Fatal neonatal meningitis and ventriculitis caused by multiresistant *Achromobacter xylosoxidans*

A case report

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Summary

Meningitis and ventriculitis in a 6-day-old neonate caused by a Gram-negative glucose-non-fermenting organism, *Achromobacter xylosoxidans*, was resistant to most antibiotics except ceftazidime and imipenem. The organism became resistant after 28 days' treatment with ceftazidime. When the infant was 7 weeks old, imipenem became available but, in spite of 3 days of intravenous treatment, the organism was still recovered from ventricular cerebrospinal fluid and the child died. This would appear to be only the second report of neonatal meningitis caused by this organism.

*A. xylosoxidans*, a non-fermenting Gram-negative peritrichous rod, was named and described by Yabuuchi and Ohyama in 1971, who isolated it from ear discharges of 7 patients with chronic otitis media. In 1974, they described in detail the characteristics of 55 strains (including the original 7) of this organism and demonstrated the uniformity of the species. *A. xylosoxidans* has been isolated from many clinical sources including blood, urine, wounds, sputa, ear discharge and lungs. Although many isolates of *A. xylosoxidans* are colonisers, some are clinically significant. *A. xylosoxidans* has also been isolated from cerebrospinal fluid and has been associated with meningitis and ventriculitis.

In 1971, Sindhu reported 3 cases of neonatal meningitis caused by an organism described as *Achromobacter* species, but no characteristics of the species were described. A year later Lee and Tan reported 3 similar cases attributed to *Achromobacter* species but they also described no characteristics. Since no proper definition of the genus *Achromobacter* existed at that time, no characteristics of the organism were described, and the fact that these authors would not then have seen a description of *A. xylosoxidans*, there is no evidence that the species mentioned in their reports was *A. xylosoxidans*. The first report of a case of meningitis caused by *A. xylosoxidans* was in 1974 in a 9-year-old girl. Six cases of cerebral ventriculitis caused by nosocomially acquired *A. xylosoxidans* infection were reported in 1978. The first case of neonatal meningitis caused by this organism was reported in 1985.

The second known case of neonatal meningitis definitely caused by *A. xylosoxidans* is described.

Case report

A 6-day-old female infant (birth weight 3500 g), born normally at a clinic, presented to hospital with fever, stiffness of the body and poor sucking of a day's duration. The child was pyrexial (temperature £90°C), mildly jaundiced, very irritable, jittery, hypertonic and hyperreflexic. The anterior fontanelle was normotensive. The Moro reflex was absent. The head circumference was 37.3 cm. The haemoglobin level was 17.7 g/dl, leucocyte count was 10.9 x 10⁹/l and platelet count was 148 x 10⁹/l. The serum urea value and electrolytes were normal. A lumbar puncture produced a drop of thick yellow cerebrospinal fluid and simultaneous Bactec radiometric, aerobic and anaerobic blood cultures were taken. The child was started on intravenous cefotaxime and oral phenobarbitone. From the blood sample tested aerobically, oxidase-positive, motile Gram-negative bacilli were cultured. Since this organism was glucose non-fermenting, it was identified by the Analytical Profile Index 20 NE system and other biochemical tests including xylose oxidation and Christensen's urea agar tests, and flagella staining, as *A. xylosoxidans*. On antibiotic disc diffusion susceptibility testing, the *A. xylosoxidans* was resistant to ampicillin, carbenicillin, tetracycline, co-trimoxazole chloramphenicol, gentamicin, netilmicin, tobramycin, amikacin, cephalothin, cefamandole, cefuroxime, cefotaxime, piperacillin and initially sensitive to ceftazidime. The therapeutic bio was changed to ceftazidime 100 mg/kg/d after obtaining sensitivities (on day 4 after admission). Repeated attempts at lumbar puncture failed. The initial lumbar cerebrospinal fluid was not cultured.

On the 2nd day of treatment with ceftazidime, the child developed apnoeic spells and became hypotonic. The head circumference had increased to 40 cm with suture diastases. Computed tomography confirmed a communicating hydrocephalus with ventriculitis. The neurosurgical decision was to manage the patient conservatively.

After 5 days on ceftazidime the patient's temperature settled. A lumbar puncture done on the 14th day of ceftazidime treatment contained 1250 polymorphs, 210 erythrocytes, no lymphocytes, chloride 109 mmol/l. No organism was isolated. The head circumference increased progressively and a ventricular tap on the same day revealed 576 polymorphs, 30 lymphocytes, protein 3.85 g/l, globulin 2+, chloride 106 mmol/l, sugar 0.6 mmol/l. No organism was isolated. Ceftazidime was continued for 21 days, after which a lumbar puncture revealed 50 polymorphs, 6 lymphocytes, total protein 4.48 g/l, globulin 2+, chloride 114 mmol/l, sugar 0.7 mmol/l. No organism was isolated. Ventricular CSF obtained simultaneously revealed 80 polymorphs, 4 lymphocytes, protein 4.48 g/l, globulin 2+, chloride 114 mmol/l, sugar 0.7 mmol/l and growth of *A. xylosoxidans* that was of intermediate sensitivity to ceftazidime and sensitive only to imipenem (which at the time was an unregistered antibiotic in the RSA and undergoing trials). Repeat ventricular tap the next day also grew *A. xylosoxidans*, which at first was thought to be sensitive.
only to chloramphenicol (because of the slow growth of the organism), but on further testing was found to be resistant.

In view of the unavailability of imipenem and the initial microbiological sensitivity report the infant was started on oral chloramphenicol (25 mg/kg/d). The child had remained apyretal. The ventricular tap was repeated on day 38 and daily thereafter (to reduce cerebrospinal fluid pressure) and the cerebrospinal fluid grew A. xylosoxidans, which was sensitive only to imipenem and resistant to other antibiotics. Using the tube broth dilution method, minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) were done on A. xylosoxidans isolated from ventricular fluid, for chloramphenicol, amikacin, cefotaxime, ceftazidime and imipenem (Table I). In view of the high MIC and MBC indicating resistance to chloramphenicol and ceftazidime and the unavailability of imipenem we continued with chloramphenicol.

On the 43rd day after admission we obtained imipenem (by special permission of the Medicines Control Council). Despite 3 full days of intravenous imipenem (100 mg/kg/d) the organism was still isolated from the ventricular fluid, but was sensitive to imipenem. The child died 3 days after starting imipenem. No immunological studies were done.

**TABLE I. MINIMUM INHIBITORY AND MINIMUM BACTERICIDAL CONCENTRATIONS FOR A. XYLOSOXIDANS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>MIC (µg/ml)</th>
<th>MBC (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloramphenicol</td>
<td>64</td>
<td>&gt;256</td>
</tr>
<tr>
<td>Amikacin</td>
<td>128</td>
<td>&gt;256</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>&gt;256</td>
<td>&gt;256</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>64</td>
<td>256</td>
</tr>
<tr>
<td>Imipenem</td>
<td>2</td>
<td>64</td>
</tr>
</tbody>
</table>

**Discussion**

There are many similarities in the patient described by Namnyak et al. (1985) and our patient. Both developed A. xylosoxidans meningitis without having undergone any neurosurgical procedures. This is in contrast with the patient described by Shigeta et al. (1985), who developed A. xylosoxidans meningitis on two occasions after a ventriculoperitoneal shunt had been created. The patient described by Namnyak et al. (1985) and our patient are the only documented cases of neonatal meningitis caused by A. xylosoxidans. The only other case of A. xylosoxidans meningitis, that described by Shigeta et al. (1985), was in a 9-year-old girl. Namnyak et al. (1985) patient and our patient both initially responded to antimicrobial therapy but subsequently developed hydrocephalus and ventriculitis unresponsive to antimicrobial therapy. A. xylosoxidans was grown from the ventricular fluid of our patient despite 3 full days of imipenem therapy. This was probably because there was insufficient imipenem in the ventricular cerebrospinal fluid. Since imipenem is known to cross the blood-brain barrier well, the reason for the poor concentration was probably a dilutional effect because of the gross ventricular dilatation or because of the presence of purulent material in the ventricle. The same experience was encountered with Namnyak et al. (1985) patient in whom, despite heavy doses of ceftriaxone to which A. xylosoxidans was sensitive, the cerebrospinal fluid still yielded a heavy growth of the organism 41 days after admission to hospital. It seems therefore that a communicating hydrocephalus is a characteristic accompaniment of A. xylosoxidans meningitis and so intraventricular antibiotics would be more appropriate for obtaining adequate cerebrospinal fluid drug concentrations. The patient described by Namnyak et al. (1985) was a premature infant, whereas our patient was full-term. Why these neonates developed A. xylosoxidans meningitis is not clear, although their relative immunodeficiency may have rendered them more susceptible. A. xylosoxidans has been well described as a causative infective agent in immunocompromised individuals.

The genus *Achromobacter* is used to describe glucose-negative fermenting Gram-negative peritrichous flagellated rods that are oxidase-positive, attack carbohydrates aerobically, and do not produce 3-ketolactose from lactose. (1985) The natural habitat of *Achromobacter* species has not been established, but an aseptic environment has been suggested. The organism has been isolated from a swimming pool, dialysis fluids, distilled, de-ionised and tap water, respirators and humidifiers, chloride solutions and incubators. Several publications have reported the isolation of A. xylosoxidans from humans. It has been suggested by Tatum et al. that A. xylosoxidans can be found in normal stools. Thus, although many isolates of the organism are colonisers, some are clearly significant. The patient described above probably acquired his organism from the clinic where he was born. The organism isolated from the blood on admission to hospital was sensitive to ceftazidime but that grown from ventricular fluid on day 20 was of intermediate sensitivity, and that grown from ventricular cerebrospinal fluid on day 28 was resistant. It seems unlikely that a different strain of A. xylosoxidans was introduced into the ventricular cerebrospinal fluid during the first ventricular tap. It appears more likely that the organism developed resistance to ceftazidime.

From our experience and from that of others, it is evident that A. xylosoxidans is resistant to most antibiotics. The MIC and MBC for imipenem was 2 g/ml and 64 g/ml respectively. It seems that imipenem has good *in vitro* activity against A. xylosoxidans. Imipenem is thus far the broadest spectrum antibiotic known. It has demonstrated efficacy against many infections caused by aerobic, anaerobic Gram-positive and Gram-negative bacteria resistant to ceftazidime, ceftriaxone, and aminoglycosides. However, efficacy and tolerability in infants and children has not been established. Further studies need to elucidate its safety in the paediatric age group.

We wish to thank Professor P. Folb of the Medicines Control Council for permission to use imipenem in this patient, Merck, Sharp & Dohme for supplying imipenem and V. Nombath, N. Pillay and Z. Solwa for technical assistance.

**REFERENCES**

Left ventricular myxoma

A case report

A. C. OTTO, J. HOUGH

Summary

A 27-year-old woman with a systolic ejection murmur caused by a left ventricular myxoma is described. The diagnosis of this potential fatal condition was made by echocardiography. The clinical differences between atrial and left ventricular myxoma are discussed.

Myxomas are the most common type of primary cardiac tumour, comprising 30 - 50% of the total in most series describing the pathological features of heart tumours. Yet the incidence of primary cardiac neoplasms remains low. Over 90% of myxomas occur in the atria with 3 - 4 times as many occurring on the left as on the right.1 Involvement of the ventricular cavities are rare and only 17 cases of left ventricular myxoma had been reported up to 1986.2 A case of a relatively asymptomatic young woman, who was referred to hospital with a systolic ejection murmur detected by routine examination and who turned out to have a large left ventricular myxoma, is reported.

Case report

A 27-year-old woman was referred to cardiology outpatients at Pelonomi Hospital by her general practitioner because of a systolic ejection murmur. She denied any cardiovascular symptoms and had only nonspecific and vague complaints of fatigue and headache for 3 years. There was no previous history of serious disease or operations. She was not taking any medication. Although married, she had no children.

Physical examination revealed a patient in good general condition. The body hair was quite prominent but with normal distribution. There were no specific signs of systemic embolism. The patient was normotensive with a systemic blood pressure of 120/80 mmHg and in sinus rhythm with pulse rate of 70/min. Cardiovascular examination revealed no clinical signs of cardiomegaly or cardiac failure. The heart sounds were normal but a systolic thrill was present. A grade 4 systolic ejection murmur was present over the aortic area but did not radiate. The intensity of this murmur decreased with deep inspiration and was clinically suggestive of aortic stenosis. Examination of the other systems revealed nothing abnormal.

Special investigations included biochemical screening and ECG, which were both within normal limits. The full blood count showed a leucocyte count of 5,91 × 10⁹/L with a normal distribution. The haemoglobin concentration was 13,7 g/dl and the erythrocyte sedimentation rate was 22 mm/1st h (Westergren).

The diagnosis of a left ventricular myxoma was made by M-mode and two-dimensional echocardiography. The myxoma was situated on the interventricular septum, anterior and inferior to the anterior mitral leaflet and was partially ejected through the aortic valve in systole (Fig. 1). The tumour was also demonstrated by a left ventricular angiogram from the