Case report

Fatal *Listeria monocytogenes* meningitis in two previously healthy adults

A C Uprichard, Kathleen R Logan

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Two patients, previously healthy, presented with *Listeria monocytogenes* meningitis within nine months of each other to a district general hospital with a catchment population of 85,000. Early disturbances of consciousness, with haematuria, proteinuria and minimal signs of meningism were similar in each. Neither responded to recommended antibiotic therapy and both died. The serological types were dissimilar. Epidemiological studies in the second case failed to identify a source of infection.

CASE ONE

A 74-year-old builder was admitted on 24 October 1982, in a semiconscious state. Headache, myalgia and fever the previous day had been attributed to a viral illness, but on the morning of admission he was found unrousable in bed having been incontinent. His only past history was of surgery for duodenal ulceration in 1968. He had a pyrexia of 39.5°C and was moving all limbs purposefully to pain. There were no localising neurological signs. Pulse 80/minute, blood pressure 160/90 mmHg, fundoscopy revealed no abnormality. He had minimal neck stiffness but Kernig's sign was negative and he had no photophobia. There were no chest signs and the abdomen was soft. Urinalysis showed moderate haematuria and proteinuria but no pus cells and sterile on culture. Haemoglobin was 15.4 g/dl, white cells 14.6 (a differential count was not done), blood urea 7.7 mmol/l, chest X-ray moderate cardiomegaly with clear lung fields.

By the following morning he had deteriorated, with a fall in the level of consciousness and increased neck stiffness. Lumbar puncture revealed cloudy fluid, pressure 24 cm. Pyogenic meningitis was confirmed: CSF protein 3.75 g/l (normal value 0.15 – 0.45 g/l), glucose 0.85 mmol/l, (plasma glucose 10.5 mmol/l), 76 leucocytes/μl (70% polymorphs). No organism was isolated for two days but empirical therapy was started 24 hours after admission with intravenous benzylpenicillin, 12g/day, chloramphenicol, 3.6g/day, and sulphadimidine, 4g/day. Forty-eight hours after admission, due to the persisting pyrexia (39.5°C), therapy was changed to ampicillin, 8g/day, erythromycin, 2.4g/day, and, for 24 hours only (because of deteriorating renal function), netilmicin.
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450 mg/day. He initially showed some improvement: his pyrexia fell slowly over the succeeding 48 hours and he was able to answer questions. The following day, five days after the onset, he became apnoeic with fixed dilated pupils and unrecordable blood pressure and died despite resuscitative attempts. There was no post-mortem. Subsequent bacteriological investigations identified the organism as Listeria monocytogenes serotype IV.

CASE TWO

A 53-year-old farmer’s wife was admitted on 15 July 1983, in a barely rousable state. She had been weak for two days with severe dizziness and nausea on standing and presented with a 24-hour history of increasing drowsiness, headache and restlessness. Her only past history was of joint pains since 1978, but rheumatoid serology was negative. She had been treated with phenylbutazone but never with corticosteroids. She kept a cow and drank unpasteurised milk. She had a pyrexia of 38°C. She was restless and responded only to pain. There were no localising neurological signs. Pulse rate was 80/minute, blood pressure 110/70; fundoscopy revealed no abnormality. There was ill-defined right hypochondrial pain but no organomegaly or peritonism. The chest was clear. Urinalysis showed marked haematuria and minimal proteinuria. Haemoglobin was 10.1 g/dl, white cells 12.7 (no differential), blood urea 6.2 mmol/l. AST was 251 U/l (normal range 2–35) but other liver function tests were normal. On admission there was no neck stiffness and Kernig’s sign was negative, but these developed over the next four hours. Lumbar puncture then revealed cloudy fluid (pressure not recorded). Protein was recorded as 5.4 g/l, glucose 0 mmol/l, leucocytes 250/μl, mainly polymorphs.

Empirical therapy was started with benzylpenicillin, 12g/day, chloramphenicol, 3.6g/day, and sulphadimidine, 4g/day, and continued for 12 hours until an organism was grown (although not identified), with sensitivities to gentamicin, co-trimoxazole, ampicillin and erythromycin. Then, 20 hours after admission, therapy was changed to ampicillin, 10g/day and co-trimoxazole, 6.4g/day, both intravenously. Later that day Listeria monocytogenes was isolated both from CSF and blood culture. She began having generalised tonic-clonic convulsions and short periods of apnoea within 11 hours of admission. The pyrexia persisted. Conjunctival oedema, which developed on the day after admission, became progressively worse. She died after four days, never having regained consciousness. There was no post-mortem. The organism was identified as Listeria monocytogenes, serotype I.

Environmental veterinary studies were subsequently carried out on the beef cattle and milking cow on the farm. No sheep were kept and no silage was available for study. No illness was detected and Listeria monocytogenes could not be isolated from the animals, the environment or the milk.

DISCUSSION

Listeria monocytogenes is a gram-positive bacillus capable of producing a spectrum of disease in man of which meningitis is the most common.\textsuperscript{1} Although rare, it has been reported with increasing frequency in recent years, probably because of greater awareness of its potential pathogenicity.\textsuperscript{1,2} It has a wide range of hosts including mammals, birds and fish, but no constant link has been found between animals and man.\textsuperscript{3} Unpasteurised milk has been implicated as a source of human infection\textsuperscript{4} and asymptomatic carriers described.\textsuperscript{5}
Listeria monocytogenes meningitis has been found to occur more often in neonates\(^2\) and in immunosuppressed patients.\(^1,6\) The latter commonly include patients with chronic renal disease both on dialysis and post-transplant.\(^1\) Underlying malignancy, connective tissue diseases and alcoholism are also predisposing factors.\(^1,2,3,7,8\) Age (50 and over) may be the only apparent risk factor.\(^2,6,7\)

Listeria monocytogenes meningitis is a rare condition with 49 reported cases in adults in the UK during the period 1982/83 (unpublished: PHLS Communicable Disease Surveillance Centre; Communicable Diseases (Scotland) Unit). These include three adults from Northern Ireland. The UK figures do not accurately separate previously healthy adults, but our two patients had no identifiable risk factor except age. It must be considered as a possible cause of purulent meningitis especially when acute disturbance of consciousness and mild meningeal signs are the presenting features, and also when the CSF suggests a purulent meningitis but no organism is immediately identified. In one study, no organism was seen on gram stain of the admission CSF in 19 out of 25 patients.\(^8\) The CSF examination in Case 1 was delayed because of the paucity of meningeal signs. This is well recognised. In a study of 40 cases, signs of meningeal irritation on admission were questionable in seven and absent in three.\(^7\)

Our mortality is higher than that reported: 46 per cent in the over-50 age group.\(^8\) 13 per cent in adults without underlying disease\(^1\) and 20 per cent in the over-50 age group without underlying disease.\(^2\) Our experience with antibiotic therapy in these two cases is similarly at variance with the literature. It has been suggested that ampicillin alone is adequate.\(^6,8\) Chloramphenicol has been advocated\(^8\) although others found it either ineffective,\(^2,9\) or associated with an increased mortality.\(^6\) Other reports suggest that additional aminoglycosides improve survival,\(^8,9\) and synergy has been observed in vitro using ampicillin with an aminoglycoside.\(^10,11\)

The organism is ubiquitous; its ability to survive is well known (several months in moist soil), as is its lack of consistent route of entry or mode of transmission.\(^3,5\) Most cases are reported from urban areas in the United States, whilst in Europe rural cases are more prevalent. Our epidemiological study in Case 2 failed to show either illness or a carrier state in the stock. Neither was Listeria monocytogenes isolated from milk samples or the environment. The different serotypes described suggest that chance and not a reservoir of infection resulted in these two cases of a rare and virulent infection.

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REFERENCES
1. Nieman RE, Lorber B. Listeriosis in adults: a changing pattern. Report of eight cases and review of the literature, 1968-1978. Rev Infect Dis 1980; 2: 207-27.
2. Busch LA. Human Listeriosis in the United States 1967-1969. J Infect Dis 1971; 123: 328-32.
3. Kalis P, Le Frock J, Smith W, Keefe M. Listeriosis. Am J Med Sci 1976; 271: 159.

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4. Sielaff H. The significance of Listeriosis in food hygiene. *Proc 3rd Int Symp on Listeriosis* 1966: 283-90.
5. Gray ML, Killinger LH. *Listeria monocytogenes* and Listeric infection. *Bact Rev* 1966; 30: 309-86.
6. Cherubin LE, Marr JS, Sierra MF, Becker S. Listeria and gram negative bacillary meningitis in N.Y. City 1972-1979. Frequent cause of meningitis in adults. *Am J Med* 1981; 71: 199-209.
7. Bouvet E, Suter F, Gilbert C, Witchitz JL, Bazin C, Bachon F. Severe meningitis due to *Listeria monocytogenes*: a review of 40 cases in adults. *Scand J Infect Dis* 1982; 14: 267-70.
8. Lavetter A, Leedom JA, Mathies AW, Ivler O, Wehrle PF. Meningitis due to *Listeria monocytogenes*. *New Engl J Med* 1971; 285: 598-603.
9. Stamm AM. Chloramphenicol: ineffective for treatment of Listeria meningitis (letter). *Am J Med* 1982; 72: 830.
10. Moellering P, Medoff G, Leech I, Wennersten C, Kunz LJ. Antibiotic synergism against *Listeria monocytogenes*. *Antimicrob Agents Chemother* 1972; 1: 30-4.
11. Trautmann M, Wagner J, Chahin M, Weinke T. Listeria meningitis: report of 10 recent cases and review of current therapeutic recommendations. *J Infect* 1985; 10: 107-14.

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