Enterobacter cloacae Endophthalmitis: Report of Four Cases

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Members of the genus Enterobacter are commensal organisms of the gastrointestinal tract and are considered pathogenic only for patients with lowered resistance to infection (e.g., chronic infection, cancer, or diabetes mellitus) or those with impaired immunity (congenital, acquired, or impaired immunity secondary to therapy). We report on four cases of endophthalmitis caused by Enterobacter cloacae: two in patients with acute postoperative endophthalmitis, one in a patient with delayed bleb-related endophthalmitis, and one in a patient presenting with presumed posttraumatic endophthalmitis. Each patient presented with severe disease many days after the onset of ocular symptoms, and two patients had systemic risk factors accounting for a reduced resistance to infection. Endophthalmitis caused by gram-negative bacilli is characterized by acute onset, rapid progression, and poor final visual outcome. Each of these patients was treated by a standard protocol with intravitreal, systemic, and topical antibiotics and systemic steroids. Despite treatment, the final visual outcomes for three of these patients was no perception of light, and that for one patient remained perception of hand movements only. In common with endophthalmitis caused by other gram-negative organisms, intraocular infection secondary to Enterobacter cloacae infection is a devastating disease which, despite treatment, results in extensive ocular damage and severe visual loss. Since 1966, only four cases of endophthalmitis secondary to infection with members of this genus have been reported. This report presents four cases which occurred over a period of 14 months and, to the best of our knowledge, the first case of bleb-related endophthalmitis secondary to E. cloacae infection.

Gram-negative organisms are the causes of 16 to 18.5% of all cases of culture-proven postsurgical endophthalmitis (1, 3, 4, 11) and of up to 30% of posttraumatic cases in rural areas (2). A variety of gram-negative bacilli have been reported to cause postsurgical endophthalmitis; the most common include Pseudomonas spp., Haemophilus influenzae, Proteus spp., Serratia marcescens, Morganella morgani, Citrobacter spp., Escherichia coli, and Klebsiella pneumoniae.

The earliest case reports of postsurgical endophthalmitis caused by Enterobacter cloacae were published in 1966 (12) and 1975 (5). Other than these two cases, only two other separate cases of post-surgical endophthalmitis secondary to E. cloacae infection have been reported, and those were in 1992 (4) and 1993 (6). E. cloacae has more commonly been reported as a causative agent of posttraumatic endophthalmitis, often as part of a mixed infection (2, 11). Irrespective of the etiology, the clinical picture at presentation is usually that of a severe, rapidly progressive disease with acute onset which results in a poor final visual outcome and often loss of the eye. We report on four cases of endophthalmitis in patients treated at Moorfields Eye Hospital between June 1995 and August 1996.

CASE REPORTS

The patients’ clinical details are presented in Table 1. The details of the standard treatment protocol have been reported previously (8), and brief descriptions are provided in Table 1.

Patient 1. An 89-year-old lady underwent uncomplicated cataract surgery and was admitted 3 days later with a clinical picture of endophthalmitis. She was treated with intensive topical gentamicin, cefuroxime, and dexamethasone hourly, and she received one subconjunctival injection of gentamicin and cefuroxime and intravenous fluocxacillin and ciprofloxacin over the next 5 days. At 10 days postsurgery, clinical deterioration was evidenced by the visual acuity in the left eye, which was perception of light and the presence of a dense relative afferent pupillary defect (RAPD). Examination revealed pus in the anterior chamber and a dense fibrin plaque over the pupil. No fundal details or red reflex was visible.

Gram staining and microscopy were not performed because the sample volume obtained was small. Two days later culture of aqueous fluid in cooked meat broth revealed gram-negative bacilli identified as E. cloacae by using the Analytical Profile Index Biochemical Identification System for members of the family Enterobacteriaceae (API 20 E system; Bιомérieux Vetek Products Incorporated). Culture of the vitreous fluid sample was negative.

Over the next 4 weeks the inflammation continued to settle, but despite this, the visual acuity remained perception of light. Two weeks later, the patient presented with a painful red eye and a visual acuity of no perception of light and was treated symptomatically.

Patient 2. A 50-year-old man with poorly controlled insulin-dependent diabetes was referred for management of recurrent and persistent vitreous hemorrhage in his left eye. Vitrectomy with delamination and endolaser treatment were undertaken on 25 May 1996. At the end of surgery Betamethasone (0.1%) and cefuroxime were injected subconjunctivaly. The patient was then seen 1 week later with a clinical picture suggestive of endophthalmitis, but he had in fact suffered ocular pain and rigors since the first postoperative day. Ocular examination revealed visual acuity of poor perception of light, evidence of intraocular inflammation, no fundal view, or a RAPD. Ultra-
**Endophthalmitis**

**Table 1. Clinical and Microbiological Details**

| Patient | Admission | Age/sex | Uncomplicated surgery | Eye operation performed at Moorfields Eye Hospital | Initial symptoms reported | Operation | Date of admission | Final visual outcome | A1c levels elevated | Prednisolone therapy | Oral antibiotics | Oral prednisolone treatment |
|---------|-----------|---------|-----------------------|---------------------------------------------------|--------------------------|----------|------------------|---------------------|---------------------|-------------------|-------------------|-----------------|--------------------------|
| 1       | 11/7/95   | 89/F    | Y                    | Y                                                  | N                        | ECCE     | 11/7/95          | NPL, phthisical      | 9.4 & 7.2%          | 1 week           | 24 days          | 4 weeks        | 3 weeks                  |
| 2       | 5/6/95    | 50/M    | Y                    | Y                                                  | Y                        | IOL      | 5/6/95           | NPL                 | 9.4 & 7.2%          | 1 week           | 24 days          | 4 weeks        | 3 weeks                  |
| 3       | 22/6/96   | 24/M    | NA                   | Y                                                  | NA                       | IOL      | 22/6/96          | NPL                 | 9.4 & 7.2%          | 1 week           | 24 days          | 4 weeks        | 3 weeks                  |
| 4       | 16/8/96   | 70/M    | Y                    | Y                                                  | N                        | ECCE     | 16/8/96          | NPL, phthisical      | 9.4 & 7.2%          | 1 week           | 24 days          | 4 weeks        | 3 weeks                  |

**Note:** A1c, hemoglobin A1c; API, Automatic Identification and Phenotyping System; CMB, chocolate brain heart infusion broth; CMBV, chocolate brain heart infusion broth with vancomycin; CMBBHI, chocolate brain heart infusion broth with amphotericin B; ECCE, extracapsular cataract extraction; E. cloacae, Enterobacter cloacae; IOL, intraocular lens; MMC, mitomycin C; NPL, no light perception; RAPD, relative afferent pupil defect; V1, oral ciprofloxacin (0.1 ml); C, oral ciprofloxacin (750 mg twice daily for 10 days); Cl, oral clarithromycin (500 mg once daily for 14 days); CMB, chocolate brain heart infusion broth; CMBV, chocolate brain heart infusion broth with vancomycin; CMBBHI, chocolate brain heart infusion broth with amphotericin B; CMBVBHI, chocolate brain heart infusion broth with amphotericin B and vancomycin; Y, yes; N, no; F, female; M, male; NA, not applicable; BHI, brain heart infusion broth; BST, benzyl alcohol starch tub; Vitreous, vitreous fluid; Aq, aqueous fluid; MES, minimum essential salt broth.
oral hypoglycemic medication, with a random glucose level of 17 mmol and 2% glycosuria.

Two days prior to admission he had arrived back from Nigeria, where he had been treated with topical medication for the previous few days for ocular infection. On presentation, the visual acuity of the left eye was hand movements. Advanced glaucomatous cupping and optic neuropathy in the fellow eye precluded the accurate assessment for a RAPD. Ocular examination revealed a thin avascular bleb inside which a fluid level of pus could clearly be distinguished, as could evidence of severe intraocular inflammation occluding the view of the intraocular lens, red reflex, and fundus. Ultrasound examination revealed no evidence of retinal detachment. The patient was treated by the standard protocol. Topical treatment with ceta- zidime and gentamicin (1.5%) was also instituted every alternating half hour. Gram staining and microscopy of the ocular samples did not reveal the presence of any organisms. Oral prednisolone was reduced gradually over the next 3 weeks. Broth culture of both aqueous and vitreous samples yielded gram-negative bacilli later identified as E. cloacae by using the API system for members of the family Enterobacteriaceae. Staphylococcus aureus was isolated from broth cultures of conjunctival swabs taken before treatment. The patient attended one follow-up appointment only 3 weeks later, at which time his eye was comfortable, but he had a visual acuity of hand movements only.

MATERIALS AND METHODS

Methods. The methodology for the sampling of intraocular fluids has been reported previously (8). Briefly, at the time of admission intraocular fluids (aqueous and vitreous fluids) were collected under sterile conditions and were processed immediately. Intraocular samples were examined by Gram and Giemsa staining and were cultured on blood agar, in brain heart infusion broth, and in Robertson's cooked meat broth. Because the volumes of the samples obtained were often small, Gram staining was performed only if the volume of the intraocular fluids obtained was greater than 100 µl. Intraocular fluid from patients 2, 3, and 4 were identical. Each of seven isolates obtained from these four patients demonstrated resistance to ampicillin, erythromycin, and vancomycin. Each of these isolates was found to be sensitive to chloramphenicol, cefuroxime, cefotaxime, ciprofloxacin, ofloxacin, amikacin, gentamycin, tobramycin, ticarcillin, mezlocillin, and tetracycline.

Discussion. Between 11% (postoperative) (15) and 30% (posttraumatic) (2) of culture-positive cases of bacterial endophthalmitis are caused by gram-negative bacilli. The disease usually has an acute onset and is rapidly progressive. Gram-negative organisms are highly virulent, their toxins and pro- teases cause extensive damage to ocular tissues, and ocular infections with these organisms result in a poor final visual outcome for the majority of patients (4–7, 13). The damage is compounded by the sequelae of intraocular inflammation and the host's subsequent healing response. All four patients described here were seen in a 14-month period, and all infections were caused by E. cloacae, which is not considered a common cause of gram-negative endophthalmitis (1, 11, 15). The infections were characterized by a delay in intraocular sampling and treatment, because the patients themselves did not seek attention in the early stages of the infection. Earlier presentation may have resulted in a better final visual outcome.

Members of the genus Enterobacter are commensals of the gastrointestinal tract and are considered patho- genic only for patients with lowered resistance to infection (e.g., chronic infection, cancer, or diabetes mellitus) or those with impaired immunity (congenital, acquired, or impaired immunity secondary to therapy). Patients with diabetes mellitus are also known to have a higher incidence of postoperative endophthalmitis secondary to infection with gram-negative organisms than patients who are not diabetic (10), and it is interesting that two of our three postoperative patients (patients 2 and 4) were diabetic. Although for each patient the diabetes was deemed under control at the time of surgery, at the time of admission for endophthalmitis, these patients were poorly controlled on their medication for diabetes, and may therefore have been more prone to infection.

In 1994, Mirza et al. (7) reported an epidemic of postsurgical E. cloacae endophthalmitis in seven patients, all of whom developed the disease 1 day after surgery. The disease was traced to contaminated cotton swabs. The consequences of infection with a large inoculum of this organism were reflected in the final visual outcomes for the patients: four of the seven patients required enucleation, two of the seven patients developed phthisis, and only one retained any vision (reported as 9/10). In the case of the four patients under our care, it is not possible to accurately judge the size of the infecting inoculum, because in all cases growth was obtained only in broth cultures and not on plates where the colonies could be counted. The absence of growth on solid medium would suggest low numbers, and the possibility of contaminated broth cultures or collection vessels, or both, was considered. The ocular samples from all the patients had, however, been dealt with by different members of staff at different locations. Only the surgery performed on patients 2 and 4 was carried out at Moorfields Eye Hospital, and these were performed by different surgeons and were performed 18 months apart. Because isolates with identical antibiotic susceptibilities were obtained from all patients, from multiple broth culture bottles (patients 2 and 4), and from both aqueous and vitreous samples for three patients (patients 2, 3, and 4) and because the infections in all four patients progressed in a manner characteristic of gram-negative endophthalmitis, it is unlikely that the isolated organisms were contaminants. The occurrence of four cases of E. cloacae endophthalmitis in such a short time span at different centers may indicate an increasing incidence of this disease or may indicate improved microbiological techniques and species-specific diagnosis. Patient 3 demonstrated persistent endophthalmitis 2 days after ocular and systemic antibiotic treatment had commenced. Shaarawy et al. (14) have reported that one of five patients from whom repeat intraocular samples were taken 3 to 8 days after initial therapy was found to be persistently culture positive for gram-negative organisms (Serrata spp.). The visual outcomes for all five of these patients were less than 20/300, and only two patients showed any improvement in visual acuity after treatment (both patients were culture negative on repeat sampling) (14). Of the four antibiotics used in the emergency treatment of the patients described here, two (ciprofloxacin and amikacin) were likely to be effective. Despite treatment, the final visual outcomes for all these patients presenting late in the course of the infection were very poor. Perhaps in the presence of severe infection with virulent organisms a second intravitreal injection of antibiotics should be considered. In patient 3, it is likely that the organism gained entry via the corneal wound, although the patient denied any history of
trauma. Although *E. cloacae* was not isolated in conjunction with other organisms, as is usually the case for intraocular samples from patients with posttraumatic endophthalmitis (2, 11), *Enterobacter* spp. have previously been reported to be the sole species causing disease in such patients (1).

Patient 4 had a case of delayed postoperative endophthalmitis secondary to bleb infection. This was the eye to which 5-fluorouracil as well as intraoperative mitomycin C had been applied postoperatively (9, 16), resulting in an avascular conjunctiva which may have been more vulnerable to infection. To our knowledge, *E. cloacae* has not previously been reported to be a cause of this type of endophthalmitis.

No common factor could be found to explain the increased frequency of isolation of *E. cloacae* from samples from patients with endophthalmitis. Interestingly, the onset of ocular symptoms (patients 3 and 4) and time of surgery (patients 1 and 2) for all four patients was between late May and early August 1995, and patients 3 and 4 had both recently returned from Nigeria. These observations may indicate a possible climatic or geographic risk to infection with this organism.

In conclusion, patients should be made aware of the need to seek medical attention should problems arise in the days following intraocular surgery, and clinicians should be aware of the devastating effects of endophthalmitis, especially when it is caused by virulent organisms such as *E. cloacae*, and should promptly treat all cases of postoperative inflammation as infective endophthalmitis until proven otherwise.

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