Listeria monocytogenes meningitis in adults

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Adult patients with impaired cell-mediated immunity are more prone to *Listeria monocytogenes* (*L. monocytogenes*) meningitis.[1] In contrast to other countries Listeriosis is not frequently reported in Saudi Arabia. This may be related to misidentification of such organism, coupled with a low index of suspicion, as well as poor communication between clinicians and microbiologist. The microbiology database of the University Hospital of King Khalid, Riyadh, Kingdom of Saudi Arabia was searched for cases with *L. monocytogenes* infection between January 2000 and December 2006. *Listeria monocytogenes* meningitis and meningoencephalitis occurred in 3 patients.

The first case was a 51-year-old Saudi male admitted to the accident and emergency department with a one-day history of severe headache and lethargy. He had a history of renal failure secondary to IgA nephropathy since 1998 with recurrent urinary tract infection. One month prior to admission, he was started on prednisolone (20 mg, once daily) and azathioprine (150 mg, once daily) for his deteriorating renal function and increasing proteinuria. On examination, high fever (39.3°C), tachycardia, drowsiness, disorientation, neck stiffness, and an acutely ill appearance were found. A presumptive diagnosis of meningitis was made, blood cultures were obtained, and a lumber puncture was performed. The white blood cell (WBC) count was 5.9 x10^9/L. The urea was 15 mmol/L and creatinine was 278 umol/L. His CT scan was normal. The CSF showed 400 cells/ml with 80% polymorphs and 20% lymphocytes. Protein concentration was 1.14 mg/dl and glucose concentration was 2.4 g/L. A gram stained-smear of the CSF showed gram-positive bacilli and cultures of both blood and CSF grew *L. monocytogenes*. He was treated empirically with ceftriaxone (2 gm intravenous [iv]/12h) and vancomycin (1 gm iv/12h). After culture results, ampicillin (1 gm iv/12h) was started and continued for 3 weeks. His condition steadily improved, and he was discharged free of any symptoms.

The second case was a 52-year-Saudi female presented to the emergency room with a 4-day history of low-grade fever, confusion, visual and auditory hallucinations. Her history was significant for hepatitis C infection and liver cirrhosis diagnosed before 5 years by serological tests and liver biopsy, which revealed portal and lobular inflammation grade 2 and stage 4 liver cirrhosis. Eleven months before admission, she started treatment with pegylated interferon alfa (3MU subcutaneously once a week) and ribavirin (tablets 200 mg twice daily). On examination, she appeared ill, pale, drowsy, disoriented, and had nuchal rigidity. The temperature was 38°C. Lumbar puncture revealed a traumatic CSF and BacT-Alert blood culture bottle after 24 hours incubation disclosed gram-positive bacilli, which was initially though to be diphtheroids. Subculture on blood agar plate grew *L. monocytogenes*. Her MRI evidenced signs of meningitis (**Figure 1**). Since admission patient remained febrile and confused. On day 5, after culture results, ceftriaxone was discontinued and intravenous ampicillin (2 g, 4 hourly) was started. Within 48 hours, she showed extreme improvement in her clinical condition, level of consciousness, and became afebrile. After 22 complete days of therapy, she was discharged in a stable condition.

The third patient was a 23-year-old Saudi male, known case of high-grade malignant melanoma and widespread metastasis. He received multiple courses of radiotherapy and chemotherapy, and was admitted with a 2-day history of fever, vomiting, and diarrhea. On examination he was acutely ill, irritable, and had neck rigidity. His temperature was 38.7°C, heart rate was 110/min, respiratory rate 50/min and blood pressure 156/80 mm Hg. Short generalized tonic colonic convulsion appeared and phenytoin was initiated. Clinical suspicion of bacterial meningitis or brain metastasis was made, blood cultures were obtained, and after attempts to perform a lumbar puncture had failed, ceftazidime (1 g/8 hour) was commenced. His CT brain was normal. Blood culture grew *L. monocytogenes*. Ceftazidime was suspended, and synergistic intravenous ampicillin (2 g/4 hour) and gentamicin (80 mg/8 hour) were started. During the following days, he developed

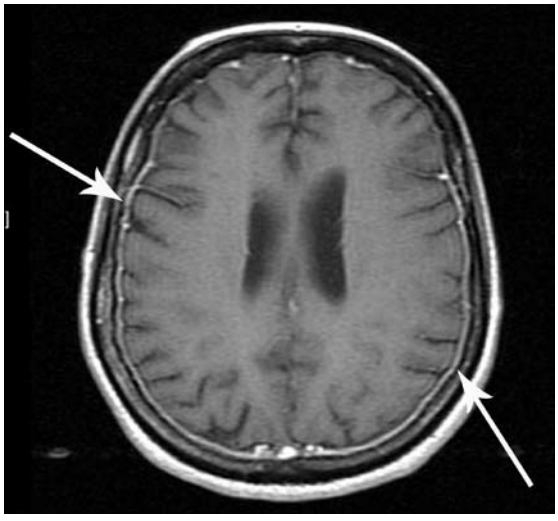

Figure 1 - An MRI brain at different levels showing mild to moderate dural thickening and uniform enhancement all over the cerebral convexity on both sides indicating pachymeningitis.

pulmonary embolism and brain death. He died 10 days after being admitted to our hospital.

Listeria monocytogenes is widespread in nature and has been isolated from the stool of 5% of healthy adults. A variety of foods are contaminated with *L. monocytogenes*. It has been recovered from raw vegetables, raw milk, fish, poultry, soft cheese, and meats at rates ranging from 15-70%.[2] Infection is rare in patients with normal immune status. Most reported cases have been associated with immunosuppression produced by drugs (steroids and cytotoxic drugs), chronic renal disease, diabetes, malignancy, and HIV.[3] Additional groups include neonates, pregnant women, and the elderly. Liver cirrhosis and chronic hepatitis C infection treated by interferon Alfa and Ribavirin have also been implicated as a risk factor.[4] Interferon-alfa and ribavirin are considered to be first line therapy for patients with chronic hepatitis C. The combination has significantly increased the number of patients, with clinical improvement. Both drugs have antiviral and immunomodulatory activity. Interferon-alfa inhibits T cell immunity in several ways. It inhibits interleukin 2 induced proliferation of the peripheral T lymphocyte, inhibits production of interleukin-12, the central immunomodulatory cytokine of the CD-4 T cells, and maintains the survival of anergic CD-T cells.[5] Ribavirin is a nucleoside analogue that may also inhibit proliferation of T cells. The immunosuppressive effect of both drugs is enhanced by their combination.[6] Clinically, Listeria meningitis frequently manifests as a benign illness characterized by a low-grade fever and personality changes. Seizures, both focal and generalized, occur in at least 25% of patients. The diagnosis is based on symptoms and laboratory data. Infection can be confirmed by culture of the CSF and blood. On gram stain, *L. monocytogenes* rods are often mistaken for contaminating diphtheroids accounting for much of the misdiagnosis. Delay in diagnosis and management would increase the risk of complication and death. The case fatality rate can be as high as 30%.[1] Combined synergistic therapy with ampicillin and gentamicin continues to be the treatment of choice. Other options include rifampin and carbapenems.

In conclusion, physicians should always consider *L. monocytogenes* among the possible etiologies of bacterial meningitis in adult immunocompromised patients. A high index of suspicion should be kept if gram-positive bacilli are seen on CSF or when neuralgic deterioration occurs after the first few days of antibiotics. One should at least consider additional treatment of listeria due to poor activity of 3rd generation Cephalosporins against it.

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