six week old male infant was referred by his local paediatricians for assessment of a thigh mass. He also had a mass in the left neck and one on the right chest. The thigh mass was noticed by his mother a week before who took him to the Emergency Department for assessment.

Prior to his admission he had been well, fully breastfed and thriving. He was born with multiple superficial haemangiomas and a cavernous haemangioma situated on his back, under his right shoulder. At the age of three weeks, he was noted to have a lump over left side of his neck, within the sternocleidomastoid muscle. This was evaluated with a USS and was thought to be benign, secondary to traumatic forceps extraction. The tumour had no effect on baby's posture.

On examination he looked well and thriving. On his left thigh, anteriorly there was a large mass measuring 8cm x 7cm, located above the knee (Figure 1 shows MRI). It was hard, non mobile non tender with normal overlying skin. Initially the thigh lump was thought be due to an infectious process and he was commenced on intravenous antibiotics (iv Cefotaxime and iv Amoxicillin).The antibiotics were stopped after four days, following negative blood culture and CRP of< 0.3 mg/l.

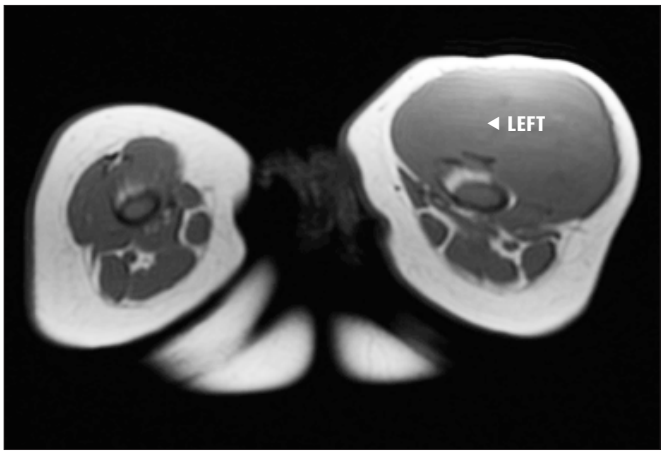

Figure 1: MRI showing mass in left thigh muscle.

An USS and MRI scan were performed, which showed the presence of the tumour. He underwent biopsy, histology of which confirmed the diagnosis of fusion negative (NTR K3-ETV6) infantile fibrosarcoma. There was a 2cm mass along the sternocleidomastoid muscle on the left. Under his right scapula on his back there was 2cm lesion with the typical clinical features of an infantile haemangioma. Whole body MRI and a Bone scan did not reveal evidence of metastatic disease.

The treatment options for infantile fibrosarcoma are a choice between primary surgery and chemotherapy .The main concern about a primary surgery approach was that this would lead to long term impairment of leg function. Cytotoxic chemotherapy on the other hand could reduce the size of the tumour and even obviate the need for surgery. Because the tumour continued to grow he was commenced on cytotoxic chemotherapy with Vincristine and Actinomycin D. Following one course of chemotherapy there was a visible reduction in the size and change in the appearance of the tumour.

The sternomastoid tumour and right chest wall haemangioma needed no further management.

Discussion

This child presented with three separate masses, one of which caused immediate concern as a result of its size and rapid growth. The diagnostic approach in this child required the establishment of the nature of all three lumps. It is unusual to have a clinical picture where the presenting features are unrelated. Thus the mass in the right chest was not immediately identified as an infantile haemangioma because it had a deeper rather than a superficial location in the skin.

The concern over the nature of this lesion was the reason for the whole body MRI. Increasingly in children MRI is preferred for staging purposes over CT scanning because of the lack of radiation dose. There is a finite risk of cancer associated with diagnostic CT2 in children and risk benefit analysis must be part of the decision making for all such scans.

However, with a rapidly changing mass the necessity of urgent imaging must also be taken into account and on occasion a limited CT scan may be considered appropriate if a diagnosis of malignancy is confirmed. In this child however, the working diagnosis for the thigh mass was a tumour that does not metastasise and therefore the right chest wall mass was not consistent with being of the same nature as the thigh mass. Under these circumstances the risk of CT was not justified and MRI was used.

Infantile fibrosarcoma represents less than 1% of all childhood cancers, but it is the most common soft-tissue sarcoma in those under 1 year of age. It has favorable course, compared to adults, with rare metastatic spread (3).

A CASE OF A BABY MULTIPLE CONGENITAL LUMPS

GAA Burke, L Uzunova

However it has high local recurrence rate. The preferred treatment method usually is primary surgery which involves wide local excision, however in situations where the operation would be challenging due to any anatomical relation to vessels and other structures, upfront use of chemotherapy is considered. In our case due to concerns about long term impairment of the limb and loss of function we opted following discussions to use cytotoxic chemotherapy with the hope that we would be able to preserve the limb function as much as possible. Indeed, there was an obvious clinical response only after one course of chemotherapy.

The management of this child was more complicated because there is degree of uncertainty in the behavior of infantile fibrosarcomas, moreover fusion negative infantile fibrosarcomas are poorly understood and documented making discussions with parents more difficult. The central issue in deciding what to do about this mass was to balance potentially curative but mutilating surgery (possibly needing amputation) with the expected unpredictable response to chemotherapy. A poor response to chemotherapy might further compromise the chances of preserving the limb with good function.

Following the initial treatment with chemotherapy, which was poorly tolerated, our patient underwent resection of the mass, histology results of which are still pending. Currently, there is no plan for further chemotherapy. We are going to institute regular surveillance scans following recovery from recent surgery.

Communication with parents had to take into account factors that might influence their ability to make decisions. This child was the first child of these parents and the expected joy of the first few weeks of life had been replaced by anxiety and hospital appointments. Rare disease in a child can result in significant stress and emotional strain particularly for mothers whereas fathers may experience stress from incompetence in the face of illness (4).

The literature in this area is sadly very inadequate to inform best practice. Continuance of breastfeeding was essential to maintain and this was achieved with encouragement from hospital and community specialist nursing staff and support from dieticians especially as chemotherapy reduced the infant desire to feed regularly. Support for the impact of diagnosis on work and finances was also provided.

Honest and detailed discussion is needed in such a situation and the parents were supported and their anxieties addressed by the members of the multidisciplinary team including invaluable input from a clinical psychologist.

MCQs

1. Which primitive reflex disappears by age of 4 months?

a) Moro
b) Sucking
c) Palmar grasp
d) Tonic neck reflex
e) Plantar reflex

2.What is the NICE guideline intravenous antibiotic of choice for an ill, febrile baby of 4 weeks?

a) Ceftriaxone
b) Cefotaxime
c) Cefotaxime + Amoxicillin
d) Co-amoxiclav
e) Piperacillin with tazobactam

3. What is the current NICE guideline cut off for neutrophil count in patients with Febrile Neutropenia?

a) Neutrophils 0.5 x 10^9 per litre or lower
b) Neutrophils 0.0 x 10^9 per litre
c) Neutrophils 1.0 x 10^9 per litre or lower
d) total WCC 1.0 x 10^9 per litre or lower
e) Neutrophils 0.75 x 10^9 per litre or lower

4. What is a sternomastoid tumour

a) Low grade malignancy
b) Birth injury
c) Haematoma in sternocleidomastoid
d) Fibrous mass in sternocleidomastoid
e) Complication of Breech delivery

5. Infantile haemangiomas

a) Are typically of the cavernous type
b) Are vascular malformations
c) Are congenital
d) Always involute
e) Can require treatment if interfering with function

A CASE OF A BABY MULTIPLE CONGENITAL LUMPS

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Answers

Answer 1

Moro reflex normally disappears by age of 3-4 months, palmar grasp age 5-6 months , tonic neck reflex 4 months and plantar reflex by age 9-12 months.

Answer 2

When parenteral antibiotics are indicated for infants younger than 3 months of age, a third-generation cephalosporin (for example cefotaxime or ceftriaxone) should be given plus an antibiotic active against listeria (for example, ampicillin or amoxicillin)

Answer 3

Diagnose neutropenic sepsis in patients having anticancer treatment whose neutrophil count is 0.5 × 10^9 per litre or lower and who have either temperature of 38 degrees or higher other signs or symptoms consistent with clinically significant sepsis.

Answer 4

A sternomastoid tumour is a fibrous mass in the sternocleidomastoid muscle. It is a cause of congenital muscle torticollis and treatment is early physiotherapy usually taught to parents.

The aetiology is not clear but associations with breech and traumatic deliveries or abnormal intrauterine positioning, leading to intramuscular compartment syndrome and ischaemic muscle injury with subsequent fibrosis and contracture of the sternomastoid muscle are recognised. There are other associations such as congenital hip dysplasia and brachial plexus injury (1).

1) Carenzio G, Carlisi E, Morani , et al: Early rehabilitation treatment in newborns with congenital muscular torticollis. Eur J Phys Rehabil Med. 2015 Oct;51(5):539-45. Epub 2015 Feb 18.

Answer 5

Infantile haemangiomas may be of differing type. Most are superficial capillary haemangiomas. They have a typical growth pattern of rapid growth in the first year of life followed by a period of involution which is variable in length. Vascular malformations by contrast are clusters of blood vessels that develop in arteries, veins, capillaries, or lymphatic vessels.

Common types include arteriovenous malformations (AVMs) and vascular ectasias. They have a slow growth pattern and since do not resolve and may require treatment. Infantile haemangiomas may be present at birth but most become apparent within the first few months of life. If infantile haemangiomas of capillary type cause significant problems with function (such as when involving an eye) they can be treated effectively with drugs such as beta-blockers under specialist care.

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INSERTION OF PAEDIATRIC CHEST DRAINS

L Selby

History

A one year old boy developed symptoms of chicken pox. Four days later he developed high fevers up to 39 degrees, grunting and difficulty in breathing. Clinical examination revealed signs of a pleural effusion and a chest x-ray was performed. It showed a white out of the right hemithorax, and an ultrasound was performed showing the presence of a large pleural effusion.

British Thoracic Society guidelines for the management of pleural effusion in children suggest that if pleural fluid is causing respiratory compromise then it should be drained (1,2).

Insertion of a Paediatric Chest Drain

Indications

- *An empyema (pus in the pleural cavity) or a pleural effusion which is significant or enlarging and compromising respiratory function.*

- *Pneumothorax compromising respiratory function, haemothorax (caused by trauma) and post operatively after thoracic surgery (3). It should be noted a tension pneumothorax should be aspirated immediately with needle decompression in the second intercostal space, mid-clavicular line.*

Contraindications

- *Any indication the effusion is not secondary to infection, when a small volume diagnostic tap for cytological analysis is carried out (1).*

Explanation of Procedure

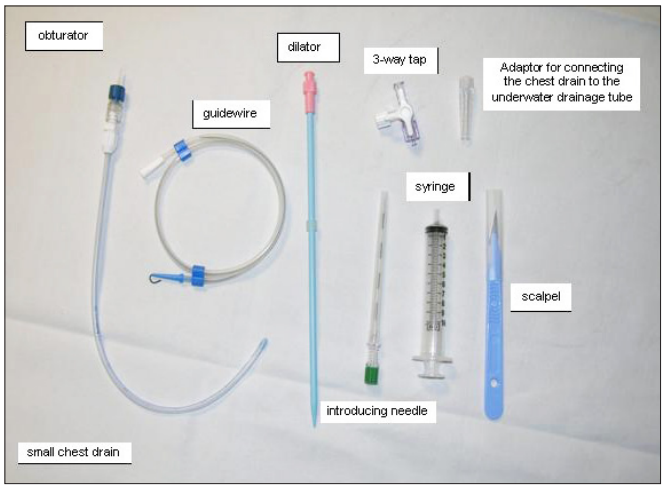
This involves insertion of a chest drain to drain fluid from the space between the inner and outer membrane of the lung (pleura). A needle will be inserted into the chest and a wire will be passed through the needle. There will be a small cut made at the skin. The drain will then be passed over the wire and the wire removed, leaving the drain in place. The drain will be secured to the skin.

There is a risk of lung injury, pneumothorax ('air leak' between the pleura), bleeding around the site of insertion and there will be a small scar. The anaesthetist should explain to the parents about the risk of a general anaesthetic.

The equipment and procedure listed refers only to insertion of chest drains in children.

Equipment

- *Sterile gloves and gown.*
- *Skin antiseptic solution, e.g. povidone iodine (Betadine) or chlorhexidine in alcohol.*
- *Sterile drapes.*
- *Sterile gauze swabs.*
- *A selection of syringes (2 ml, 5 ml, 10ml, 20ml) and needles.*
- *Local anaesthetic, e.g. 0.25% bupivacaine (Marcaine).*
- *Scalpel.*
- *Suture (e.g. 2/0 or 3/0 silk).*
- *Guide wire with dilators.*
- *Chest drain: 8.5, 10–12 French Gauge appropriate for most children.*
- *Connecting tubing including 3-way tap.*
- *Closed drainage system (including sterile water for the underwater seal).*
- *Sterile universal containers for collection of pleural fluid samples.*
- *Large adhesive dressings.*



Photograph courtesy of Royal College of Emergency Medicine Learning website, taken from the URL: **http://www.rcemlearning.co.uk/references/spontaneous-pneumothorax/**

Most chest drains in children are inserted under general anaesthetic with a paediatric anaesthetist at a tertiary respiratory centre.

Ultrasound shows the location of the fluid and the skin can be marked to indicate the optimum site for drain insertion. Alternatively, an ultrasound probe can be used in theatre by a radiologist to show the clinician the exact location of the deepest pocket of fluid.

INSERTION OF PAEDIATRIC CHEST DRAINS

L Selby

Procedure

- *Position the patient with the operating table at the desired height of the clinician inserting the chest drain, with the child's arm out of the way.*
- *Scrub and put on sterile gown and gloves.*
- *Clean the skin.*
- *Draw up and infiltrate local anaesthetic at insertion site.*
- *Attach a 10 or 20ml syringe to the introducer needle and insert slowly, aiming posteriorly and inferiorly while pulling back gently on the plunger.*
- *When the needle tip is intrapleural, withdraw pleural fluid.*
- *Detach the syringe, ensuring the needle stays in place.*
- *Pass the syringe to the assistant to place into sterile containers for microbiology, cytology and biochemistry (for albumin and lactate dehydrogenase testing).*
- *Take the wire and pass it in through the needle into the pleural space. Stop when you meet resistance or when you reach the mark engraved on the wire.*
- *When the wire is in place, withdraw the needle back over the wire, holding the wire in one hand to ensure it does not move.*
- *Take the scalpel and make a small incision (a few mm) in the skin at the entry point of the wire, in the line of the rib space. Be careful not to cut through the wire.*
- *Pass the smallest dilator over the wire into the pleural space through the skin incision. Larger drains have 3 dilators. If there is resistance to the dilator, initially extend the incision in the skin. Otherwise, try rolling the dilator gently whilst advancing or changing the angle of entry. If there is still resistance, it may be that the wire has become dislodged; if so, reinsert the needle and start again.*
- *Remove the dilator and then pass the drain over the wire into the pleural space.*
- *Remove the guidewire and pleural fluid should drain back. Be sure to get the theatre assistant to witness your removal of the wire with a theatre assistant and ensure it is disposed of safely.*
- *Clamp the drain and secure into position using a ('drainfix') dressing.*
- *Attach the chest drain to the 3 way tap and underwater seal and release the clamp but ensure not too much fluid is drained initially.*
- *Dispose of all sharps safely.*

Aftercare

The procedure should be documented including specific mention that the wire was removed, seen and disposed of. A chest x-ray should be requested immediately to check position of the drain. To avoid rapid loss of large volumes of fluid, the drain should be clamped for one hour after 10ml/kg fluid has drained.

Samples should be sent to cytology for cell count and to look for presence of malignant cells and to microbiology for gram stain, microscopy, culture and in some cases PCR analysis. Lactate dehydrogenase and albumin should be estimated in fluid by biochemistry. The chest x-ray should then be reviewed.

Best of 5

1: Indications for a chest drain in a child include:

a. A likely malignant pleural effusion.
b. A small pleural effusion seen on ultrasound.
c. An empyema.
d. A large pleural effusion causing respiratory compromise or a pneumothorax.
e. A large pleural effusion causing respiratory compromise, pneumothorax, haemothorax or post-operatively.

2: Risks and complications of insertion of chest drains in children include:

a. Pneumothorax.
b. Large amounts of bleeding.
c. Large scar at the insertion site.
d. Pneumothorax, lung injury and a small scar at the insertion site.
e. Pneumothorax, lung injury, a small amount of bleeding and a small scar at the insertion site.

3: Samples obtained from the insertion of chest drain should be tested for:

a. Gram stain, microscopy, culture and cytology for cell count.
b. Gram stain, microscopy, culture, cytology for cell count and electrolytes.
c. Gram stain, microscopy, culture, cytology for cell count, albumin and lactate dehydrogenase.
d. Gram stain, microscopy and culture only; most effusions in children are infectious in origin.
e. Gram stain, culture and cell count.

4: Concerning imaging and chest drain insertion in children:

a. Ultrasound scan must confirm the location of deepest pocket of fluid prior to insertion of the chest drain.
b. CT scan is required pre-operatively.
c. A chest drain can be inserted after visualising an effusion on chest x-ray.
d. The drain is inserted using an ultrasound probe for direct vision.
e. CT scan is required post-operatively.

5: Concerning post-operative care of chest drains:

a. A chest x-ray must be performed the next day.
b. Repeat ultrasound is required to assess adequate drainage of the fluid.
c. A chest x-ray must be performed immediately after the procedure to ensure the drain is in the correct place, but a maximum of 10ml/kg fluid should be allowed to drain at once before the drain is clamped.
d. A chest x-ray should be performed immediately after the procedure and fluid allowed to be freely drained.
e. Once the drain is removed a follow up ultrasound scan is recommended to assess the volume of remaining fluid.

INSERTION OF PAEDIATRIC CHEST DRAINS

L Selby

Answers

1. Answer: E

Small pleural effusions or suspicion of a malignant pleural effusion should not have a chest drain inserted. In the case of the former the effusion should be enlarging or causing respiratory compromise and in the latter a diagnostic tap should be considered in the first instance. Pnuemothorax and haemothorax are usually as a result of trauma and do require a chest drain.

2. Answer: E

The drain should be inserted into the pleural space to drain the effusion, however a pneumothorax or tension pneumothorax can result from interpleural pressure exceeding atmospheric. This may be caused by an incorrect seal on the chest drain and not having an adequate underwater seal. Bleeding can occur by injury to vessels at the point of insertion of the drain. Additional complications include displacement of the drain and surgical emphysema if the holes within the drain itself migrate to outside the pleural space.

3. Answer: C

Pleural fluid must be sent for microbiological analysis including gram stain and bacterial culture as well as differential cell count to try to identify a responsible organism. Tuberculosis and malignancy must be excluded if there is presence of pleural lymphocytosis. Biochemical analysis of pleural fluid allows determination of whether the pleural fluid is transudate or exudate.

4. Answer: A

Ultrasound can reveal the exact location of the fluid collection and the skin can be marked to indicate the optimum site for drain insertion. Alternatively, an ultrasound probe can be used in theatre by a radiologist to show the clinician the exact location of the deepest pocket of fluid.

CT scans are not indicated unless requested pre-operatively by a surgeon if the child is likely to need video assisted thorascopic surgery or thoracotomy

5. Answer: C

A chest x-ray should be requested immediately after the procedure to check position of the chest drain. To avoid rapid losses of large volumes of fluid, the drain should be clamped for one hour when 10ml/kg fluid has drained. It should then be unclamped and accurate observations of the chest drain and the child's fluid balance should be commenced.

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EARLY RECOGNITION OF SUBTLE SEIZURES IN NEONATAL MENINGITIS MAKES A DIFFERENCE TO THE OUTCOME

S Shah, A Thirunavukarasu, G Oligbu

Abstract

Group B Streptococcus (GBS) is the leading cause of neonatal meningitis in many countries. Although following the use of intrapartum antibiotics, mortality due to early onset GBS infection have reduced with little effect on late onset GBS infection.

In addition, the morbidity following neonatal meningitis has not changed dramatically over the last 20years (1), with 2-8% meningitis presenting with neonatal seizures, and its long term adverse outcomes (2).

Recognition of neonatal seizures can be difficult in this particular group of infants as the signs could be subtle and not appear to be pathological. Awareness of these is essential to effectively manage a complicated case of meningitis, where seizures may be the only presenting feature of severity.

Case History

Baby AS is a 17 day old female infant, born by spontaneous vaginal delivery with no antenatal or postnatal concerns. She presented with 12 hours history of fever. Examination revealed an irritable infant with no other focus of infection. She had a full septic work up, including urine and lumber puncture for CSF (cerebrospinal fluid) analysis (Table 1). She was empirically started on Cefotaxime and Amoxicillin for suspected sepsis.

The next morning, AS had an episode of right handed jerky movement described by the mother with no associated bradycardia or desaturation, a cerebral Function monitor was attached. This revealed further seizure like activity before obvious clinical seizures. She was loaded with Phenobarbitone and continued on a maintenance dose. These subtle seizures persisted despite being on a Midazolam infusion, and therefore required intubation, and subsequent transfer to the tertiary Neonatal Intensive Care Unit (NICU). An urgent CT scan showed swelling of the brain, with leptomeningeal enhancement and a slight focal density in the left frontal region.

Her blood and CSF cultures were positive for Beta-haemolytic Group B streptococcus, fully sensitive to Penicillin. In view of this, Amoxicillin was discontinued and she remained on Cefotaxime.

Her last episode of seizures was on Day 20, and she was extubated onto Bilevel Positive Airway Pressure (BIPAP) initially and then nasal cannula oxygen. By day 23 of life, she had no oxygen requirement.

An MRI on Day 23 of life showed decreasing brain swelling with leptomeningeal enhancement with features of cerebritis on the left frontal region, and no evidence of empyema. The electroencephalogram (EEG) on the same day was normal for her age with no focal abnormalities.

AS remained apyrexic with improving inflammatory markers and no further seizures, and went onto full enteral feed. She was then transferred back to her local hospital on Day 25 of life on Cefotaxime (Day 8) and her femoral line was also removed.

However, on Day 10 of Cefotaxime, AS spiked temperature to 39^{0}C, with deterioration in her clinical condition. A soft systolic murmur was noted, but her Echocardiogram showed a small patent foramen ovale (PFO) but no obvious vegetation and a structurally normal heart. Other investigations, including blood, urine, stool cultures, nasopharyngeal aspirate (NPA) were all negative. In addition, abdominal ultrasound and cranial ultrasound scan did not reveal any abscess collection.

AS continued to spike temperatures despite being on day 14 of Cefotaxime. This was changed to Ceftriaxone, as she was now 1 month old. Her repeat MRI following discussion with the neurosurgical team was suggestive of an area of gyral enhancement, in keeping with meningitis, and a small possibility of a left parietal area collection with no mass effect. The collection was not suitable for surgical intervention or drainage. A repeat lumbar puncture (LP) was performed, and the CSF showed a raised white cell count with 100% polymorphs, low glucose, raised protein, and no organisms on gram stain (Table1).

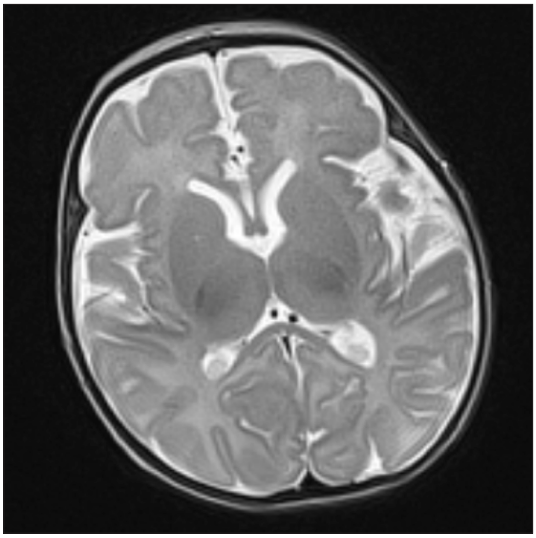

Figure 1: AS MRI Scan.

Days	2/6	3/6	4/6	12/6	13/6	14/6	15/6	17/6	19/6
CRP	3	138.5	155.7	16.9		10.8	12.3	5.9	3.1
ESR								48	
Hb		145	127			100	109	92	
Plts		269	247			429	500	414	
WCC		14.8	16.2			13.5			
Neut		7.7	8.1			6.8	5	3.8	
Lymph		5.6	6.7			4.4	7.8	5.1	
Blood culture	GBS +ve				Negative at 48hours		Negative at 48hours		
CSF	GBS +ve Isolate identification - Streptococcus agalactiae serotype III						No organism seen, no bacterial growth WCC 379 (100% Polymorphs)		

Table 1: AS Laboratory Results. +ve = positive.

On discussion with the Infectious Diseases (ID) team they felt that this CSF result could represent either a post infection inflammatory response or a quiescent infection. As per their advice, AS was commenced on Meropenem (Ceftriaxone was stopped on Day 2). Her repeat CSF, including viral PCR was negative.

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At this time her MRI images were reviewed in the Neuroradiology Multidisciplinary team meeting (MDT) which concluded that there had been no increase in size of the collection from previous images and the on-going inflammation and enhancement in the basal meninges was in keeping with meningitis.

She had an additional 5 days of Meropenem bringing the total duration of antibiotics (since commencing on Cefotaxime and Amoxicillin initially) to 3 weeks. They also advised to perform an immunological screen on AS, and there was no evidence of immunodeficiency found.

Baby AS was discharged on Day 38 of life and with no reported complication on follow up.

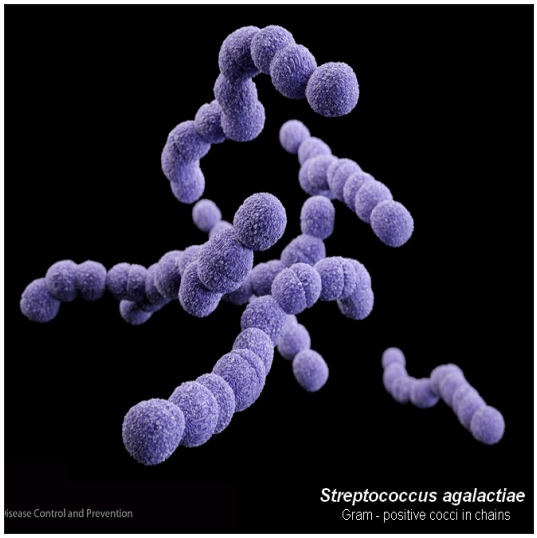

Figure 2: Group B Streptococcus.

Discussion

The incidence of bacterial meningitis in the newborn ranges from 0.21-1 per 1000 live births in the UK (1). The most common pathogens causing early onset neonatal sepsis (within 7days of life) are GBS and Escherichia coli (E coli), with GBS being the most common cause of early and late onset neonatal bacterial meninigitis (1,3). Pregnant women with GBS positive bacteruria are offered intrapartum antibiotics (IAP) as there is a higher risk of chorioamnionitis and neonatal disease in these cases. Although this has been shown to reduce the incidence of early onset GBS disease, it has not been shown to reduce all causes of GBS related mortality (4).

One prospective study over a 7 year period looking at 444 cases of neonatal bacterial meningitis found that GBS was more often involved in neonates presenting with seizures compared to E coli infection (3). Furthermore, seizures at admission have been found to be a significant risk factor for adverse outcomes at discharge (5).

Therefore the early recognition and management of neonatal meningitis and seizures is imperative for reducing long term morbidity and mortality. Most neonatal seizures (>50%) are caused due to hypoxic ischaemic encephalopathy, with 2-8% of cases due to meningitis (2).

In this case, AS had late onset GBS meningitis. Initial management in the Paediatric A&E was rapid with early antibiotic treatment. The classical signs of meningitis (bulging fontanelle, high pitched cry, neck stiffness) are often absent in infants (6) as these signs, as well as seizures, are often advanced presentation (2). Most cases of neonatal seizures occur within the first 3 days of life (2).

AS's presenting complaint was a fever, which in neonates triggers investigations for a full septic screen. She then went on to have a very subtle right-handed jerky movement with no other associated clinical signs. The use of Cerebral Function Monitoring (CFM) enhanced our clinical suspicion, and therefore early aggressive treatment to control this subtle movement.

In addition, 20-50% of children with neonatal seizures experience epilepsy later in life (12) In a prospective study looking at the aetiology, burden and short term outcome of neonatal seizures, of 426 neonates, seizure burden was high with a mortality of 17% and 49% of survivors with an abnormal neurological examination at discharge. Their findings highlighted a potential for improved outcome if seizure burden is reduced (13).

Recognition of seizures in the neonate can be challenging as in 50% of cases the signs are subtle. Types of seizures can be broadly classified (2):

SUBTLE

- Facial: eye flickering, deviation, fixed staring. Lip smacking, mouthing and chewing.

- Limbs: Cycling, stepping, swimming and boxing movements of limbs.

- Other: Apnoea.

These manifestations have a variable correlation with electrical activity on the EEG, but the ocular signs are more likely to present with EEG changes. AS had unilateral movements of one upper limb, 'boxing movements' with no ocular involvement. Her parents noted these movements initially. Caregivers are more familiar with their baby's normal behaviour and thus may be an important source to verify any potentially new or abnormal movements.

CLONIC

Clonic seizures present with repetitive, rhythmic jerking movements and can be unifocal or multifocal. These are the next most common type.

EARLY RECOGNITION OF SUBTLE SEIZURES IN NEONATAL MENINGITIS MAKES A DIFFERENCE TO THE OUTCOME

S Shah, A Thirunavukarasu, G Oligbu

MYOCLONIC

Sudden, brief, irregular, arrhythmic jerky movements typify Myoclonic seizures, tending to occur in the flexor muscle groups.

TONIC

These are the least common seizure form characterised by stiffening and decerebrate posturing.

However, an important distinction should be made between clinical seizures and other benign movements. Jitteriness is extremely common in newborns and is usually benign or may be associated with hypoglycaemia. These fine movements are symmetrical and do not involve the face and normally cease when the baby is held (2). Neonatal sleep myoclonus is another benign condition whereby myoclonic movements occur during Rapid Eye Movement (REM) sleep and is a diagnosis of exclusion (7).

AS's initial MRI changes showed inflammation with no early evidence of a collection. With further temperatures despite antibiotic treatment, she had numerous investigations to try to identify the source of the pyrexia. Clinically there was no evidence of raised intracranial pressure or worsening neurology to immediately suggest an intracranial abscess.

With all other investigations proving negative she had a repeat MRI scan, which at this point was suggestive of a small collection. This may have been present in the previous scans but this was unclear. For this reason she was treated with 3 week course of antibiotics.

Early recognition and management of neonatal seizures gives increased opportunities to treat seizures and may benefit in improving developmental outcomes in at risk neonates (12)

In high risk infants with bacterial meningitis, moderate-markedly abnormal EEG's are reliable predictors of adverse outcome. (14) In this case, the subtle clinical seizures prompted electrical monitoring to prevent delay in treatment and management.

AS's persistent subtle clinical and electrophysiological seizures benefitted from early recognition and treatment to prevent secondary brain injury (14).

Subsequent follow up of AS showed a normally developing infant with no obvious neurological deficit.

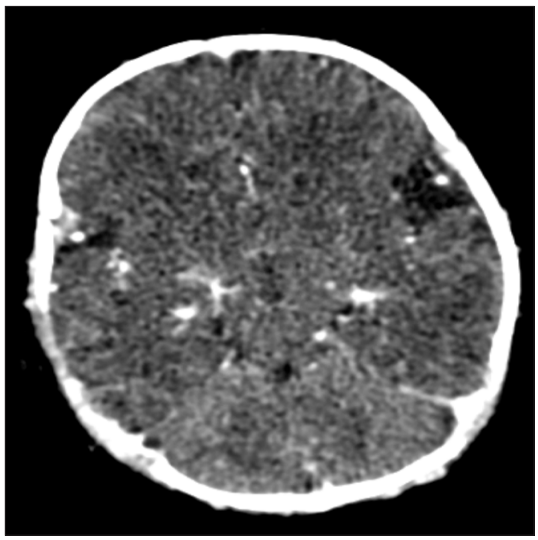

Figure 3: AS CT Scan.

MCQ Questions

1) A pregnant woman was admitted from Triage in labour. The midwife bleeps you to say her previous baby was admitted to the Neonatal Unit with GBS sepsis. The patient has not been tested for GBS in either pregnancy. What would be your advice for the management for this woman?

A. The baby should have observations for 24hours after delivery and no Intrapartum Antibiotics (IAP)

B. She should only have IAP if she spikes a temperature in labour

C. She should have IAP, specifically Benzylpenicillin

D. She should have IAP, specifically Cefotaxime

E. Postnatally the baby should have prophylactic antibiotics

2) Long term complications of bacterial meningitis include:

A. Sensorineural hearing loss and visual impairment

B. Hydrocephalus

C. Epilepsy and cognitive impairment

D. Renal failure

E. All of the above

EARLY RECOGNITION OF SUBTLE SEIZURES IN NEONATAL MENINGITIS MAKES A DIFFERENCE TO THE OUTCOME

S Shah, A Thirunavukarasu, G Oligbu

3) Group B Streptococcus (GBS):

A. Is an encapsulated gram-positive diplococcus

B. Colonises the gastrointestinal and genital tract of 15-40% pregnant women and is symptomatic

C. GBS is the most common cause of early and late onset neonatal meningitis, and meningitis in young children

D. Group A and Group B streptococcus may affect pregnant women and both can cause invasive disease in the form of skin and soft tissue infections including streptococcal toxic shock syndrome

E. Mainly colonises the oropharynx and is asymptomatic

4) What is the correct treatment for your 2 week old patient who has been having subtle seizures with cycling of the right leg and the EEG is mildly abnormal?

A. Sodium Valproate

B. Lamotrigine

C. Levetiracetam

D. Phenobarbitone

E. Carbamazepine

5) You are an F2 in Paediatrics A&E and are called to the bedside of a 6month old baby who the A&E nurse states has just started 'jerking his left leg continuously, eyes wide and not responding to his mum calling him'. What should you do?

A. Ask the nurse to complete a set of observations and talk to mum to get a full history

B. Note the time, apply high flow facial oxygen and manage the airway and ask the nurse to urgently contact your senior

C. Ask the nurse to get some help whilst you manage the airway and apply oxygen

D. Go and find your Registrar and ask the nurse to observe the baby

E. Pull the emergency buzzer

Answers

1. Answer B.

The RCOG guidelines suggest that IAP should be offered to women with a previous baby with GBS disease. (4) Subsequent infants are likely to be at increased risk of GBS disease, likely related to persistence of low levels of maternal anti-GBS antibodies. 3g of Intravenous (IV) Benzylpenicillin should be administered as soon as possible as a loading dose, and subsequent 1.5g four hourly until delivery. The baby should be observed for the first 12-24hours after birth (as should any baby at increased risk of early onset GBS disease). (4)

2. Answer E.

NICE recommends the following morbidities to be specifically considered: Hearing loss, orthopaedic complications, skin complications (including scarring from necrosis), psychosocial problems, neurological and developmental problems and renal failure. All children need audiology follow up and review in an outpatient clinic by a Paediatrician. The child's health visitor and GP should be informed of the episode.(6)

Adverse neurological problems occur in 30-50% of survivors in most cases, and babies with normal or mildly abnormal EEG background were shown to have a normal outcome. (2) Predictors of mortality and moderate/severe disability include presence of seizures/come, use of inotropes and leukopenia.(2)

Mortality in neonatal meningitis is higher in pre term neonates, very low birth weight infants, as well as in neonates in general compared to older children. Although mortality has declined in the last 20years, morbidity has remained unchanged. (1,9)

3. Answer A.

Group B streptococcus is an encapsulated gram-positive diplococcus that colonises the GI and genital tracts of 15-40% of pregnant women. Colonisation is usually asymptomatic. It is the most common cause for early onset neonatal meningitis. GBS bacteruria in the pregnant woman is associated with a higher risk of chorioamnionitis and neonatal disease. Vertical transmission occurs in labour and with rupture of membranes. (4,10)

EARLY RECOGNITION OF SUBTLE SEIZURES IN NEONATAL MENINGITIS MAKES A DIFFERENCE TO THE OUTCOME

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4. Answer D.

Phenobarbitone is the most common first line anti epileptic medication in neonatal seizures and is effective in approximately 50% of cases. One study found the reduction in seizures was not permanent and seizures were likely to represent within 4hours of treatment. (11)

The effect of anti epileptic medication is unclear on the immature and developing brain and it is unclear whether the short or long term treatment alter cognitive function. (12)

The clinical recommendation is that clinically apparent seizures which last longer than or up to 3mins, or are brief serial seizures should be treated. (12) Phenytoin is also commonly used although it has more severe side effects and a narrower therapeutic range than Phenobarbitone. (12)

5. Answer B.

It is important in any emergency situation to remember the ABC management. Make sure the airway is safe and if there is any compromise pull the emergency buzzer. Noting the time is especially important to ensure how long the seizure is continuing for. You will need extra people to gain some access and gain a full history from the baby's mother.

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AN EXPERIENCE FROM COMMUNITY PAEDIATRICS

C Nunn, J Williams

Using Your Own Data Mine - Collecting Meaningful Data In The NHS, An Experience From Community Paediatrics

Objectives

The RCPCH recommends that data about patients with neurodisability be collected. Over 3 months, data using national standards was collected on patients attending neurodisability clinics. This data maps patient need. Using our data, I will discuss how it is possible to obtain meaningful patient data and its' applications.

Methods

Data on 93 patients attending paediatric neurodisability clinics was collected in an ad hoc fashion over 3 months. Data included basic characteristics, diagnoses, sensory deficits, neuroimaging, and risk of death within the next 12 months. Data were analysed using excel, to gauge broad patient characteristics, rather than statistical significance.

Results

The patients were 0-19 years old, with an even spread. 32% of patients had sensory impairment, and 30% had learning difficulties. 45 percent of patients had a movement disorder. 1 patient had 1 diagnosis, but another had 30 separate diagnoses and the mean number of diagnoses was 10.

Discussion

We gained concrete information on complexity of need in our patients. Doctors are trained to analyse information on a single patient, but with large IT databases, that information can be scrutinised on a different scale. It can be used for recognition of need, service planning and development, training plans and therefore contribute to delivery of high quality care. We are retrospectively auditing what we've done and learnt; we ought to be gathering information on what needs to be done and what we need to know.

How To Make Your Own Data Mine - Collecting Meaningful Data In The NHS, An Experience From Community Paediatrics

Objectives

The RCPCH has recommended that data about complex patients with neurodisability be collected via clinically accurate and useful codes (1). Over a period of 3 months, data using these nationally agreed standards was collected on patients attending a series of neurodisability clinics. The initial purpose of the exercise was to analyse how complex these patients are in order to better facilitate their care.

However on examining the data, it became apparent that this data could be used for a wide variety of purposes, and that by routinely coding according to patient need and complexity, we are collecting a detailed map of service need. Using our data as an example I would like to discuss how it would be possible to easily obtain swathes of meaningful patient data and the many ways this could be applied.

Methods

Data on 93 patients attending paediatric neurodisability clinics was collected in an ad hoc fashion over a 3 months period. Data included basic characteristics, NHS number to avoid duplication, outcome of consultation, diagnoses, sensory deficits, neuroimaging, barriers to participation, and risk of death within the next twelve months.

Any patient attending the clinic could be included and data were collected either on an electronic form, or scribed on a paper version during the clinic, and manually entered later. There were no formal inclusion of or exclusion criteria, as the aim was get broad information about attendees.

This information was simply analysed using excel, as we were looking for broad patient characteristics, rather than statistical significance.

Results

The patients ranged from 0-19 years old. They had a mean age of 7.8 with the interquartile range between 3 and 12, reflecting a fairly even spread and considerable diversity of need. Just under a third of patients had some kind of sensory impairment(30/93, 32%), and a similar proportion had learning difficulties (28/93 30%).

45 percent of patients had some kind of movement disorder. Perhaps most interestingly, only 1 patient had 1 diagnosis, with one patient having 30 separate diagnoses recorded and the mean number of diagnoses being 10. 71 out of the 93 patients had undergone neuroimaging, and of those were abnormal.

A significant proportion (17 patients, 18%) had behavioural difficulties, which is perhaps partially explained by the high proportion of patients with ASD as an additional diagnosis (21 patients, 23%). A third of patients required continual support, but only 2 were considered to be at risk of death before 18.

Discussion

This data collection exercise gave us as a team concrete information about the complexity and diversity of need in our patient population. Consultation with patients often involves collecting significant amounts of information. As doctors, we are trained to analyse this information on an individual basis, but with increasing use of large IT databases, that same information can be scrutinised on a much larger scale.

This example shows that with a simple input form it possible not just to gauge but to accurately quantify the range of care patients are likely to require. The data demonstrates that this clinic would not be possible in a facility that was not wheelchair friendly. In practice this means large clinic rooms, and seated scales as well as wheelchair accessible scales.

Although randomised controlled trials are the gold standard for comparing treatments, retrospective data may be equivalent in certain circumstances (2). For trainees looking to help improve the NHs in small ways, retrospectively collected data could be the basis for many quality improvement projects.

AN EXPERIENCE FROM COMMUNITY PAEDIATRICS

C Nunn, J Williams

All the data we collected would be part of a routine consultation and although there is undoubtedly controversy about the use of NHS data for any purpose other than NHS care (3), it is being increasingly recognised that the NHS cannot afford not to use this data.

Training is becoming increasingly complex, with an emphasis on hospitals being able to prove what they can teach and doctors proving what they have learnt. Having access to data on patient need allows deaneries to prove that trainees are likely to have adequate exposure to certain problems, and crucially over what timescale. For trainees, documenting you have attended clinic for six months, knowing that means you will have seen a specific range of conditions and problems is far more time efficient that documenting each clinic or patient interaction.

Although the NHS and each consultation generates vast amounts of useful data, how to store it, analyse it, and code it remain big questions, with even big research projects finding these questions difficult to answer (4). However real time and data collection is becoming a reality for doctors in a variety of environments (5-8).

NHS managers are not always aware of data already available to them, data that they could make useful changes with (8), but large commercial companies routinely collect huge amounts of data and then see what they could do with it. We have already access to massive amounts of information about our patients, it is time for us to start mine it more efficiently.

MCQs For Paediatric Neurodisability

1. There are many definitions of cerebral palsy. Which one of the following answers best incorporates all aspects of the condition?

A - An evolving motor problem that presents differently depending on the age of the patient

B - A brain injury occurring prenatally, in the neonatal period or in early infancy

C - An umbrella term for an evolving motor disorder resulting from a brain injury occurring prenatally, in the neonatal period or in early infancy

D - Generalised spasticity

E - Generalised hypotonia

2. You are seeing a two year old boy who is not yet walking with no history of trauma. Which of these tests is essential to perform?

A - Bilateral hip X-ray

B - Full blood count

C – Renal function

D – Liver function

E – Creatinine Kinase

3. An eight year old with moderate learning difficulties needs a team based approach to help her reach her potential. Which of the following would normally be part of their supporting team? You may choose more than one answer.

A - Teacher

B - Parents

C - Health visitor

D - School Nurse

E - Paediatrician

4. A three year old presents with unclear speech and behavioural difficulties. Which one of these tests should be done with the most urgency?

A – Full assessment for autism

B – Hearing screen

C – ENT referral

D - ECG and genetic screening

E – Renal screen for Allports

5. Which of the following are risk factors for developing seizures later on in childhood? You may choose more than one answer.

A - Isolated neonatal hypoglycaemia with a low BSL of 2

B - Severe neonatal hypoxic ischaemic encephalopathy

C - A baby born after placental abruption who is delivered and breathes normally

D - Rett syndrome

E - Peri-ventricular leukomalacia

AN EXPERIENCE FROM COMMUNITY PAEDIATRICS

C Nunn, J Williams

Answers

1. Answer C

Cerebral palsy symptomatology vary with age, as do the needs of the child. However the underlying pathology remains unchanged

2. Answer E

It is essential to either rule out Duchenne muscular dystrophy, or diagnose it quickly

3. Answer C

Health visitor would be part of a team looking after pre-school children, but wouldn't normally be involved with a school aged child as they discharge them to the school nurse.

4. Answer Hearing Screen

Hearing loss is common and potentially treatable. Given that there is a window of learning for speech development it is important to diagnose this as quickly as possible.

5. Answers B, D and E.

Neonatal hypoglycaemia is common and usually responds to feeding. There aren't usually complications unless the baby is very sick. Severe neonatal encephalopathy is a known risk factor for seizures, as is peri-ventricular leukomalacia. Rett syndrome is a condition largely affecting females, causing speech loss or delay, autistic features and with stereotyped repetitive hand movements. Seizures are commonly associated.

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A CASE STUDY OF STAPHYLOCOCCAL TOXIC SHOCK SYNDROME FOLLOWED BY 'SACRIFICES': A MNEMONIC TO GUIDE MANAGEMENT OF SEPTIC SHOCK

L Ahmed, A Hargadon-Lowe, S Sahi, G Oligbu

Early identification of patients with sepsis is key to the delivery of the sepsis six bundle including antibiotic therapy within an hour. (1). This approach is recommended to improve the effective management of septic patients, although promoted by the Survive Sepsis organisation in the UK, builds on the bundles developed by the international Surviving Sepsis Campaign (2)

However, compliance with the Sepsis Six remains poor and interventions to improve reliability of completion have shown only modest success, partly due to high demand in the Emergency Department (ED) and a significant strain put on staff memory.

In this paper we present an interesting case of toxic shock syndrome and then propose an easy mnemonic for the assessment and management of septic shock.

Case Summary

A 15 year old girl, presented to the emergency department and booked in as 'unwell child'. In the waiting room she was noted to be pale and listless, and then she collapsed. At this time she had a HR of 148/min (tachycardic), saturations of 99% in air, a blood pressure of 94/62mmHg and temperature of 39.1^{0}C. Her blood sugar was 6.1mmol and she remained alert at this stage (A on AVPU scale).

The history at this stage noted a headache for 24 hours, vomiting since noon that day, a fever, and talking 'gibberish' throughout the preceding night. She denied alcohol or drug intake and her urine toxicology screen was negative. The differential diagnosis at this stage included toxic shock syndrome; meningo-encephalitis; and ingested toxins although urine toxicology screen was negative. A lumber puncture was deferred as she was noted too unwell unwell and not clinically fit for the procedure

Initially she was treated with a 0.9% sodium chloride bolus of 20mls/kg followed by 10mls/kg shortly after. Her initial blood gas had shown a metabolic acidosis (pH of 7.20, PCO_2 6.3, Bicarbonate (Bicarb) 19.4 and Base Excess (BE) -9.4.). She was started on intravenous ceftriaxone, clarithromycin for atypical organisms, and acyclovir to cover for herpes.

After this fluid she temporarily improved and her systolic blood pressure was 90mmHg, and her repeat gas showed a PH of 7.43, BE −6.7, lactate 7.0. Blood results showed acute renal failure (Urea 10.6, Creatinine 296) and deranged clotting with an APTT of 1.6. Her amylase was 244, her CK 6000, white cells 22 and CRP 122.

Subsequently she acutely deteriorated becoming confused and delirious and pulled out her cannula. This was replaced with 2 large bore cannulas. Her repeat gas on reinserting the cannulas had a PH of 7.31, BE − 9.5. At this stage, her capillary refill was 3-4 seconds, with poor pulses and a heart rate of 160-170, temperature 41^{0}C and her saturations were deteriorating, saturating < 90% in 10 litres/min of oxygen, and only 92% in 15 litres/min. She was delirious and moved to 'Resus'.

Two paediatric consultants were called along with the anaesthetic team. A dopamine infusion was prescribed and a gelofusin bolus of 20mls/kg given followed by a bolus of Hartmann's solution same volume. She remained drowsy and agitated. The dopamine was increased to 20micrograms/kg/minute and a noradrenaline infusion started as her BP was not improving. She was intubated with thiopentone and suxamethonium, and sedated with midazolam. A central jugular line was placed.

Eventually the BP started to improve – at this stage BP = 82/30mmHg, HR = 143/min, sats 100%. The retrieval team were updated and advised starting an adrenaline infusion and placing an arterial line. She had a dose of clindamycin on advice from PICU. In total she received up to 80mls/kg fluid resuscitation. At this time she was transferred to PICU. She was also noted to have an evolving macular erythematous rash over her arms with some petechiae over her right triceps, and extremely red conjunctival injection. A Brain CT prior to deterioration was normal.

Further history emerged as she became increasingly unwell that she had complained of headache, myalgia and arthralgia, with vomiting and faecal incontinence associated with severe diarrhoea. She had had a tampon in situ for 14 hours and was currently menstruating. Apart from iritis for which she was under the care of ophthalmology, the rest of her past medical history is unremarkable.

In PICU she required 3 days of inotropic support and was ventilated for 3 days. She received haemofiltration as she was anuric with acute renal failure, and she developed a thrombocytopaenia. She also had pulmonary oedema and effusions, and an echo showed moderate mitral regurgitation. She returned to the district general hospital on day 5 and was discharged home well on day 14 after completing her antibiotics. In confirmation of TSS, she grew staphylococcus aureus on her high vaginal swab.

Staphylococcal Toxic Shock Syndrome

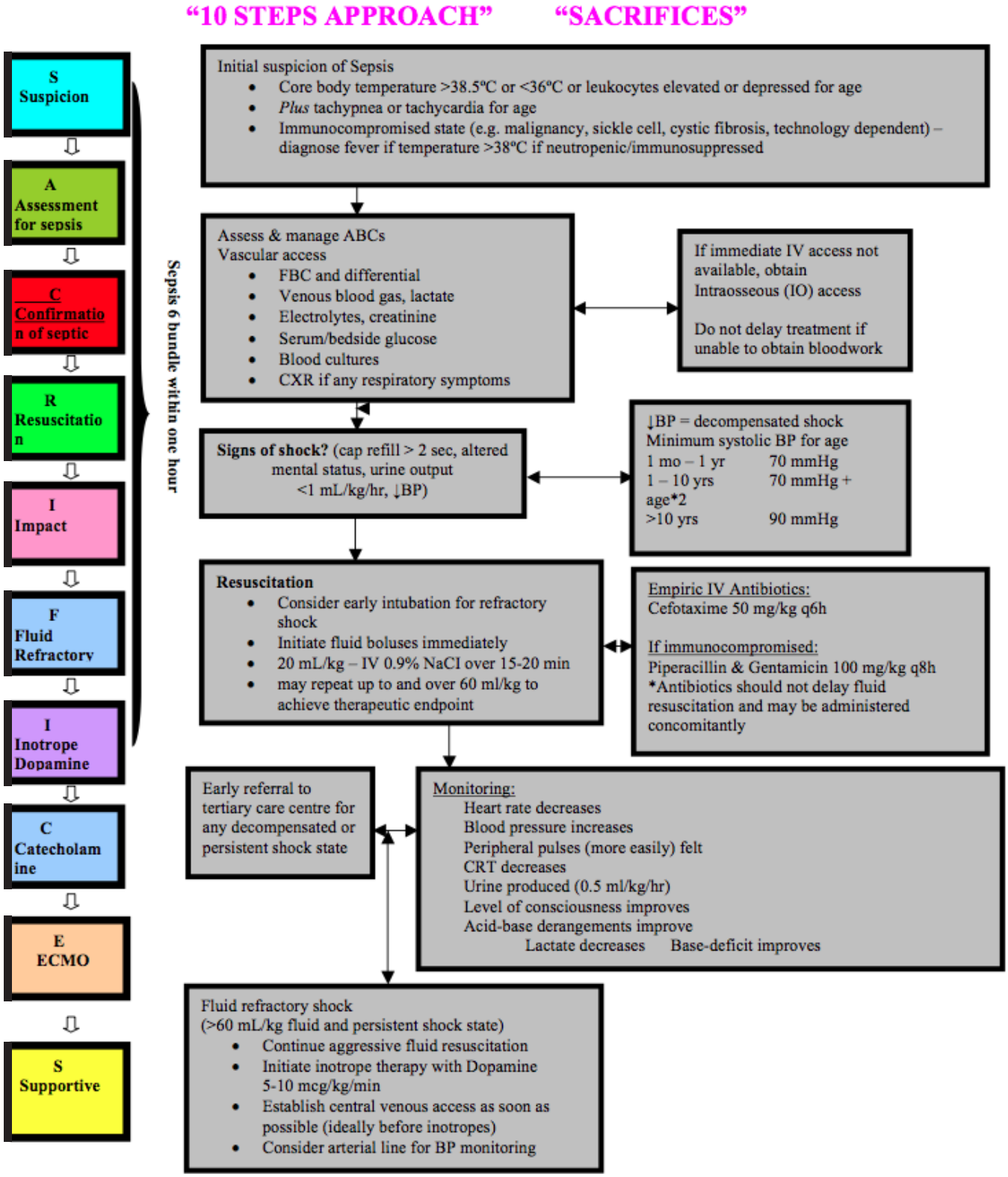
This is an acute, multi-system, toxin-mediated illness that often results in multi-organ failure (1). Staphylococcus aureus (S. aureus) is known to be a colonising bacteria; persistently in 20% of the population, and up to 60% intermittently (most commonly in the nares) (2). When host defences are down it makes infection more likely. S. aureus expresses a variety of cell-associated and secreted virulence factors making it a very adaptable pathogen (2).

Its secreted factors include enzymes, cytotoxins and exotoxins. The main aim of the enzymes is to turn parts of the host into nutrients for the bacteria. The exotoxins include staphylococcal enterotoxins (SE) and toxic-shock-syndrome-toxin-1 (TSST-1), and the latter and SE'B' have been shown to be most commonly responsible for staphylococcal toxic shock syndrome (2,3).

A CASE STUDY OF STAPHYLOCOCCAL TOXIC SHOCK SYNDROME FOLLOWED BY 'SACRIFICES': A MNEMONIC TO GUIDE MANAGEMENT OF SEPTIC SHOCK

L Ahmed, A Hargadon-Lowe, S Sahi, G Oligbu

Flow Diagram For Management Of Septic Shock"



A CASE STUDY OF STAPHYLOCOCCAL TOXIC SHOCK SYNDROME FOLLOWED BY 'SACRIFICES': A MNEMONIC TO GUIDE MANAGEMENT OF SEPTIC SHOCK

L Ahmed, A Hargadon-Lowe, S Sahi, G Oligbu

Very similar properties are shared with group A streptococcus (GAS) which leads to streptococcal toxic shock syndrome. These exotoxins are known effectively as superantigens and have the ability to activate large numbers of T-cells (up to 20-30%) by interacting with the cells at an area separate from the classical antigen recognition site.

This, combined with binding to class II MHC (major histocompatibility complex) molecules leads to an uncontrolled release of inflammatory cytokines including TNF-ß, IFN-gamma, IL-1ß, IL-6 and IL-8, the key chemokines to producing acute inflammation, tissue damage and shock (1,2).

However 70-80% of people develop an antibody to TSST-1 by adolescence and 90-95% by adulthood – those who lack this protective antibody are susceptible to the clinical manifestations (3).

It was first found in children in 1978 (4) but was not well recognised until a few years later when it was linked to women using highly absorbent tampons (5). This is thought to be due to the decline in the highly absorbent tampons on the market. Today roughly 50% are caused in relation to menstruating (6). Other important causes include wound infections including post-operative and postpartum, burns, and osteomyelitis (3).

Prevalence is not well documented but STTS is more common than GAS-TTS, although a history of recent varicella infection significantly increases the risk of GAS-TTS (3). The BPSU (British Paediatric Surveillance Unit) are likely to soon be releasing data they have collected on prevalence in children in the UK from 2008 – 2009 (7). Mortality rate for menstrual TSS is now <5%, but significantly higher in GAS-TTS and TTS caused by SEs (3,6).

Common presenting symtoms include fever, myalgia, vomiting, diarrhoea, and headache. Patients are often hypotensive and cannot respond to fluid resuscitation. Confusion or altered mental state is frequently present. Other signs include a maculo-papular rash / petechiae, mucosal involvement, desquamation, and soft tissue infection / necrotising fasciitis.

The case definition from the Centre for disease Control and Prevention, 2011 states that a probable case will have 4 of the 5 following criteria plus meet laboratory criteria, and a definite case will meet 5 out of 5.

The clinical features include: 1) fever (≥= 38.9); 2) rash - diffuse macular erythroderma; 3) desquamation after 1-2 weeks; 4) hypotension; 5) multisystem involvement (with 3 or more) – Gastrointestinal (vomiting or profuse diarrhoea at onset); renal (urea or creatinine at least twice normal, sterile pyuria); hepatic (total bilirubin, ALT or AST at least twice normal); haematological (platelets less that 100); Central nervous system (altered consciousness without focal neurology when fever and hypotension are absent); pancreatitis; muscular (severe myalgia or creatine kinase at least double normal upper limit); mucous membrane (vaginal, oropharyngeal or conjunctival hyperaemia) (8).

Laboratory criteria include isolation of staphylococcus aureus on culture, and negative serologies for Rocky Mountain spotted fever, leptospirosis, or measles (8). GAS-TSS case definition is similar but less and slightly different criteria, and isolation of GAS (8).

Systemic Inflammatory Response Syndrome is defined as 2 or more of the following: temperature >38.5 / <36^{0}C; heart rate above 90/min; respiratory rate > 20/min; white cell count (WCC) >12,000 or less that 4,000 per µL9. This is altered in Paediatrics using limits of 2 standard deviations (SDs) above or below the mean, WCC 'elevated or depressed for age', and altered temperature or leucocyte count must be present (10).

Sepsis is defined as ≥ 2 criteria for SIRS plus evidence or strong suspicion of infection. Severe sepsis is defined as sepsis plus at least one organ dysfunction (if cardiovascular, or acute respiratory distress syndrome), otherwise 2 or more organ dysfunctions (10). Septic shock is severe sepsis with cardiovascular dysfunction - mainly hypotension with the systolic blood pressure < 2 SDs below the mean for age, or need for a vasoactive agent to maintain blood pressure in the normal range despite fluid resuscitation (other criteria involving lactate, base excess, oliguria, core-peripheral temperature gap, and capillary refill time) (10).

Sepsis is a significant cause of mortality, whatever the initial cause of the sepsis, and early recognition and appropriate management has been shown to significantly improve outcome. We propose a tool to be used in all cases of septic shock in order to most effectively manage these patients and there-by lead to improved outcomes.

It has been created using evidence and guidelines from the 'Surviving Sepsis Campaign' Paediatric section (11) and the South Thames Retrieval Service guidelines (12) both of which have produced those guidelines based on gathered evidence from all available relevant studies.

The 'Surviving Sepsis Campaign' use 'recommend' to imply the desirable outcomes clearly outweigh the undesirable effects, however use 'suggest' to mean they probably outweigh the negatives but the panel is not confident either due to poor quality evidence or because the positives and negatives are closely balanced (11).

'SACRIFICES' is the mnemonic to remember this tool. Divided up, this stands for:

- S – Suspicion: *initial suspicion of sepsis due to fever >38.5 or <36^{0}C, raised or depleted leucocytes (if already known), plus tachypnoea or tachycardia (fever >38^{0}C if immunocompromised);*

- A – Assessment: *assess and manage ABCs including obtaining vascular access, a bedside blood sugar and gas with a lactate, and sending blood for culture, full blood count, urea and electrolytes, and C-reactive protein. Assess level of consciousness. If vascular access is difficult and child considered to be in septic shock then intraosseous access is advised.*

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• C – Confirmation: *shock confirmed following assessment – delayed capillary refill, reduced urine output (<0.5ml/kg/hr, altered mental status, low blood pressure (decompensated shock) – systolic BP should be ≥ 70 mmHg (<1year), ≥ 70 + (age x 2) mmHg (1-10yrs), ≥ 90mmHg (>10years old). Remember hypotension is a late sign in children, making the recognition and management of septic shock in children different from adults.*

• R – Resuscitation: *initiate fluid boluses immediately at 20mls/kg 0.9% NaCl, and continue to repeat until therapeutic endpoint is achieved. This may require up to and over 60mls/kg. Consider early intubation for refractory shock (>40-60mls/kg fluid), altered consciousness, hypoxia, or signs of raised intracranial pressure. Early intubation for shock is proven to improve outcome (12).*

The most experienced person should intubate, and be aware that anaesthetic drugs can cause cardiovascular instability so ketamine should be considered. Broad spectrum antibiotics should be given during fluid resuscitation, which should be within the first hour of recognition of sepsis (11).

• I – Impact: *assess impact of resuscitation at regular intervals – heart rate, blood pressure, peripheral pulses, capillary refill time, urine production, level of consciousness, acid-base derangement improves (lactate and base deficit)*

• F – Fluid Refractory: *>60mls/kg fluid and persistent shock state – start inotrope therapy-dopamine at 5-10mics/kg/min and continue aggressive fluid resuscitation. Contact PICU if not already done so. Intubation should already have been done at this stage but intubate and ventilate if not. Obtain central venous access and consider an arterial line.*

• I – Inotropes – dopamine: *see above. If resistant to dopamine, move onto the next stage. Dobutamine can be considered in cold shock (low cardiac output, high systemic vascular resistance leading to cool extremities, prolonged capillary refill, decreased urine output but normal blood pressure following resuscitation) – this is 'suggested' by the Surviving Sepsis Campaign authors11 – see above for the implications of 'suggest'.*

• C – Catecholamines – *adrenaline or noradrenaline: for cold shock (as above) use adrenaline and for warm shock (brisk capillary refill, bounding pulses, hypotensive or wide pulse pressure) use noradrenaline, both starting at 0.1micrograms/kg/min (12). When patients remain in cold shock despite the above, the use of a phosphodiesterase inhibitor could be considered e.g. milrinone (11,12). IV hydrocortisone is advised if resistant to catecholamines as a 2mg/kg bolus (12) however SSC suggest only using it in those with suspected or proven adrenal insufficiency (11).*

• E – ECMO: *Extra Corporeal Membrane Oxygenation (ECMO) can be considered if the child is fluid, inotrope and catecholamine resistant. There are 4 centres in the UK – Leicester, Newcastle, Glasgow and London – and they work together to co-ordinate a national neonatal service. However, for older children, this is available in all the cardiac centres.*

• S – Supportive Therapies: *DVT prophylaxis is 'suggested' in postpubertal children when clotting is normalised. Most DVTs in young children are associated with central lines. SSC states there is no data on the efficacy of low molecular weight heparin to prevent catheter related DVT in children. Stress Ulcer Prophylaxis – again there is limited data according to SSC but coagulopathy and mechanical ventilation are risk factors for gastrointestinal bleeding and prophylaxis is often used, although effects are not known (11).*

Renal Replacement Therapy in the form of continuous veno-venous haemofiltration or dialysis can be used for anuria / severe oliguria or fluid overload but there is limited data on comparison of the two (11). Glycaemic control is also important as there are reports of hyperglycaemia and hypoglycaemia being associated with an increased risk of death and length of stay (11).

It is advised insulin should be used in children as is shown to be beneficial in adults but the optimal glucose is not known. Appropriate sedation and analgaesia are important and it is recommended to follow local protocols, and although no specific drugs are recommended, propofol should not be used as it is associated with fatal metabolic acidosis (11). Blood products should be considered with low a haemoglobin level. Intravenous immunoglobulin is 'suggested' as an adjunct to the treatment of sepsis (11).

Conclusion

We have described a case of toxic shock syndrome and how it was managed, given some background on the illness and proposed an easy mnemonic in how to remember the current best evidence guidelines on how to manage septic shock. This is also adaptable to future updates in evidence as well. Ideally this could be taught to medical students and junior doctors as a memory aid and will help improve outcomes in a condition that is so dependent on accurate and rapid management.

MCQ

1. A mother brings her 24 day old baby to the emergency department as the baby developed a fever a few hours ago. She has been otherwise well, feeding and wetting her nappies as normal. She was born at term with no complications and did not require antibiotics or SCBU admission. Her physical examination is unremarkable but she is noted to be pyrexic at 38.9ºC. What is the most appropriate management for this patient?

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A. Observe the baby in the unit for 4 hours and send home with safety netting advice if no further temperatures.

B. Explain to mother that examination was normal and reassure that fever is common in children. Discharge home with paracetamol and advice to return if fever persists.

C. Perform a full septic screen including lumbar puncture and commence empirical parenteral antibiotics until culture results are known and adjust as appropriate.

D. Take blood for full blood count (FBC) and C- reactive protein (CRP) and start antibiotic therapy if markers are elevated.

E. The most common reason for neonatal sepsis is Group B streptococcal (GBS) infection and thus both mother and child should be commenced on IV antibiotics as soon as possible.

2. With regards to physical examination in the context of meningism, Brudzinski's sign refers to?

A. Applying pressure to both cheeks inferior to the zygomatic arches. A positive sign results in spontaneous flexion of forearm and arm.

B. Passive flexion of the neck with patient in supine position. A positive sign results in reflex flexion of the patient's hips and knees.

C. Inability to passively extend a flexed knee due to spasm of the hamstring muscles.

D. Reflex flexion of a lower limb on passive flexion of the opposite limb.

E. Pain on anterior but not lateral compression of calf.

3. Which of the following does not form part of the criteria of a paediatric Systemic Inflammatory Response Syndrome (SIRS)?

A. Temperature <36^{0}C or >38.5^{0}C.

B. Heart rate greater than 2 standard deviations above or below the mean.

C. A white cell count (WCC) elevated or depressed for age with altered temperature or leucocyte count.

D. A systolic blood pressure <90mmHg or diastolic <60mmHg.

E. A respiratory rate greater than 2 standard deviations above or below the mean.

4. A 4 year old boy has been brought to the emergency department by his parents as he has been increasingly lethargic that day. He has been coryzal with a cough and intermittent fevers up to 38.5^{0}C for the past few days. Mom reports that he has been off his food. She became worried as he appeared sluggish to her since this morning when he woke up.

On examination, he is warm to touch with a temperature of 38^{0}C. He has a flash central capillary refill time. He has a bounding radial pulse with a heart rate of 144bpm. A wide pulse pressure is noted. He appears lethargic and uninterested in his environment.

He is commenced on a fluid bolus challenge of 20ml/kg with 0.9% Saline. Despite 4 boluses, he remains tachycardic and lethargic. His work of breathing appears worse and he has bilateral crackles on auscultation. On abdominal examination, hepatomegaly is noted. What is the next most appropriate step in the management of this patient?

A. Continue with fluid boluses at same volume as these children may require > 100ml/kg.

B. Give adrenaline.

C. Give noradrenaline.

D. Give stat dose of furosemide.

E. Continue with fluid boluses but reduce bolus dose to 10ml/kg.

5. The main organism implicated in Toxic Shock Syndrome is:

A. Gram positive, coagulase positive, catalase positive coccus.

B. An obligate intracellular parasite.

C. Gram positive, coagulase negative, catalase positive coccus.

D. Gram negative, aerobic coccus.

E. Gram negative, lactose positive, bacillus.

Answers

1. C

A child under one month presenting with fever requires a full septic screen even if they appear well. This includes bloods for FBC, CRP, blood and urine cultures and a lumbar puncture. A chest X-Ray if chest signs are present and stool culture if diarrhoea present should also be performed. NICE Guidelines also advise commencing the child on a 3rd generation cephalosporin parenterally.

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In infants younger than 3 months, if antibiotics therapy is indicated, then adding an antibiotic active against Listeria, such as amoxicillin, is recommended. The most common cause for neonatal sepsis is (GBS), however appropriate cultures should be taken prior to commencement on parenteral antibiotics and it is not necessary to treat the mother unless she is symptomatic.

2. B

A is Brudzinski's cheek sign. C is Kernig's sign. D is Brudzinski's contraletral leg sign. These are all used in the context of examination for meningism although the most popular are Brudzinski's neck sign and Kernig's sign. E is Bancroft's sign and is sought in the context of suspected deep vein thrombosis.

3. D

Blood pressure does not form part of the criteria for SIRS. Hypotension in children is a late sign of shock and does not form part of the diagnosis. However if present in a child with suspected shock, then the diagnosis is confirmed.

4. C

The child has symptoms of warm shock: flash capillary refill time, bounding pulse, wide pulse pressure. He also has symptoms of fluid overload. Although pulmonary crackles may be signs of a pulmonary manifestation of disease, worsening work of breathing and hepatomegaly are indicative of fluid overload. The next appropriate step therefore is inotropes. In warm shock, noardrenaline is advised and in cold shock (cold and mottled peripheries, increased capillary refill time >3 secs and narrow pulse pressure), adrenaline is the main inotrope.

5. A

Staphylococcus aureus is the main organism implicated in Toxic Shock Syndrome, although other organisms such as group A streptococci also have a role. An example of option B is Chlamydia. C describes staphylococcus epidermidis, implicated in infection from catheters and prostheses. Examples of D and E are Neisseria spp. and Enterococci respectively.

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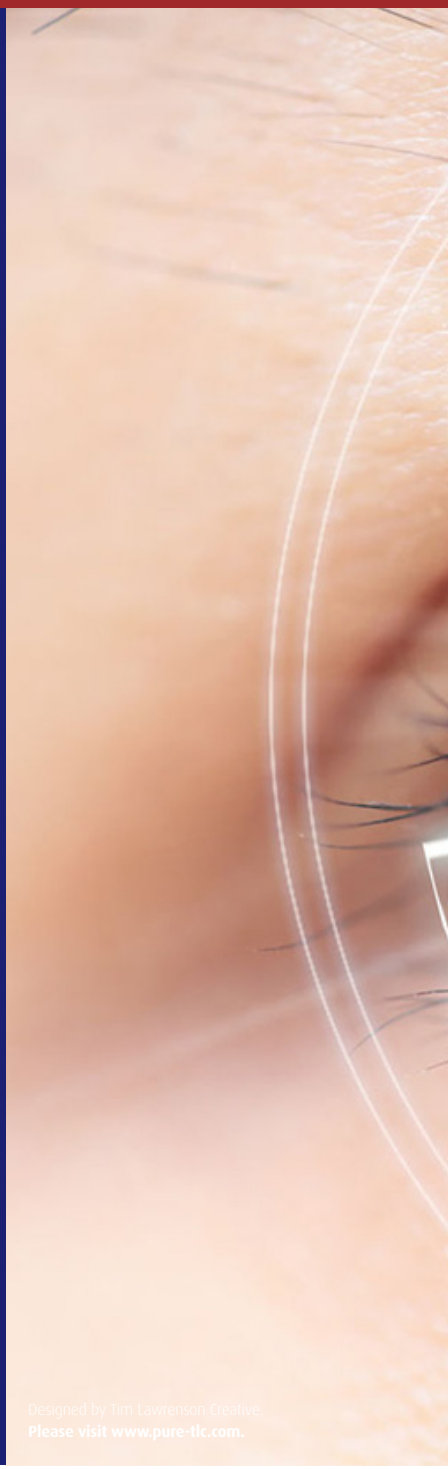

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