Reminder of important clinical lesson

High-dose amoxicillin should be included in the empirical treatment of suspected meningitis in patients at risk of HIV infection

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Summary

The authors report on a case of *Listeria rhomboencephalitis* in a previously undiagnosed HIV positive man. This case is of interest as the incidence of *Listeria* has increased dramatically in recent years and so may increase in the HIV-infected population. The organism is inherently resistant to cephalosporin antibiotics, empirically employed in the treatment of central nervous system infections and thus highlights the need to include amoxicillin in meningitis treatment regimes in patients at risk of HIV infection as well as the older and those known to be immunocompromised.

BACKGROUND

This presentation of Listeriosis in a previously undiagnosed HIV-infected individual emphasises the importance of considering *Listeria* meningocerebritis in all potentially immunocompromised hosts with relevant clinical presentations. It also highlights the need to add amoxicillin to empirical treatment regimes for such patients particularly in the context of an increasing incidence of the infection. It also reiterates the need to appropriately test for HIV infection in patients with unusual infectious syndromes and provides reinforcing evidence to the argument for universal HIV testing in acute medical admissions.

CASE PRESENTATION

A 39-year-old UK resident from Uganda who had been found unconscious on the floor, having headache, neck stiffness and fever with increasing confusion for the preceding 4 days. He had no significant medical history. On examination he was febrile (39.8°C) with a stiff neck and a Glasgow coma score (GCS) fluctuating between 11 and 14 but without focal neurology.

INVESTIGATIONS

Blood tests revealed a normocytic anaemia (haemoglobin 11.9 g/dl), white cell count (WCC) of $9.2 \times 10^9/l$ (neutrophilia and lymphopenia) and a C reactive protein of 244 mg/l. A head CT scan revealed no intracranial abnormality and therefore a lumbar puncture was performed with an opening pressure >40 cm H₂O. Cerebrospinal fluid (CSF) analysis revealed a WCC of $2235 \times 10^6/l$ (95% polymorphonuclear cells), protein 5730 mg/l and glucose 1.1 mmol/l (serum glucose 6.5 mmol/l). CSF microscopy revealed no bacteria, acid fast bacilli or encapsulated fungi and a cryptococcal antigen test was negative.

TREATMENT

He was initially empirically treated with intravenous ceftriaxone (2 g twice daily) and acyclovir (10 mg/kg three times a day) before being transferred to an intensive care unit in view of his fluctuating GCS where his antibiotics were changed to intravenous meropenem (2 g three times a day) and amoxicillin (1 g three times a day) with continuation of the aciclovir. He remained febrile and, although his GCS stabilised at 14/15, he developed right-sided VIth and VIIth cranial nerve palsies and ataxia. An HIV test sent on admission was positive and a CD4 count was 3 cells/mm³ and HIV viral load 2265 copies/ml. He was therefore transferred to our specialist HIV Unit (Brighton and Sussex University Hospital). Two days following admission, *Listeria monocytogenes* was cultured from both CSF and blood cultures and his antibiotics were therefore rationalised to intravenous amoxicillin (2 g every 4 h) with gentamicin (1.7 mg/kg three times a day) for the 1st week of a 3 week treatment course.

OUTCOME AND FOLLOW-UP

He made a good recovery with normalised inflammatory markers. At discharge, his cranial nerve palsies had improved though he was left with staccato speech and bilateral finger-nose and gait ataxia. At 6 month follow-up, he was much improved and continued to have physical therapy rehabilitation. He was able to walk unaided but had residual speech difficulties. He was started on tenofovir, emtricitabine and darunivir/ritonovir as initial highly active antiretroviral therapy as an inpatient and at 6 months had made a slow response with CD4 count of 49 cells/mm³ and aviral load of 55 copies/ml. He had a fully sensitive wild-type virus and was therefore switched to tenofovir, emtricitabine and efavirenz (as Atripla).

DISCUSSION

Listeria meningitis is the third most prevalent cause of bacterial meningitis in adults.¹ However, Listeria brainstem encephalitis is a rare disease which characteristically consists of a non-specific prodrome of headache, nausea and fever lasting for several days followed by progressive asymmetrical cranial-nerve palsies, cerebellar signs, hemiparesis or hypaesthesia and impairment of consciousness. It is reported to be an unusual presentation of Listeriosis and carries a poor prognosis, being universally fatal if untreated.² The syndrome of rhombencephalitis is more commonly seen in previously healthy individuals with Listeriosis, which is in contrast to the classical Listeria meningitis which affects primarily the immuno-compromised.

Case series describe Listeriosis in individuals with impaired cellular immunity (eg, attributable to immunosuppressive therapy, immunosenescence, diabetes or malignancies), though cases are relatively rare in HIV patients.³ It is now well acknowledged that the incidence of Listeriosis has increased significantly in recent years, with more than a twofold increase in the number of cases seen between 1990 and 2008 in the UK. It is postulated that this is due to the increasing numbers of older people and immuno-compromised patients in the population.⁴ Interestingly, the risk to HIV patients may be higher in those with a CD4 count >200 cells/mm³ as they are unlikely to be taking prophylactic co-trimoxazole to which the organism is sensitive.⁵

The importance of considering Listeria in empirical treatment regimes is also therefore increasing and the changing epidemiology may herald more cases in HIV-infected individuals. The current British Infection Society guidelines are to add Ampicillin to the empirical treatment of any patient over the age of 55 years presenting with symptoms suggestive of meningism, however only referral for specialist advice is recommended for immunocompromised patients. Listeria are inherently resistant to cephalosporins which are the treatment of choice for suspected bacterial meningitis.⁶ A combination of amoxicillin plus gentamicin has generally been the antibiotic regime of choice though a small study of 22 cases suggests that amoxicillin plus co-trimoxazole may be superior.⁷ We suggest that ampicillin should be used in addition to a cephalosporin in all cases of suspected meningitis in an immuno-compromised patient or patients at risk of immuno-compromise. This case also reiterates the need to appropriately test for HIV infection in patients with unusual infectious syndromes and provides reinforcing

evidence to the argument for universal HIV testing in acute medical admissions.

Learning points

- Listeria meningitis is the third most prevalent cause of bacterial meningitis in adults. It is much more prevalent in the immuno-compromised population with a significant increase in incidence in recent years.
- Listeria brainstem encephalitis is a rare disease which characteristically consists of a non-specific prodrome of headache, nausea, and fever lasting for several days followed by progressive asymmetrical cranial-nerve palsies, cerebellar signs, hemiparesis or hypaesthesia and impairment of consciousness.
- Listeria are inherently resistant to cephalosporins. A combination of amoxicillin plus gentamicin has generally been considered the antibiotic regime of choice and therefore should be used empirically in the treatment of suspected meningitis in the immuno-compromised.
- HIV testing should be considered in all patients presenting with unusual infectious syndromes.

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Patient consent Obtained.

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