

Listeria meningitis presenting in an immunocompetent adult patient

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A case of fatal *Listeria meningitis* in an immunocompetent 39-year-old female is presented. Although most patients with CNS listeriosis are immunosuppressed, infection in immunocompetent individuals may also occur.

The possibility of listeriosis should be considered in all patients presenting with evidence of CNS infection, particularly if there is an unusual CSF picture. The immediate antibiotic treatment

should include ampicillin plus gentamicin; third generation cephalosporins do not cover the organism.

DISCUSSION

Listeria monocytogenes is a Gram positive rod, first recognized as infecting humans by Nyfeldt in 1929. Indirect transmission through contaminated food products has been clearly implicated in epidemic listeriosis, although

the mode of transmission in sporadic cases, which account for the majority of cases of human infection, is less clear. Possible means include a food-borne inoculum affecting an immunocompromised host or invasive infection developing in asymptomatic carriers when they become immunosuppressed.

Direct transmission from animals to man has occasionally been documented in veterinarians, abattoir workers and farmers. Person to person spread is thought to be rare, except from mother to fetus. Of healthy humans, 1–5% carry *Listeria* in the gut and it is therefore likely that the majority of persons exposed to *Listeria* do not develop symptoms.

CASE REPORT

A 39-year-old female was brought to hospital after neighbours heard her falling repeatedly in her flat. She lived alone and had last been seen 24 hours before admission by neighbours when she had complained of headache and was noted to be mildly confused. She was previously fit and well with no significant past medical history. She was not taking any regular medication.

On examination, she had a pyrexia of 39°C. There was no rash. Apart from a tachycardia, there were no abnormal signs in the cardiovascular, respiratory or abdominal systems. On CNS examination she was alert but profoundly confused with a mental test score of 0/10. There was mild nuchal rigidity but no photophobia. Cranial nerve examination revealed bilateral sixth nerve palsies. Pupils were equal and reacting to light. Fundi were normal. Examination of the peripheral nervous system was normal. Full blood screen was normal apart from a sodium concentration of 129 mmol/litre and a leucocytosis of 14.2×10^9 /litre (neutrophils 9.20×10^9 /litre, monocytes 2.80×10^9 /litre). Chest X-ray and electrocardiography were normal.

The clinical impression was of a meningoencephalitis. Blood cultures were drawn and intravenous cefotaxime started. A computed tomography scan of the brain was normal. Lumbar puncture showed clear and colourless CSF at raised pressure (21 cmH₂O). CSF analysis showed: 160 white blood cells/mm³ (80% lymphocytes, 20% neutrophils); protein: 2.59 g/litre; glucose: 0.8 mmol/litre (blood glucose: 4.5 mmol/litre); Gram and Ziehl–Nielsen stain: negative.

In view of the unusual CSF picture with clinical evidence of brainstem involvement the patient was treated with intravenous ampicillin, cefotaxime, gentamicin, acyclovir and quadruple antituberculous therapy to cover the possibilities of bacterial (including *Listeria*) and tuberculous meningitis and herpes simplex encephalitis. The change from cefotaxime monotherapy was made approximately 6 hours after admission.

Three hours after the lumbar puncture the patient became obtunded and suffered a respiratory arrest. She was intubated and ventilated. The left pupil was noted to be fixed and dilated. In spite of full intensive care support the patient showed no sign of recovery. She subsequently developed bilateral fixed unreactive pupils and died 3 days after admission.

Listeria monocytogenes was cultured from the CSF, 24 hours before death. Antibiotic treatment was continued with high dose ampicillin and gentamicin (the organism subsequently proved to be sensitive to both). Blood cultures were sterile.

At autopsy the brain was swollen, soft, hardened poorly in formalin and had lost the distinction between grey and white matter: changes typical of ventilation following brain death. Microscopic examination revealed an additional widespread predominantly lymphocytic leptomeningitis, most severe in the medulla where there was also subependymal and vascular necrosis, choroid plexitis and cuffs of lymphocytes surrounding deeply penetrated vessels. There were no microabscesses, viral inclusions or identifiable organisms (Figure 1). There were no significant extracranial findings and, in particular, no evidence of occult neoplasm.

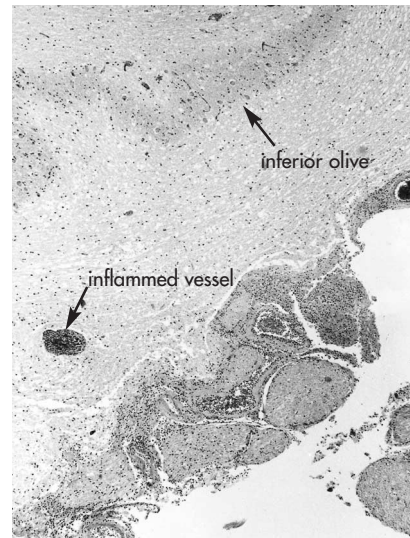


Figure 1. Low power photomicrograph of the inferolateral medulla, showing inflammatory infiltrate in relation to the XII cranial nerve and an engorged parenchymal vessel (haematoxylin and eosin stain).

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Listeriosis currently affects around 100 people each year in the UK (Communicable Disease Report, 1997). The incidence has fallen in recent years following government health warnings pertaining to the consumption of various foods such as soft cheeses and pate.

Pregnant women account for about one-third of cases in the UK. Others classically affected are those at the extremes of age and immunosuppressed adults. Excluding pregnant women, 70% of adult cases have clear predisposing factors such as immunodeficiency (including AIDS), neoplasia (particularly haematological), or treatment with immunosuppressant therapy (Barza, 1985; Lorber, 1997). Other conditions associated with an increased incidence of listeriosis include diabetes, chronic renal or liver disease, alcoholism and conditions associated with iron overload.

In pregnancy *Listeria* causes mild maternal disease (most commonly a mild 'flu-like' illness: CNS involvement is extremely rare), although it may cross the placenta causing fetal loss, perinatal meningitis or septicaemia.

In non-pregnant adults, *Listeria* most commonly presents as CNS infection, accounting for 60% of cases (Sen, 1987). Other modes of presentation include septicaemia or endocarditis, and, less commonly, pneumonia, hepatitis and peritonitis. There is recent evidence that it may present as a gastroenteric illness (Dalton et al, 1997).

Ninety per cent of cases of CNS listeriosis present as a meningitis (Pollock et al, 1984). Non-meningitic presentations include encephalitis (classically affecting the brainstem: the 'rhombencephalitis syndrome'), cerebritis and abscesses affecting the cortex, brainstem or spinal cord. Listeriosis is the fourth commonest cause of bacterial meningitis in adults, accounting for 1–2% of cases (Barza, 1985), although it is the commonest cause of bacterial meningitis in patients with cancer (Nieman and Lorber, 1980).

Few clinical features set *Listeria* meningitis apart from other causes of bacterial meningitis, although movement disorders such as ataxia and tremor are said to be prominent features (Nieman and Lorber, 1980). The

tropism of *Listeria* for the brain parenchyma (particularly the brainstem) as well as the meninges is of interest, and is not seen with the other common causes of bacterial meningitis.

CSF findings are variable. A predominance of neutrophils is seen in 70% of cases, although a predominance of lymphocytes may occur or a mixture of both. CSF glucose is low in only 40% of cases and Gram stain negative in 60% (Nieman and Lorber, 1980). Protein is usually elevated. It is notable that low CSF sugar and positive Gram stain occur less frequently than with other causes of pyogenic meningitis.

The CSF findings may mimic tuberculous meningitis or viral meningitis/encephalitis: indeed a partial response may be seen with antituberculous drugs as rifampicin has excellent in-vitro activity against *Listeria* but induces only a partial remission (Sen, 1987).

Given the variable CSF findings, blood cultures are an essential part of the diagnostic workup as they are positive in 75% of cases. There has been interest in the use of antibodies against Listeriolysin O in cases where bacteria cannot be isolated, although this technique requires further evaluation before it enters routine clinical practice (Berche et al, 1990). Polymerase chain reaction (PCR) techniques exist but remain a research tool (Jaton et al, 1992).

The average mortality of *Listeria* meningitis is 30% (Nieman and Lorber, 1980), although this is affected by the presence or absence of factors such as underlying malignancy or immunosuppression. Untreated, the mortality approaches 90%. Poor prognostic features include septicaemia, fits and low CSF sugar.

Listeria encephalitis appears to be a separate entity from meningitis with a lower incidence of positive blood cultures, less abnormal CSF and better prognosis. It may represent a modified response to *Listeria*, possibly in patients with previous subclinical exposure (Pollock et al, 1984). *Listeria* rhombencephalitis is a rare entity that appears to affect predominantly immunocompetent individuals. Classically it presents as a biphasic illness with a prodrome of fever, headache and vomiting for

4–10 days followed by progressive brainstem dysfunction.

The treatment of choice for CNS listeriosis is high dose ampicillin plus gentamicin. Treatment should last for 3 weeks in *Listeria* meningitis, although a 6-week course is recommended for brain abscess or rhombencephalitis (Lorber, 1997). Third generation cephalosporins, e.g. cefotaxime, have poor bactericidal activity against *Listeria* and should not be used as monotherapy in meningitis cases where *Listeria* is suspected. A combination of cefotaxime and ampicillin is reasonable initial antibiotic therapy while awaiting cultures in cases of pyogenic meningitis where *Listeria* is suspected. In penicillin allergic individuals, co-trimoxazole is the best alternative (Jones et al, 1997).

CONCLUSIONS

Careful consideration should be given to the possibility of *Listeria* in any patient presenting with meningitis or encephalitis and suspicion should heighten if there are factors causing immunosuppression or underlying neoplasia. This case serves as a reminder that CNS listeriosis can occur in immunocompetent individuals, and is not covered by third generation cephalosporins which are being increasingly used as first-line treatment for pyogenic meningitis. **HM**

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