

## A 28 Years Old Woman with Severe Headache and Few Episodes of Vomiting: A Case Report

<sup>1</sup>Ahmad Reza Nakhayi, <sup>1</sup>Tasnim Eghbal Eftekhaari, <sup>1</sup>Hossein Montazerghaem,  
<sup>1</sup>Seyedhamid Moosavy and <sup>2</sup>Abdoulhossain Madani

<sup>1</sup>Department of Infectious Disease,  
<sup>2</sup>Department of Epidemiology,  
Infectious Disease Research Center,  
Hormozgan University of Medical Sciences, Bandarabbas, Iran

**Abstract: Problem statement:** Cryptococcosis neoformans is commonest central nervous system infection in individuals infected with HIV. Most of the patients infected with *Cryptococcus neoformans* present with headache and visual changes. **Approach:** A 28 year old woman presented to Emergency Department (ED) with a chief complaint of headache, fever and vomiting and developed seizures during the first hour of admission. Firstly, diagnosed as cryptococcal meningitis, then, because of having a low White Blood Cell count (WBC) and low Total Lymphocyte Count (TLC) she was checked for HIV Ab and P24 Ag. **Results:** A diagnosis of HIV was made then her family members were checked for HIV and they were also HIV positive. Patient was discharged with a two month course of Fluconazole and after completion of antifungal treatment, Antiretroviral Treatment (HAART) was started. **Conclusion:** This case indicated that Cryptococcosis neoformans may develop in Immune-deficient patients, so complete laboratory workup and high index of suspicion to HIV should be under diagnosis.

**Key words:** HIV, episodes of vomiting, *Cryptococcus neoformans*, Total Lymphocyte Count (TLC)

### INTRODUCTION

**Case report:** A 28 year old woman with severe headache and few episodes of vomiting was referred to our outpatient clinic and admitted in emergency ward. Her headache had been present since last two months beginning in frontal area extending to both parietal areas during her pregnancy for which she had been treated with amoxicillin diagnosed as sinusitis. Headache was persistent after her delivery. In her physical exam she was pale and had a generalized wasting. Her right eye was adducted, had diplopia and blurred vision. Pupils were reactive to light. No neck rigidity was seen in examination. Lymphadenopathy was absent and her lungs were clear with a normal breathing sound. Abdomen was soft with no organomegaly. Her extremities were also normal except for nail bed pallor. Presenting ED vital signs were a temperature of 40°C (axillary), blood pressure 95/60 mm Hg, pulse was filiform with a rate of 100 min<sup>-1</sup> and respiratory rate was 20 min<sup>-1</sup>. Blood was sampled for diff count, Hb, ESR, wright, widal, 2ME, BUN, Cr and urine was sampled for analysis and culture. Laboratory

evaluation revealed a serum white blood cell (WBC) count of  $3.4 \times 10^3$  with 72% neutrophils, 25% lymphocytes, 3% monocytes, a hemoglobin of 8.5 gm/dl and platelets 88 k/cumm. Peripheral blood smear showed hypochromia, ovalocytosis, elliptocytosis, microcytosis, schistocytosis, spherocytosis and tear drop RBC. While her basic electrolytes were unremarkable except for serum potassium which was 2, the liver function panel revealed a total bilirubin of 0.8 mg dL<sup>-1</sup>, alkaline phosphatase 100 units L<sup>-1</sup>, SGOT (AST) 40 units L<sup>-1</sup>, SGPT (ALT) 13 units L<sup>-1</sup>, ALP 147 and LDH 314. Urinalysis had gross hematuria and pyuria and urine was positive for nitrite. Wright, widal and 2ME were not remarkable. Sputum and CSF were negative for AFB and culture. The patient's condition aggravated during the first hour of admission, she had an episode of focal seizures and her level of consciousness decreased. She was admitted in ICU and her seizures were treated with diazepam 10 mg IV immediate (stat) dose and as needed (p.r.n.), phenytoin 750 mg IV infusion in 250cc normal saline and valproic acid 300 mg twice daily. Chest x ray was not remarkable and abdominal sonography was normal.

**Corresponding Author:** Abdoulhossain Madani, Department of Epidemiology, Infectious Disease Research Center, Hormozgan University of Medical Sciences, Bandarabbas, Iran

Brain computerized tomography scan was performed to rule out any contraindications of lumbar puncture (LP). Brain had mild cortical edema and no focal lesions were present. LP was performed and cerebrospinal fluid (CSF) was sampled for cell count, protein and glucose level, adenosine deaminase (ADA) and gram stain. Infectious disease specialist was consulted. CSF revealed 370 white blood cells with 53% lymphocytes, 0 monocytes 47% polymorphonuclear cells, low glucose at 37 mg dL<sup>-1</sup> and high protein at 1000 mg dL<sup>-1</sup>. Gram stain was negative and empirical treatment was started with antituberculous regimens (four regimen treatment with isoniazid, rifampicin, ethambutol and pyrazinamide) because of high prevalence of tuberculosis in south of Iran. ADA was 0.5 and LP was performed again for Indian ink stain. Indian ink stain was positive for *Cryptococcus neoformans*. According to this finding and persistence of fever, anti-tuberculosis agents were discontinued and antifungal treatment was started with Amphotericin B 35 mg IV infusion/day in D5%; because of unavailability of Flucytosine in this area, Fluconazole was substituted and administered 400 mg daily. Valproic acid and phenytoin were discontinued. Because of low WBC count (3500) and a total lymphocyte level of 850 and fungal meningitis, HIV Ab and P24 Ag were checked and were positive. Patient was discharged with a two month course of Fluconazole and after completion of antifungal treatment, antiretroviral treatment (HAART) was started. Following a detailed and in-depth history revealed that her husband was an intravenous drug user (IDU) and resided outside Iran having unprotected sex. Her husband and children were checked for HIV and were positive. Consent was obtained from the patient to report this case anonymously.

## RESULTS AND DISCUSSION

Headache being a symptom is seen in most patients presenting to ER. Chronic headaches are often a sign of chronic meningitis, which is often caused by infectious, inflammatory, neoplastic causes and toxic exposures. *Cryptococcus* is common and fatal in immunocompromised patients (Cheung *et al.*, 2003; Hong *et al.*, 2007) and being a major cause of fungal meningitis (especially in patients with AIDS) (Cheung *et al.*, 2003; Ginsberg and Kidd, 2008), has been the AIDS defining illness for 60% of HIV-infected patients in whom it is diagnosed (Coyle, 1999). As an opportunistic T cell modulated mycosis, Cryptococcosis is an important disease in patients with a weak or suppressed immune system (Ginsberg and Kidd, 2008).

Cryptococcus is the fourth most common source of life-threatening infection in AIDS patients after infections of cytomegalovirus, *Pneumocystis carinii* and *Mycobacterium avium intracellulare* (Hong *et al.*, 2007). A study has reported that approximately 60% of headache presentation in patients with AIDS headache is due to cryptococcal meningitis or presumed bacterial sinusitis (Shih *et al.*, 2000).

Globally, it is estimated that approximately 957,900 cases of cryptococcal meningitis occur each year, resulting in more than 600,000 deaths (Sar *et al.*, 2004). Neurological dysfunction as the first manifestation of AIDS has been found in 10-20% of symptomatic HIV infections (Botha and Wessels, 1999). In most cases neurologic involvement in patients with AIDS is due to infection with *Mycobacterium tuberculosis* and *Cryptococcus neoformans* and they account for 75% cases of meningitis; because of their frequency and morbidity, they should always be considered first in evaluation of a headache in a patient with AIDS but only 1.9% of cases initially present with cryptococcal infection (Hong *et al.*, 2007). Patient described in this case had a rare etiology of a common presentation to ED. Classic meningitic findings, such as neck rigidity, are absent in 75% of cases. The most common presentation of cryptococcosis is a subacute meningitis or meningoencephalitis with fever, malaise and headache (Shih *et al.*, 2000). Visual changes have been reported and most of visual changes in HIV infected patients are attributable to Cryptococcus meningitis (Hong *et al.*, 2007), as well as new onset seizure activity.

Clinical disease is rarely fulminant; in these cases the patient may present with coma and rapid progression to death (Coyle, 1999). Clues to the diagnosis in this case included an atypical headache (sub acute), high grade fever and new onset seizures. Computed tomography of the brain is normal in 50% of proven cases; however, a focal neurological exam and abnormalities on brain CT or MRI have both been linked to a poorer prognosis (Lakshmi *et al.*, 2007) but this patient had no focal lesions except for mild cortical edema. The CSF WBC count is typically low (<50 microL<sup>-1</sup>) with a mononuclear predominance and the protein and glucose concentrations are usually only slightly abnormal (Coyle, 1999) but in our case CSF WBC count was high (350 microL<sup>-1</sup>) with a lymphocytic predominance (53%), which was favorable for aseptic meningitis and normal gram stain of CSF suggested a probability of TB meningitis and normal Zeehl Neilsen staining for TB, indicated for Indian ink staining which was positive for yeast cells. CSF staining with India ink will show the typical

encapsulated yeast forms in approximately 75% of patients (Coyle, 1999). This patient had a low WBC count (3500 microL<sup>-1</sup>) and a low total lymphocyte count (850) and presence of a fungal meningitis in addition to decreased total lymphocyte count guided us to check for HIV status, regarding this fact that cryptococcal meningitis is seen in 89.3% of patients with TLC less than 200 (Leite *et al.*, 2004). Although number of people infected with HIV in Hormozgan province (in south of Iran) was 927 with 54 new cases till end of 2009 in a population of 1450000, but HIV infection is not suspected in many cases and is only checked in people having high risk behaviors. Precise prevalence of fungal infections in HIV infected patients are not known which may be due to under reporting of these infections. Patients with chronic headache and fatigue should be screened for possible aseptic meningitis and detection of fungal infections may improve in patients (whether immunocompetent or immunocompromised) suspected of meningitis if CSF fluid was sent for Indian Ink stain besides gram stain. A study has shown that immunosuppressed patients present with less typical clinical symptoms of meningitis (Lakshmi *et al.*, 2007). Our patient presented with sinusitis and headache. She was not suspected and diagnosed for meningitis until she developed seizures. Delayed diagnosis is an important issue with this disease and has reported to increase morbidity and mortality (Juhi *et al.*, 2009) and undiagnosed HIV in a pregnant woman, caused birth of an infected newborn. Diagnosis of one patient with HIV and checking the HIV status of her family members, resulted in diagnosis of 3 more HIV patients. As number of Persons Living with HIV/AIDS (PLWAs) increases, caring for them is a new rising problem. Adequate knowledge and positive attitude are important factors in providing better care for a patient (Mahin *et al.*, 2010).

### CONCLUSION

Clinicians should be informed that fungal meningitis should be suspected in patients with chronic headache and fatigue; high index of suspicion and full laboratory workup is required for more survival and diagnosing hidden cases of HIV.

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