

# Nosocomial Meningoencephalitis In Medical Patients

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## Abstract

Nosocomial central nervous system (CNS) infections are rare in the absence of head trauma or neurosurgical interventions which led some investigators to doubt the need for lumbar puncture in hospitalized febrile patients without headache or meningismus. We describe two cases of meningoencephalitis with unusual nosocomial CNS pathogens to emphasize the need for lumbar puncture in making the diagnosis even in the absence of headache and meningismus.

## INTRODUCTION

Fever and mental status changes are commonly seen in hospitalized patients and are rarely due to central nervous system (CNS) infection in the absence of head trauma or neurosurgical interventions. In fact, a recent study found that all 51 lumbar punctures performed to evaluate for nosocomial meningitis were negative, while 14% of those performed for suspected community acquired meningitis were positive. This led to the conclusion that lumbar puncture might not be necessary in low-risk hospitalized patients with fever and mental status changes [1]. We describe two cases of nosocomial meningoencephalitis with unusual pathogens to illustrate the need for cerebrospinal fluid (CSF) sampling in the hospitalized patient with an unexplained fever and mental status change.

## CASE PRESENTATIONS

### CASE 1

A 34-year-old female was transferred to the Intensive Care Unit with acetaminophen overdose. En route, she required intubation because of vomiting and declining mental status. On admission, her acetaminophen level was 452 (g/ml with unclear timing of ingestion. Despite treatment with N-acetylcysteine and activated charcoal, she developed fulminant hepatic failure with her INR peaking at 7.3 (normal 0.9-1.1) on day # 3. The patient was treated with ticarcillin/ clavulanic acid and ciprofloxacin for aspiration pneumonia. Liver function tests improved gradually over the following two weeks. Her mental status improved and she was able to communicate on day # 8. On day # 9, she became febrile (39°C) and unresponsive. She had no signs of meningismus, however. She was started empirically on

ceftriaxone and ampicillin for possible bacterial meningitis. Lumbar puncture (day# 9) showed 545 nucleated cells/(l with 25% neutrophils, 70% lymphocytes and 4% macrophages. Protein level was 42 mg/dl and glucose 35 mg/dl. Serum glucose was 94 mg/dl. Gram stain, bacterial culture, cryptococcal antigen and acid-fast stain were negative. A vesicular skin lesion appeared on the left anterior thigh which was positive by Tzanck smear for multineucleated giant cells, therefore acyclovir was added for presumed herpes encephalitis. Subsequently, herpes simplex virus polymerase chain reaction (PCR) came back positive from the cerebrospinal fluid. Her mental status improved and she was extubated on day #13 and discharged in good condition on day #30.

### CASE 2

A 58-year-old male was hospitalized with two weeks of dyspnea, myalgia, nausea, vomiting and diarrhea. Chest x-ray showed left lower lobe infiltrate. BUN was 104 mg/dl and creatinine 17.5 mg/dl. The patient was treated with ceftriaxone and erythromycin for community acquired pneumonia. Further workup revealed a positive urinary Legionella antigen. His condition improved over the following week. On day # 8, he was noted to be confused and progressively less responsive. His exam revealed 4th cranial nerve palsy but no meningismus. The patient was continued on ceftriaxone for presumed bacterial meningitis. Lumbar puncture, performed on day #9, showed 3500 nucleated cells/(l with 91 % neutrophils and 5% lymphocytes. Protein level was 337 mg/dl and glucose 77 mg/dl. Serum glucose was 102 mg/dl. Gram stain and bacterial culture, cryptococcal antigen, VDRL and acid-fast stain were negative. HIV serology was negative. He required

intubation because of the development of respiratory distress. New bilateral pulmonary infiltrates appeared, and multiple sputum cultures revealed *Aspergillus fumigatus*. MRI of the brain showed slight enhancement around the fourth ventricle, hydrocephalus and maxillary sinus fluid levels. Aspirate of the right maxillary sinus grew *Aspergillus fumigatus*. He was started on Amphotericin B. However, the patient developed respiratory failure, renal failure and septic shock. Blood cultures remained negative. He expired on day # 20. Autopsy showed ventriculitis, meningitis and focal encephalitis with aspergillus invasion. Extensive invasive pulmonary aspergillosis was also seen.

### DISCUSSION

Nosocomial central nervous system (CNS) infections occur in patients who undergo neurosurgical interventions, those with ventricular shunts and those with CSF leak [2]. These infections are usually bacterial with gram-negative bacilli and *Staphylococcus* species being the common pathogens [2]. In nonsurgical patients, nosocomial meningitis is very rare. This lead to questioning the value of lumbar punctures frequently performed on hospitalized medical patients who develop delirium and/or fever. Metersky et al found all 51 lumbar punctures performed for suspected nosocomial meningitis to be negative, while 14% of 181 lumbar punctures done for suspected community-acquired meningitis were abnormal [1]. Patients whose lumbar punctures were positive more often had headache or meningismus than those whose lumbar punctures were negative, and only 11 patients (22%) who had lumbar punctures performed for suspected nosocomial meningitis had headache or meningismus. They suggested that lumbar puncture might not be necessary in low-risk hospitalized patient with fever and mental status changes. Here we described two medical patients who presented with fever and altered mental status without headache or meningismus. Lumbar puncture was abnormal in both cases and diagnostic in one of them (Case 1). The pathogens were nonbacterial in both cases and unusual causes of nosocomial CNS infections.

The first case was of herpes encephalitis. This is the most commonly recognized cause of sporadic encephalitis in the community [3]. Typically, patients present with fever and alteration of mental status. Headache, seizures and personality changes can be present. Examination of the CSF typically reveals a lymphocytic pleocytosis of 5 to 500 cells/mm<sup>3</sup>, a mild to moderate elevation in the protein concentration, and a normal or decreased glucose

concentration [4]. Red blood cells or xanthochromia may be present. Cerebrospinal fluid polymerase chain reaction for HSV DNA is the test of choice for herpes encephalitis. The test has a very high sensitivity (95-98%) [4,5] and specificity (99-100%) [4,6]. A 100% PCR positivity has been reported for the detection of HSV DNA in the CSF of patients who have HSV encephalitis collected within 10 days after onset of symptoms [3]. False positive results are rare [7] and the test is considered diagnostic in patients with clinical presentation consistent with herpes encephalitis [3,4,5,6]. The presentation of herpes encephalitis as nosocomial CNS infection has not been reported before. The CSF findings in our patient were typical of herpes encephalitis. We believe that reactivation of latent herpes infection secondary to hepatic failure was the cause of herpes encephalitis.

The second case was of aspergillus meningitis. This is an extremely rare infection affecting primarily immunocompromized patients, such as bone marrow transplant, renal transplant patients and HIV patients [8,9]. Common clinical features include fever, altered mental status, seizures and focal neurologic deficits [9]. Meningismus and headache are rare. In a series of 17 patients with CNS aspergillosis, Walsh et al found meningeal involvement in 8 patients. Headache and meningismus were noted in only one patient who had a subarchanoid hemorrhage caused by rupture of a mycotic aspergillus aneurysm [9]. Pathologically, the meningeal involvement usually is focal occurring adjacent to regions of cerebral or cerebellar aspergillus infection [9]. The disease can affect the ventricles leading to hydrocephalus [10]. Cerebrospinal fluid findings include pleocytosis with both lymphocyte [9] and neutrophil [11,12] predominance reported. Low glucose and high protein have also been described. Culture of the organism from CSF is extremely rare [9]. Non-culture methods for diagnosis by detecting aspergillus antigens or antibodies have been described [13]. The diagnosis is established antemortum in only 7-50% of cases [8,9]. Our patient presented with *Legionella* pneumonia and acute renal failure. After showing signs of improvement, his mental status started to deteriorate and he developed 4th cranial nerve palsy. The latter could be related to involvement of the basal meninges or to direct aspergillus infection of the nerve or its nucleus. Disseminated aspergillosis in our patient was probably secondary to the uremia and use of broad-spectrum antibiotics. Meningitis was probably secondary to the aspergillus spread from the infected sinuses. Although uremia is known to increase the risk for fungal infections [14,15], aspergillus meningitis in this

context has not been reported before.

These two cases illustrate two important points. First, fever and mental status changes in the hospitalized medical patient can be related to nosocomial CNS infection. Second, nosocomial CNS infections in hospitalized patients can be due to unusual pathogens. For these reasons, early diagnosis requires clinical vigilance and early consideration of lumbar puncture.

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