Unusual association of diseases/symptoms

Reversible blindness: severe pneumococcal induced uveitis following septicaemia

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This study illustrates the case of a middle-aged woman who presented with sepsis and purpura fulminans, found to be due to *Streptococcus pneumoniae* infection. She later developed blindness from a dramatic ocular inflammatory response provoked by pneumococcal antigens.

BACKGROUND

Only one previous case report has been published of this dramatic presentation, yet pneumococcus is a common pathogen and known to be highly immunogenic.

The diagnosis-demonstration of pneumococcal DNA in ocular vitreous where Gram stain was negative, and treatment-response to immune suppression with steroids rather than targeted antibiotics, are both of interest to physicians who see pneumococcal infections frequently and sepsis regularly.

This is an extreme presentation, but given the prevalence of pneumococcal infections, could be seen by any general physician. Given the reversibility of the blindness, we feel it is important for physicians to be aware of the potential benefit from immunosuppression with steroids in this scenario.

CASE PRESENTATION

A 56-year-old woman was admitted feverish, disorientated, with generalised weakness and an extensive purpuric rash (figures 1 and 2).

She was a teacher with pet cats, but there were no other animal, occupational, travel or leisure exposures of note. Medical history consisted of nasal polyps and sinusitis. There was no history of splenectomy, functional asplenia or other immuno-compromise.

INVESTIGATIONS

Her white count was $23.4 \times 10^9/l$, C reactive protein 285 mg/l, clotting was deranged (international normalised ratio 3.17, activated partial thromboplastin time ratio 2.95, fibrinogen 1.9 g/l) and a blood film showed a leucocytoblastic picture with thrombocytopenia and red cell fragments. This suggested disseminated intravascular coagulation secondary to sepsis. Liver and renal function was abnormal (alkaline phosphatase 297 IU/l, albumin 38 g/l, bilirubin $27 \mu\text{mol/l}$, alanine transaminase 49 IU/l, urea 11.1 mmol/l , creatinine $210 \mu\text{mol/l}$).

Antinuclear antibody was negative. Antineutrophil cytoplasmic antibodies, myeloperoxidase and proteinase 3 were within the normal range. HIV serology was negative.

Chest radiograph was unremarkable.

MRI brain showed high-density material within the ethmoid (figure 3) and frontal (figure 4) sinuses of likely infective origin.

TREATMENT

She was admitted to intensive care and received ceftriaxone 2 g once daily and aciclovir 10 mg/kg 8-hourly intravenously, fluid resuscitation and vitamin K.

Gram positive cocci, later confirmed as *Streptococcus pneumoniae*, were isolated from blood cultures. The organism was sensitive to β -lactams, macrolides and tetracyclines. Antibiotics were switched to intravenous benzyl penicillin 1.2 g 4-hourly. Sinusitis was felt to be the likely portal of entry.

On day 3, she had visual disturbance and was noted to have severe bilateral conjunctival injection and haemorrhages. Visual acuity was reduced to 6/36 bilaterally. She had a small hypopyon in the left eye and there was only a hazy fundal view due to vitritis. Bilateral endogenous endophthalmitis was suspected clinically and she underwent left vitreous biopsy and intravitreal ceftazidime (2.2 mg/0.1 ml) and vancomycin (1 mg/0.1 ml) was given bilaterally.

On the first postoperative day the hypopyon was resolving and the vitritis was less. However, over the next few days, vision rapidly dropped to perception of light only in both eyes. She became very photophobic and both anterior chambers became packed with fibrin.

This marked uveitic response was treated with pulsed intravenous methylprednisolone and gradually over a week the fibrin cleared with no permanent ocular sequelae. One month later the visual acuity was 6/6 in both eyes with normal fundi.

Figure 1 Purpuric rash on face.

Figure 2 Close up of purpuric rash on face.

Microscopy (Gram stain) and culture of the vitreous fluid failed to reveal a pathogen. Given diagnostic and aetiological uncertainty surrounding the vitritis, the sample was sent for molecular microbiological investigations: 16S rDNA gene and species specific PCR assays (Dr K Harris, Camelia Botnar Laboratories, Great Ormond Street Hospital, London). Pneumococcal DNA (lytA gene) was detected by PCR from a penicillin-susceptible strain (PBP2B gene detected) on this molecular analysis- confirming this organism as the aetiological agent responsible for the ophthalmological findings.

Figure 3 T2 MRI showing infective material in ethmoid sinuses.

OUTCOME AND FOLLOW-UP

The patient made a dramatic recovery; her eye pain and photophobia improved, vision returned and the fibrin plaque contracted. At follow-up, her visual acuity was normal (6/6 and 6/5), her lenses were clear and fundi were normal.

DISCUSSION

This case illustrates a dramatic ocular inflammatory response to pneumococcal antigens which responded well to immunosuppressive rather than local antibiotic therapy. Only one such case has been described previously to our knowledge.¹

This case was also notable for its severe presentation, with purpura fulminans, occurring in an immunocompetent adult. Purpura fulminans is characterised by haemorrhagic cutaneous infarcts resulting from disseminated intravascular coagulation and vascular thrombosis.² In adults, *S pneumoniae* is the leading infectious precipitant, but this is usually in the context of pre-existing asplenia.

Infections due to *S pneumoniae* are characterised by a vigorous host immune response. Pneumococcal cell-wall and polysaccharide capsule components, as opposed to toxins, are the main stimulants of both the alternative and classical complement pathways and precipitate an inflammatory cytokine cascade.³ Individual variation in disease manifestation may result from genetic polymorphisms in host immune receptors, such as toll-like receptors and CISH receptors.⁴

Novel molecular microbiological techniques such as pathogen specific assays and broad-range 16S rDNA gene PCR molecular analysis are increasingly available.⁵⁻⁷ These innovative techniques are particularly useful for

Figure 4 T2 MRI showing infective material in frontal sinus.

direct detection of bacteria from sterile site specimens and can be invaluable in demonstrating presence of bacterial DNA from tissues even after antibiotic therapy has been commenced, possessing greater sensitivity in detection of organisms (including non-viable organisms) than routine bacteriological techniques. In our case detection of DNA of *S pneumoniae* by species-specific PCR from the vitreous sample confirmed this pathogen as the sole agent

responsible for the systemic and ophthalmological symptoms and signs (via haematogenous dissemination) thus reassuring clinicians by excluding a secondary pathogen or disease process.

Learning points

- ▶ *Pneumococcus* has antigenic activity and the potential to cause immunological sequelae.
- ▶ These sequelae may respond to immune suppression rather than antibiotic therapy.
- ▶ Diagnosis may be aided by PCR analysis of fluid which has no bacteria visible on Gram Stain.

Competing interests None.

Patient consent Obtained.

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