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# SEPTICAEMIC INFECTION WITH GROUP B STREPTOCOCCI PRESENTING WITH ENDOPHTHALMITIS IN ADULTS

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## SUMMARY

**Metastatic bacterial endophthalmitis is an uncommon and serious infection, that can be caused by a variety of bacteria. Group B streptococci have rarely been implicated. We report four cases of metastatic endophthalmitis in adults caused by group B streptococci. The organisms were isolated from the eyes and blood in each case.**

Bacterial endophthalmitis is a devastating condition, with a poor visual prognosis and most cases follow surgery or penetrating ocular trauma.<sup>1</sup> Haematogenous spread to the eye (metastatic bacterial endophthalmitis) is much less common, especially in this antibiotic era.<sup>2</sup> Group B streptococci have rarely been reported as pathogens in metastatic endophthalmitis and mostly in neonates.<sup>2,3,4</sup> To our knowledge there is only one previously reported adult case.<sup>5</sup> We report four cases of metastatic endophthalmitis in adults due to group B streptococci: Three presented to the Medical Eye Unit at St. Thomas' Hospital, between October 1989 and June 1990 and one to the Royal Berkshire Hospital in November 1990.

## CASE REPORTS

### *Case 1*

A 55 year old man was admitted to the Medical Eye Unit in October 1989, with a three day history of reduced vision, pain and redness, worse in the right eye. This was associated with fever (38°C), left loin pain and tenderness and redness of the right elbow. He had a history of left renal calculi and had recently been treated with co-trimoxazole for a suspected urinary tract infection. On admission, the right visual acuity was hand movements, with a severe uveitis, a 4 mm hypopyon, an intraocular pressure of 40 mmHg and no fundal view (Fig. 1). Left

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visual acuity was 6/36, with a mild anterior uveitis, a normal intraocular pressure, a mild vitritis and white-centred haemorrhages at the posterior pole.

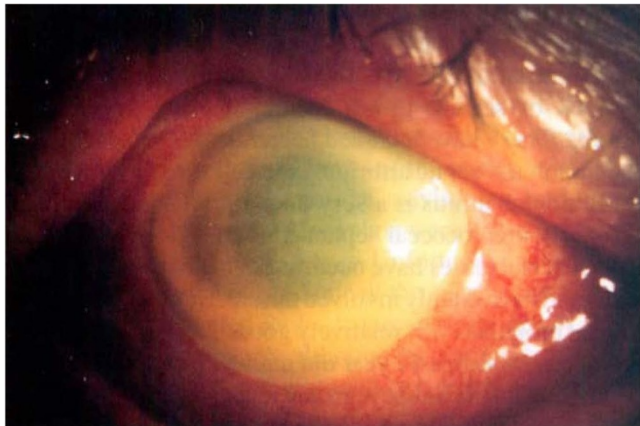
Investigations revealed a haemoglobin of 7g/dl, a peripheral white cell count of  $5.7 \times 10^9/l$ , an erythrocyte sedimentation rate (ESR) of 140mm/hr and a raised total protein (116g/l), with a reduced albumin (18g/l). Protein electrophoresis showed an IgG kappa paraproteinaemia. The serum calcium was elevated (2.97mmol/l). An aqueous tap and vitreous biopsy of the right eye were performed and microscopy revealed Gram-positive cocci in the aqueous but not the vitreous. Group B streptococci, type 1b, were subsequently cultured from the aqueous, vitreous and blood. The urine was sterile.

Treatment was started with intravenous amoxycillin and gentamicin for four days and continued with oral amoxycillin alone for twelve days. An intravitreal injection of 2.25 mg of cefuroxime was given at the time of the vitreous biopsy of the right eye. Topical methicillin, gentamicin, prednisolone and mydriatics were used in both eyes, with timoptol to the right eye only.

Within 72 hours his pyrexia settled and his general condition improved. The inflammation of the right elbow gradually resolved without intervention. Bone marrow examination showed an increase cellularity with reduced erythropoiesis and plasma cells forming 63% of nucleated cells and chemotherapy was started for multiple myeloma. The right visual acuity remained perception of light but the inflammation settled in the left eye with vision improving to 6/6, fully corrected,

### *Case 2*

A 76 year old previously healthy woman, presented to another hospital in April 1990 with an acute febrile illness, with rapid visual loss in both eyes over 48 hours. She had no urinary symptoms. On admission, she was pyrexial, confused and disorientated. There was redness and proptosis of both eyes, with reduced extraocular movements.



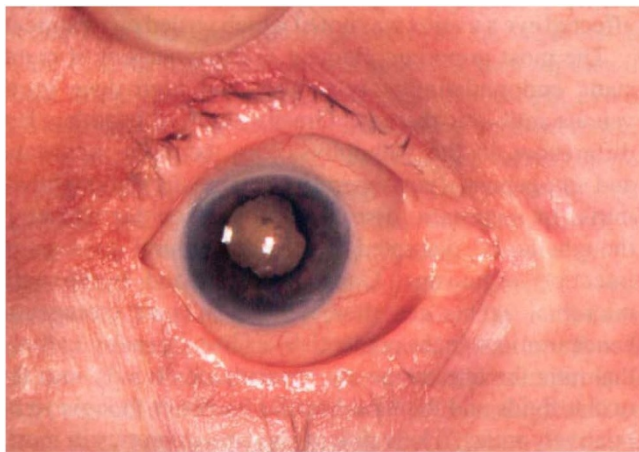
**Fig. 1.** The right eye of patient 1 showing a severely inflamed eye, with a severe uveitis and a 4 mm hypopyon.

Visual acuity was reduced to perception of light in both eyes. Treatment was started with erythromycin, ceftazidime and metronidazole.

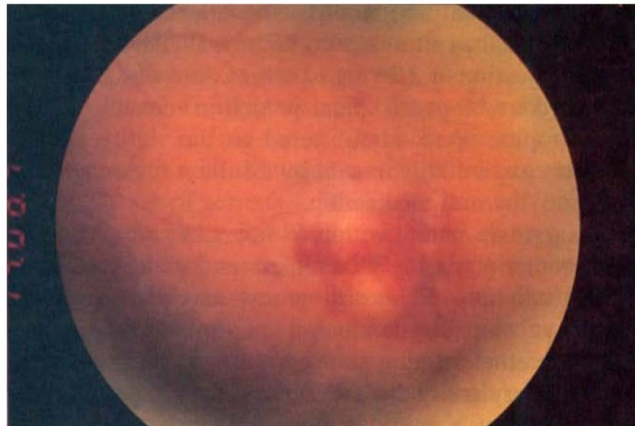
Group B streptococci, type 1b/c, were cultured from a conjunctival swab of the left eye, the urine and blood. A vitreous biopsy was not obtained in this case.

The patient was transferred to the local neurosurgical unit for investigation of possible cavernous sinus thrombosis. Treatment was changed to intravenous benzylpenicillin, gentamicin and acyclovir, with topical ceftazidime, gentamicin, mydriatics and acyclovir to both eyes. Her fever settled and her general condition improved but vision failed to return.

She was transferred to the Medical Eye Unit four weeks after the onset of her illness. On admission, she was afebrile with mitral and aortic systolic murmurs and crepitations at both lung bases. The right visual acuity was perception of light with a clear cornea, no hypopyon and dense vitreous opacification with no fundal view (Fig. 2). The left eye was blind, with pus filling the anterior chamber and a localised collection of pus beneath the conjunctiva laterally. Extraocular movements were slightly reduced in all directions of gaze. Investigations showed a haemoglobin of 8.8g/dl and a neutrophil leucocytosis



**Fig. 2.** The right eye of patient 2, four weeks after presentation, showing a quiet eye with a clear cornea and dense vitreous opacification.



**Fig. 3.** Fundus photograph of the left eye of patient 3 showing white-centred haemorrhages at the posterior pole.

( $13.2 \times 10^9/l$ ), with an ESR of 120 mm/hr. Urea, electrolytes and blood sugar were normal. Antibiotic therapy was stopped. Repeat blood and urine cultures were negative. Echocardiogram showed mild aortic incompetence with mild to moderate tricuspid and mitral valve regurgitation. No measureable electroretinogram or visual evoked response could be elicited in either eye. A presumed diagnosis of group B streptococci metastatic endophthalmitis was made. This was not culture proven as no intraocular microbiological specimens were obtained.

After discussing the poor visual prognosis, the patient refused further investigations or treatment and returned to her local hospital for nursing care.

### Case 3

A 65 year old previously healthy man was admitted to the Medical Eye Unit in June 1990, with a five day history of progressive, painless visual loss in the right eye and pain and swelling of the right knee. On admission, he was pyrexial ( $38^\circ\text{C}$ ) and tachycardic, with a mitral systolic murmur. The right knee was swollen and tender with a reduced range of movement and an effusion. The right visual acuity was vague perception of light, with a severe uveitis, a 1 mm hypopyon, an intraocular pressure of 28 mmHg and no fundal view. Left visual acuity was 6/5, with no uveitis, fundoscopy revealing haemorrhages two disc diameters temporal to the fovea, one of which was white-centred (Fig. 3), which were thought to be the result of septic emboli.

Investigations revealed a neutrophil leucocytosis ( $11.2 \times 10^9/l$ ) and an ESR of 46 mm/hr. Urea ( $15.2 \text{ mmol/l}$ ) and creatinine ( $159 \mu\text{mol/l}$ ) were raised. Blood sugar was raised ( $23.7 \text{ mmol/l}$ ), but there was no evidence of ketoacidosis. He admitted to thirst and polyuria during the preceding few months. 50 ml of green turbid fluid were aspirated from the right knee. Microscopy revealed numerous pus cells and Gram-positive cocci. Gram-positive cocci were also seen in an aqueous tap and vitreous biopsy from the right eye and in the blood cultures. Group B streptococci, type 1b, were subsequently grown from all specimens.

Treatment was started with intravenous amoxycillin

and gentamicin and continued with benzylpenicillin alone, when the culture results became available. An intravitreal injection of 2.25 mg of cefuroxime was given after the vitreous biopsy. Topical penicillin, dexamethasone, and atropine were administered to the right eye. The diabetes was initially treated by insulin infusion and subsequently by oral medication.

His pyrexia settled within 48 hours but four days later he became increasingly breathless and with atrial flutter and fibrillation. Echocardiograms revealed worsening mitral valve regurgitation but no obvious vegetations. Cardiac catheterisation showed mitral valve endocarditis and coronary artery disease. Sixteen days after admission he underwent a mitral valve replacement, a coronary artery bypass graft and a left internal mammary anastomosis. The mitral valve was sterile on culture. The right eye became blind three days after admission. The ocular inflammation gradually settled. Six weeks later pus (not cultured) discharged through the anterior sclera superonasally. This settled one week later, leaving a phthisical eye. The left eye retained good vision and the fundal lesions resolved. Turbid fluid, sterile on culture, was aspirated from the right knee on several occasions and the swelling gradually settled. Antibiotic treatment was continued for six weeks.

#### Case 4

A 60 year old previously healthy man presented to the Royal Berkshire Hospital in November 1990 with a two day history of a sore throat, generalised aching and shivering and pain and visual loss in the left eye. On admission, he was pyrexial with tenderness in the right hypochondrium, an inflamed throat and a painful, hot left wrist. The left visual acuity was 6/60, with chemosis, corneal oedema and an intraocular pressure of 55 mmHg. The right visual acuity was 6/5. An initial diagnosis of left acute glaucoma was made and he was treated with pilocarpine and acetazolamide but the left ocular inflammation persisted and the patient remained systemically unwell.

Investigations showed a haemoglobin of 11.4/dl, a white cell count of  $14.1 \times 10^9/l$  and an ESR of 65 mm/hr. Urea and electrolytes were normal and blood sugar was 11.8 mmol/l. Two days after admission, group B streptococci, type 1a/c, were cultured from the blood and treatment was then started with intravenous benzylpenicillin and topical penicillin and atropine to the left eye. Three days later intravenous gentamicin was added as his pyrexia continued. The intravenous drug regimen was continued for two weeks, after which oral amoxycillin was given.

The left eye became blind and five days after admission an evisceration was performed. A swab of the ocular contents grew group B streptococci. A few days later a right uveitis was noted but this quickly resolved on topical steroids and mydriatics. His general condition gradually improved and he was discharged twenty-three days after admission.

#### DISCUSSION

Group B streptococci are normal commensals in the female

genital tract and the lower gastrointestinal tract. Although they are predominantly pathogens in neonatal, post-abortion and postpartum sepsis, there have been several recent reports of serious group B streptococcal infections in adults. These have included bacteraemia,<sup>6-8</sup> endocarditis,<sup>9</sup> pneumonia,<sup>10</sup> septic arthritis<sup>11</sup> and cellulitis.<sup>12</sup>

Endophthalmitis is a very uncommon manifestation of group B streptococcal septicaemic infection. Most of the few reported cases have occurred in neonates with meningitis and have mainly involved the anterior segment and the visual prognosis was relatively good.<sup>2,8,9</sup> The only reported adult case was in a 42 year old man with endocarditis who went blind in his right eye from metastatic endophthalmitis and eventually died.<sup>5</sup> Severe adult eye infections, mainly microbial keratitis, but also post-operative endophthalmitis, due to group B streptococci have also recently been reported.<sup>13</sup>

In their review of 72 cases of metastatic endophthalmitis, Greenwald *et al*<sup>2</sup> showed that with severe ocular inflammation, the visual prognosis was poor, regardless of treatment. They suggested that the retina is irreversibly damaged by bacteria and inflammatory cells, with retinal ischaemia due to septic emboli contributing to the visual loss. The vision may be lost within a few hours of the first signs of infection, as in Case 2. In all four cases both eyes were involved and bilateral involvement is reported in about 25% of cases of metastatic endophthalmitis.<sup>2</sup> In five of the eight affected eyes the inflammation was severe and involved both the anterior and posterior segments. Two of these eyes maintained only vague perception of light and the other three became completely blind, despite systemic antimicrobial therapy. In the other three eyes the inflammation was less severe: in two funduscopy revealed white-centred haemorrhages and cotton wool spots, one had a mild uveitis, the other showed no signs of inflammation. These fundal lesions were probably due to small septic emboli. Both eyes retained full vision and the haemorrhages and cotton wool spots gradually resolved. Greenwald *et al*<sup>2</sup> showed that with this type of mild 'focal' inflammation, the visual prognosis was good, with early appropriate systemic antibiotic therapy. In the remaining affected eye a uveitis was noted which settled on treatment.

The most important element in the treatment of metastatic endophthalmitis is prompt and high dose intravenous antibiotic therapy.<sup>2</sup> Greenwald *et al*<sup>2</sup> postulate key differences in the pathophysiology between metastatic and exogenous (post-operative, traumatic) endophthalmitis. In metastatic disease the blood ocular barrier is thought to be disrupted by the transmural passage of infecting organisms. Consequently blood borne antimicrobial agents can more readily achieve therapeutic concentrations in the ocular tissues. In exogenous endophthalmitis the organisms are inoculated directly into the ocular fluids and the blood ocular barrier is thought to be relatively intact. The value of topical antibiotics in metastatic endophthalmitis have not been proven and Greenwald *et al*<sup>2</sup> suggested they may be omitted. They do recommend mydriatics and topical steroids, and suggest

that periocular antibiotic injections around the uninvolved eye may be used as prophylaxis. They recommend that intravitreal antibiotics be withheld in cases that are 'focal' or mainly involve the anterior segment, where there is often a favourable outcome with conservative treatment. If there is extensive involvement of the posterior segment intravitreal antibiotics may be advisable. Intravitreal injections of 2.25 mg of cefuroxime were given in Cases 1 and 3 to the worse affected eyes. Unfortunately these eyes were severely inflamed and one of the eyes went blind and the other maintained only vague perception of light. Systemic steroid therapy, although recommended in some cases of exogenous endophthalmitis<sup>14</sup> has not been evaluated in metastatic endophthalmitis and as many of these patients have underlying diseases, such as diabetes, and are systemically unwell their use is probably inadvisable.

Patients with metastatic endophthalmitis<sup>2</sup> and those with serious group B streptococcal infections often have significant underlying diseases, particularly diabetes mellitus and malignancy and such patients should be thoroughly screened for predisposing illness. Case 1 had multiple myeloma and Case 3 diabetes mellitus, both diagnosed on admission. Case 2 had only a limited number of investigations and in Case 4 no predisposing disease was discovered.

Non-ocular foci of infection, especially meningitis, endocarditis and urinary tract infection<sup>2</sup> are often present in patients with metastatic endophthalmitis. Case 3 had infective endocarditis, subsequently requiring emergency mitral valve replacement and in Case 2 the echocardiogram was abnormal suggesting that she too had probable endocarditis. Case 1 had swelling, erythema and tenderness of the right elbow, Case 4 a painful, hot left wrist and in Case 3 there was a septic arthritis of the right knee. Case 2 had a urinary tract infection. Full clinical examination and investigation is necessary to ensure that serious non-ocular infective foci are not missed.

Group B streptococci were cultured from the eyes in three cases, a conjunctival swab in Case 2 and blood in all four cases. Blood cultures are usually positive in metastatic endophthalmitis and the pathogen is found in ocular fluid and blood cultures with equal frequency.<sup>2</sup> Microscopy revealed Gram-positive cocci in the aqueous in Case 1, in the vitreous, aqueous and right knee aspirate in Case 3 and from a conjunctival swab of the right eye in Case 2. In these three cases Gram-positive cocci were seen in the initial blood cultures. Data for microscopy is not available in Case 4. Close liaison with the microbiologist and early microscopy of ocular fluids and blood can be of great value in early diagnosis and prompt treatment.

Although most serious neonatal infections with group B streptococci are caused by type III strains,<sup>15</sup> little is known of the types associated with serious adult infection. Type II strains have been isolated from most adults with group B streptococci meningitis.<sup>6,16</sup> None of the organisms isolated from our four cases were of type II or III, two were type 1b, one type 1b/c and one type 1a/c. Nor is it known why group B streptococcal septicaemic infection is becoming more common.

It is unusual for an ophthalmologist to be presented with a systemically ill, febrile patient with acute visual loss, and initial diagnostic confusion may occur as in Cases 2 and 4. Eleven of sixty-seven patients reviewed by Greenwald *et al*<sup>2</sup> were initially misdiagnosed with a delay in appropriate therapy. Metastatic endophthalmitis is a rare manifestation of serious septicaemic illness. Non-ocular metastatic foci may also occur, including, as in our cases, endocarditis and septic arthritis. Underlying systemic disease may be present and should be anticipated. Early recognition and prompt treatment with adequate intravenous antibiotic therapy, after appropriate microbiological specimens have been taken, are essential, but in most severe cases visual loss may be inevitable.

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