CASE REPORT

Group A streptococcal endophthalmitis complicating a sore throat in a 2-year-old child

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SUMMARY

A previously well 2-year-old presented to her general practitioner after 5 days of fever, lethargy, sore throat and a slightly red eye. A viral infection was diagnosed. Two days later, she re-presented with a swollen right eyelid and a moderately red eye. Oral amoxicillin and chloramphenicol eye drops were prescribed. The next day, marked periorbital swelling developed. She was admitted to hospital and parenteral ceftriaxone was started. Examination under anaesthetic showed injected globe diffuse corneal clouding and peripheral corneal opacities; ultrasound and CT suggested endophthalmitis. On transfer to a tertiary centre, intraocular vancomycin and subconjunctival cefuroxime were given. Aqueous fluid samples were positive for group A *Streptococcus* (GAS) by PCR, so parenteral clindamycin was added. GAS endophthalmitis was confirmed 1 day later from the positive intraocular fluid culture results. Visual evoked potentials revealed complete loss of vision. The eye was removed to limit potential spread. She made a good recovery postoperatively and was discharged on oral antibiotics.

BACKGROUND

Endophthalmitis is a potentially devastating infection: simple bedside tests such as checking for a red reflex can alert the general clinician for the need for urgent ophthalmological involvement.

Group A streptococcal (GAS) pharyngitis is common but complication with a severe endophthalmitis is rare in an otherwise healthy child or adult. There is an unusual increase in prevalence of scarlet fever (caused by GAS) in the UK at present and public health agencies have issued a warning to clinicians that invasive GAS infections may also increase. In this context, clinicians need to be aware of potentially devastating complications of GAS. Rapid molecular tests for GAS have been developed that enable prompt diagnosis and tailoring of antibiotic therapy. Uptake and wider usage of such tests could enable clinicians to treat invasive GAS infections promptly and limit complications.

CASE PRESENTATION

A previously well 2-year-old girl presented to her general practitioner with a 5-day history of fever, lethargy, sore throat and a slightly red eye. There was no significant medical history, particularly no history of trauma to the eye. She was developing normally and her vaccinations were up to date. There was no significant family history. A viral infection was diagnosed and managed with antipyretics. Two days later,

she re-presented with a swollen right eyelid and moderate conjunctivitis. Her throat was noted to be severely inflamed. She was prescribed oral amoxicillin and chloramphenicol eye drops, but presented to the emergency department 24 h later with more marked periorbital swelling. She was admitted and blood tests were taken; parenteral ceftriaxone was started to treat a possible preseptal cellulitis and an ophthalmological review was undertaken.

INVESTIGATIONS

Examination under anaesthetic undertaken at the local hospital revealed chemosis with a very cloudy cornea, no view from the iris and an almost total epithelial defect. There was no hypopyon or stromal abscess. Imaging with ultrasound and CT orbit showed a thickened sclera and mild vitreous opacities, and no intraocular mass; the CT head was normal. Blood tests were normal except for an erythrocyte sedimentation rate of 88 mm/h and a C reactive protein (CRP) of 80 mg/L. Antinuclear antibody and antineutrophil cytoplasmic antibody were negative as were blood cultures at 48 h. Repeat CRP 48 h after admission was 31 mg/L. She was transferred to a tertiary centre after 4 days of parenteral antibiotics. Repeat examination under anaesthesia demonstrated evidence of endophthalmitis: the cornea was diffusely hazy with areas of opacity at the limbus (figure 1). There was no view of the anterior chamber structures. A focal area of scleral necrosis was observed next to the medial limbus and the eye was hypotonous with large choroidal detachments noted on ultrasound. A Gram stain of aqueous fluid revealed Gram-positive cocci. The same sample was positive when tested with a real-time PCR assay specific for GAS. Cultures were positive for GAS 24 h later. Visual evoked potentials performed after a week of parenteral and intravitreal antibiotics showed a tiny response to very bright light. Histopathology postevacuation, performed 7 days later, revealed endophthalmitis, with severe keratitis and probable perforation.

DIFFERENTIAL DIAGNOSIS

Sudden periocular swelling in the context of an acute upper respiratory tract infection suggests orbital cellulitis, which is usually associated with sinus infection. This may be accompanied by marked inflammation of the globe with intraocular changes secondary to increased intraorbital pressure, but acute endophthalmitis is rare. Simple bedside screening tests, such as loss of the red reflex, can alert the clinician to globe involvement rather than an orbital cellulitis alone.

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Figure 1 Image of eye during examination under anaesthetic demonstrating widespread conjunctival injection. Arrows (clockwise from top right). (1) Area of widespread epithelial defect. (2) Hypopyon. (3) Area of scleral necrosis.

Autoimmune orbital inflammation may cause a similar presentation, especially in the absence of sinusitis and with negative blood cultures.

Bacterial endophthalmitis without an obvious exogenous precipitant, such as intraocular surgery, may take some time to diagnose and children notoriously fail to report significant early symptoms of intraocular inflammation, especially when unilateral. Presenting signs in children are, therefore, often atypical when compared with adults due to the progression of disease before diagnosis.

TREATMENT

After the initial diagnosis of endophthalmitis was suspected she was started on parenteral chloramphenicol in addition to ceftriaxone and topical steroid drops. When there was no improvement, she was transferred to a tertiary centre where intravitreal vancomycin and cefuroxime were given, the ceftriaxone continued and the intravenous chloramphenicol stopped. Following the positive GAS PCR result, intravenous clindamycin was added. After the confirmation of complete loss of vision in the right eye, the decision was made to proceed to enucleation of the right eye to limit potential spread of the infection via the optic nerve or via another route.

OUTCOME AND FOLLOW-UP

She made a good postoperative recovery and was discharged on oral antibiotics. She will be fitted with a prosthetic eye in due course.

DISCUSSION

GAS is a versatile pathogen causing a myriad of diseases from the common and minor to the life threatening. There are estimated to be over 600 million cases of GAS pharyngitis worldwide per annum with invasive GAS infections, such as sepsis, cellulitis, toxic shock syndrome and necrotising fasciitis being 1000-fold less common.¹ Septic complications of throat infections are rare and clinical signs have poor predictive power in adults.^{2–4} Public Health England issued a warning in March 2014, a month prior to this case, of a surge in notifications of scarlet fever, with nearly 2.5 times as many cases being reported in the winter period of 2013–2014 as compared with the same period in the previous year.⁵ They highlighted the importance of a high degree of clinical suspicion where complications of GAS infections may be involved.⁵ A recent prospective study

has highlighted the devastating impact of GAS periorbital necrotising fasciitis, with sepsis and death resulting in 10%.⁶

This case exemplifies the pitfalls confronting a clinician managing GAS infections in that a relatively mild pharyngitis led to devastating consequences within a very short space of time. The benefits of a rapid test such as real-time PCR cannot be underestimated. This real-time PCR was an inhouse assay that allowed the results to be communicated to the treating clinicians within one working day.⁷ For external samples, the turn around time is 24 h from receipt of sample.

Bacterial endophthalmitis usually has an obvious precipitant, such as intraocular surgery or trauma. Less commonly, it can be endogenous, acquired from an infection elsewhere in the body. Features include a painful red eye with decreased vision and loss of the red reflex, although with less virulent organisms the condition can be painless. Endogenous endophthalmitis usually occurs with obvious risk factors, such as immunosuppression or bacterial colonisation as seen in patients with diabetes with chronic foot ulcers and ITU patients with indwelling catheters.^{8–9} In previously fit patients, endogenous endophthalmitis may be caused by deep-seated abscesses, such as intervertebral disc abscesses. GAS is rare or unmentioned in most case series of exogenous endophthalmitis.^{10–25}

One study focusing specifically on streptococcal endogenous endophthalmitis reported a rate of 8% for β -haemolytic streptococci.²⁶ GAS endogenous endophthalmitis has rarely been reported, accounting for 2/342 (0.6%) of cases in one review,⁹ in both associated with immunocompromise; and 0/27 in another series.^{27–28} The most similar cases to this is that of otitis media in a healthy adult and that of bilateral GAS endophthalmitis following gynaecological surgery where the peripheral corneal opacities were very similar to this case and were associated with an endophthalmitis rather than a primary keratitis.^{29–30} There have been six reported cases of neonatal group B endogenous endophthalmitis reported which illustrate the diagnostic problems of ocular inflammation in children.³¹ Enucleation may be necessary, in this age group, if retinoblastoma cannot be excluded. Classical inflammatory signs, such as globe redness, periorbital oedema and hypopyon, may be absent despite endophthalmitis. Retinoblastoma may present with inflammatory signs mimicking infection.³² Nor does imaging with ultrasound and MRI provide a definitive distinction between infection, intraocular tumour or congenital posterior segment anatomical variants associated with media opacity.³¹ Intravitreal antibiotics are the cornerstone of therapy, although recent studies have highlighted a potential role for adjunctive therapy with intravenous immunoglobulin for invasive GAS infections, such as endophthalmitis.^{33–34}

The differential diagnosis between acute autoinflammatory orbital and sclerocorneal inflammation and ocular infection can be very difficult. The corneal changes in this case were actually more suggestive of a diffuse anterior segment vasculitic process than infection although diffuse corneal changes can occur from endophthalmitis.

Clinicians frequently need to presume an infectious cause or orbital and ocular inflammation at the initial presentation and this may include the administration of intraocular antibiotics despite the high risk of further intraocular damage, including perforation. Local and systemic immunosuppression may then be rapidly required once endophthalmitis has been adequately excluded.

Undoubtedly GAS pharyngitis leading to severe endophthalmitis in a previously healthy child is highly unusual. However, given the increasing prevalence of other GAS infections, there is

Parents' perspective

The first sign things were not right were on the Saturday before admission via A&E. We took our child to the local play park and unusually she was not interested in playing there. We ran into some friends on the way back to the cafe and while talking to them she was quiet and withdrawn (although she did not know them well so we thought she was being shy). She then fell asleep while we ate lunch again not alarming but a little unusual. As a parent I thought she was coming down with a cold or virus and she had been sleepy and so forth with the usual childhood coughs and colds so at this stage it didn't seem suspicious.

As the week progressed she did not show sign of improvement and it was this that rang alarm bells. She wasn't eating much just a few bites each time and mostly wanted to sleep covered with a blanket on the sofa. The main alarm bell in my mind was that there were no cold or viral symptoms and towards the end of the week this seemed strange. The NHS website provided useful advice in this respect and initiated a visit to the general practitioner. The eye problem wasn't immediately apparent until it started to look like what we thought was conjunctivitis. When it closed that was when we knew there was a potential problem. There was a rapid deterioration, that is, it started as if conjunctivitis but clearly not—the eye closed quickly (on Friday it was open at the general practitioner's surgery but by Sunday it was closed). The red area started on Thursday but was not of great concern at start. From a lay person's point of view it starts as possible conjunctivitis/burst blood vessel but in this case perhaps indicator of initial infection?

Alongside initial signs/diagnosis, we would like to raise awareness of any changes within the child among other professionals, for example, childcare settings/nurseries, etc, and possibly even health visitors/midwives—we had regular contact with the NHS midwives as I was pregnant at the time and it's quite possible that I could have expressed concerns via this route initially not GP or had it happened just after our new baby was born it could have been via health visitor.

The pregnancy and child's birth were straightforward and as a baby she met all her developmental milestones.

We have found the main impact apart from the initial problems is now from a parent's perspective a child development focus, that is, explaining to our daughter later on what has happened and meeting any additional educational needs (so far she has adapted very well but some extra thought may have to go into some activities at primary school).

She is getting on really well, entertaining us daily and last week enjoyed her birthday!

a possibility that this kind of complication of streptococcal infections will be seen in other cases. Clinicians must have a high index of suspicion for complications of GAS infections as the consequences can be devastating.

Learning points

- ▶ In the context of suspected preseptal cellulitis, an early complete ophthalmological review is mandatory.
- ▶ Simple bedside tests, such as checking for a red reflex, can alert the clinician to globe involvement and should be mandatory when assessing cases of preseptal or orbital cellulitis.
- ▶ Group A streptococcal pharyngitis can lead to a severe endophthalmitis in otherwise well children.
- ▶ Group A streptococcal infections have increased in the UK over the past year; so clinicians must be wary of devastating and rapid onset complications in patients with seemingly inconsequential infections.
- ▶ Rapid PCR-based tests are now available for Group A streptococci. In the context of clinical suspicion these tests can lend crucial and timely diagnostic support, and guide appropriate antibiotic choice.

Contributors CE and RH were responsible for the clinical care of the child and KH oversaw the laboratory investigation. The report was conceived and drafted by FF in conjunction with the other authors. All authors contributed to the manuscript.

Competing interests None.

Patient consent Obtained.

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