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Infectious pseudomonas subglottic stenosis occurring in a patient with acquired immunodeficiency syndrome

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Abstract

Pseudomonas aeruginosa is emerging as an increasingly common opportunistic infective agent in the immunocompromised human immunodeficiency virus (HIV) positive patient (Kielhofner *et al.*, 1992). Improvements in the prevention and treatment of opportunistic infections in HIV and acquired immunodeficiency syndrome (AIDS) has led to longer life expectancy (Graham *et al.*, 1992), and this has changed the incidence of *Pseudomonas aeruginosa* infection in this population (Baron and Hollander, 1993). We present a case of a patient with AIDS who developed a fulminant *Pseudomonas aeruginosa* stenosing subglottic infection. We are unaware of any previous reports of this particular manifestation of *Pseudomonas aeruginosa* infection.

Key words: Acquired immunodeficiency syndrome; *Pseudomonas aeruginosa*; Laryngostenosis

Case report

A forty-four-year-old male homosexual known to be HIV positive since 1986 presented to the emergency department with acute dyspnoea, sore throat and otalgia, all of three days duration. In the previous 18 months he had had five admissions for chest infections. During the last episode, six months prior to this admission, the AIDS defining diagnosis of *Pneumocystis carinii* pneumonia was made. He was on multiple medication including zidovudine, didanosine, fluconazole, doxycycline, dapsone and analgesics. He was allergic to penicillin, erythromycin and septrin. Examination revealed a pyrexia of 38.5°C and mild throat inflammation, but no evidence of chest infection.

A full blood count revealed a haemoglobin of 10.8 g/dl and a white cell count 2.2×10^9/l (neutrophils 1.3×10^9/l), and the CD4 count was $40/mm^3$ (0.040×10^9/l). Biochemistry screen, arterial blood gases and a chest radiograph were normal. Blood cultures and a throat swab were sent. A diagnosis of viral upper respiratory tract infection was made, and the patient was discharged. However, on review at 24 hours, his condition had deteriorated and he had developed a headache, hoarse voice and dyspnoea. He was noted to have inspiratory stridor. His arterial blood gases on air were still normal. Further blood, sputum and a throat swab were sent for culture. He was admitted and commenced on intravenous ciprofloxacin, salbutamol nebulizers and oxygen.

Two days later he developed biphasic stridor. Nasendoscopy revealed a normal epiglottis and red mobile vocal folds, but the view of the subglottic region was poor. There had been no microbiological growth of any pathogens from previous specimens. The chest radiograph was unchanged, but an antero-posterior radiograph of the neck revealed subglottic stenosis and a diagnosis of tracheo-bronchitis was made (Figure 1). He was placed on intravenous hydrocortisone and cefuroxime in addition to the ciprofloxacin. The patient deteriorated further with increasing pyrexia, stridor and neck pain. Repeat nasendoscopy revealed no change in the appearance of the larynx from the previous flexible nasendoscopic examination but his condition was such that he was unfit for bronchoscopy. The patient was assessed for transfer to the intensive care unit by the consultant anaesthetist who felt cardiopulmonary support was inappropriate at this stage. He developed a

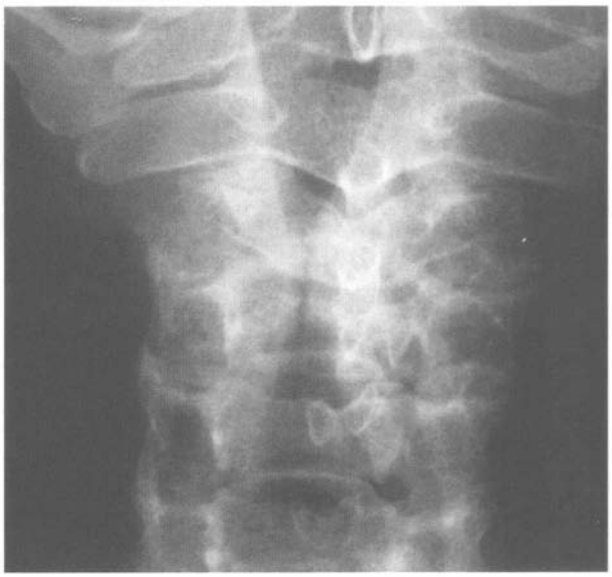

Fig. 1
Radiograph of larynx AP view.

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purulent productive cough with basal crepitations and nasendoscopy revealed swelling of the supraglottis. A swab of this area was sent for culture. A chest radiograph revealed basal shadows with diffuse interstitial opacification of the lung fields. The arterial blood gases had deteriorated. A diagnosis of pneumonia was made and the patient commenced on intravenous clindamycin, ceftazidime and anti-tuberculous therapy, but the patient failed to respond to treatment and died. *Pseudomonas aeruginosa* was isolated from the oropharyngeal swab, this was subsequently found to be sensitive to gentamicin, ciprofloxacin and ceftazidime.

A post mortem examination revealed extensive green discoloration and ulceration of the laryngeal and tracheal mucosa with stenosis of the subglottis. The supraglottis had a similar green-coloured ulcerated appearance. The lungs were oedematous with multiple sites of consolidations. Histological analysis of the larynx and the trachea revealed widespread superficial ulceration with infiltration by Gram negative bacilli and underlying inflammatory exudate and swelling. The appearances were highly suggestive of *Pseudomonas aeruginosa* infection. A similar picture with haemorrhagic necrosis was found in the lungs.

Discussion

Pseudomonas aeruginosa is a ubiquitous organism which has been associated with hospital and community acquired infections. It is found in moist environments such as soil, water, and colonises indwelling devices such as urinary catheters, peritoneal dialysis tubing, endotracheal tubes and intravascular catheters (de Latorre *et al*, 1995). The organism is an opportunist remaining in these humid sites and initiating infections when the host resistance is lowered. Patients at risk of *Pseudomonas* sp. infections include those with cystic fibrosis, chronic debility, indwelling devices, skin burns and previous antibiotic therapy. This Gram negative bacillus has gained increasing importance as a multiple antibiotic resistant organism since the 1970s. It is being increasingly implicated in infections of the neutropenic patient (Morrison and Wenzel, 1984).

The patient presented had sustained primarily an infection focused around the subglottis which slowly spread to involve the lung and supraglottis. The patient may have sustained lung injury from previous chest infections allowing for pseudomonas colonisation akin to that seen in cystic fibrosis patients who not only have lung injury but are also on antibiotic prophylaxis. HIV-infected patients have been found in increasing numbers to be contracting lower respiratory tract infections by this agent (Kielhofner *et al.*, 1992). The cases of community acquired pseudomonas infection in HIV positive and AIDS patients appears to be related to neutropenia and depressed CD4 counts, these risk factors and those common to cystic fibrosis patients were manifest by the patient in this report. However, in a study by Baron and Hollander (1993), not all patients exhibited neutropenia, low CD4 counts nor have AIDS, though pseudomonas infection rates were most common when these conditions prevailed. They suggest that prolonged survival in the face of severe immunosuppression may select this group of organisms (Baron and Hollander, 1993).

Unusual sites in the respiratory tract for infection with *Pseudomonas spp.* include the supraglottis, epiglottittis, pharyngeal cellulitis and sinusitis (Lacroix *et al.*, 1988; Connolly *et al.*, 1992; Mendelson *et al.*, 1994). The case described is unique in that *Pseudomonas aeruginosa* affected the subglottis causing stenosis. A retrospective study conducted by Mendelson and colleagues reported a higher mortality rate for patients with upper respiratory tract infections of 75 per cent compared to a figure of 33.3 per cent for pseudomonal pneumonia (Mendelson *et al.*, 1994). Hence these patients require early diagnosis and prompt treatment.

Microbiological swabs are useful in diagnosing *Pseudomonas aeruginosa* infection although in this case the organism was isolated late in the infection. The infection had spread from the subglottis and trachea to include the lungs as well as the supraglottis as revealed by postmortem examination. Late nasendoscopic examination of the larynx revealed supraglottic swelling and a postmortem examination revealed ulceration of this site. This developed late in the progression of this patient's illness and may explain the delay in isolating *Pseudomonas* spp. from the oropharyngeal swab. With the aid of a computer generated list we reviewed the results of isolates from throat swabs in HIV positive patients treated as both in-patient and out-patients at the HIV Infectious Diseases Unit of St Mary's Hospital. In our analysis, a total of 396 swabs were sent for culture in the last two years, of these 98 swabs yielded growth of organisms but only one throat swab (that from this patient) was positive for *Pseudomonas aeruginosa.* This suggests that *Pseudomonas aeruginosa* does not appear to colonise the pharynx in these patients despite immunosuppression and antibiotic prophylaxis. A review of the literature revealed that delays in diagnosis of up to eight days may occur for pseudomonal pneumonia (Schuster and Norris, 1994) and sputum analysis did not always yield *P. aeruginosa* (Kielhofner *et al.*, 1992). The diagnosis may be facilitated by the use of fibreoptic bronchoscopy, bronchoalveolar lavage, or bronchial brushings, as they are capable of diagnosing pseudomonas pulmonary infection when sputum culture remains negative (Schuster and Norris, 1994; Doyle *et al.*, 1995; Taylor *et al.*, 1995). On the rare occasions when these techniques fail to diagnose *P. aeruginosa* pneumonia an open lung biopsy may be necessary (Miller *et al.*, 1995). However, our patient deteriorated rapidly and was unfit to undergo further investigations such as flexible bronchoscopy. The patient developed abnormalities on the chest radiograph late in the illness. The appearances of basal shadowing and interstitial opacification have been reported in cases of pseudomonas pneumonia together with other changes such as cavitation, and bronchial wall thickening, but these are not diagnostic for this condition alone (Ali *et al.*, 1995).

Patients infected by *Pseudomonas aeruginosa* were found to have a poor life expectancy especially if the initial treatment was inappropriate to the sensitivity of the organism. Patients were severe infections, such as bacteraemia had a particularly high mortality despite appropriate antibiotic therapy usage throughout the course of the illness (Shepp *et al.*, 1994). When initial therapy was inappropriate for the organism's antibiotic sensitivity and later changed to appropriate antibiotics the mortality remained higher than those treated appropriately throughout the illness. However, a number of cases were reported as responding poorly to antibiotics which appeared to be appropriate to the sensitivity of the organism. This failure was in part due to monotherapy, in those patients treated with multiple antibiotic therapy, a smaller proportion of patients died. (Kielhofner *et al.*, 1992; Mendelson *et al.*, 1994; Shepp *et al.*, 1994). In the case presented, the *in vitro* studies suggested that the organism was responsive to ciprofloxacin the anti-microbial agent initially utilised in treating his condition. Further treatment was limited by multiple antibiotic allergy. However, combination therapy including a third generation cephalosporin failed to halt the progression of the infection.

The failure of treatment with combination therapy suggests that there was a deficit of the mechanisms for

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clearance of the infection and virulence factors of the organism not reflected by *in vitro* studies. The bacterial wall has a thick lipopolysaccharide layer and narrowed pore openings (porins) which resist penetration of antibiotic agents. The bacterium can also produce beta-lactamase enzymes (Morrison and Wenzel, 1984). Type-specific antibodies for the lipopolysaccharide layer may opsonize this layer facilitating the neutrophil-mediated attack on the organism. However, immunoglobulin production relies on T-lymphocyte helper cells, whose numbers are reflected by the CD4 count, which was low in this case.

Conclusion

Pseudomonas infections are increasingly common in HIV positive AIDS patients. They may be difficult to treat because of the organism's virulence as well as host immunodeficiency. The infection may present at unusual sites such as the subglottis. A high index of suspicion together with frequent microbiological sampling may yield *Pseudomonas aeruginosa* and lead to the diagnosis.

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