Case Report:

Atypical presentation of a common opportunistic infection in advanced AIDS

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ABSTRACT

Intracranial tuberculosis in immunocompromised patients can occasionally mimic central nervous system (CNS) neoplasms radiologically and complicate the decisions regarding management. A 42-year-old male presented with a history of fever and vomitings of 5 days duration. On evaluation he was found to be reactive for human immunodeficiency virus 1 infection with a CD4+ count of 63 cells/mm^3 and a viral load of 1,260,779 copies /mL. He was started on highly active antiretroviral therapy with tenofovir, emtricitabine, efavirenz, *Pneumocystis jiroveci* prophylaxis and was discharged. After 5 months he developed aggressive behaviour, irrelevant talking and memory loss. On examination, he was irritable with memory disturbances; no focal neurological signs were evident. Magnetic resonance imaging brain and magnetic resonance spectroscopy (MRS) showed a large heterogeneous enhancing ill-defined lesion in the left parieto-occipital lobe with a lipid lactate peak suggestive of infective aetiology. Cerebrospinal fluid (CSF) analysis showed glucose 33 mg/dL, protein 120 mg/dL, 40 cells/mm^3 (all lymphocytes), adenosine deaminase 40U/L; Gram's stain was negative, Ziehl-Neelsen stain did not reveal acid-fast bacilli, toxoplasma, cryptococcal antigen tests were negative. Polymerase chain reaction for Epstein-Barr virus was also negative. In view of the clinical setting, CSF analysis supported by MRS findings he was started on antituberculosis treatment (ATT) and corticosteroids. Patient showed remarkable improvement clinically and radiologically with significant reduction in the size of the lesion. MRS is a useful non-invasive technique that can help in differentiating tuberculoma from lymphoma.

Key words: *Tuberculoma, Lymphoma, Magnetic resonance spectroscopy*

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INTRODUCTION

The incidence of pulmonary tuberculosis (TB) is almost 500 times greater in acquired immunodeficiency syndrome (AIDS) patients compared with the general population.[1] Moreover, the incidence of central nervous system (CNS) TB is significantly high in AIDS patients.[2] However, primary central nervous system lymphoma (PCNSL) is also common in patients with AIDS.[3] Although meningitis is the most common presentation of CNS TB other forms including cerebritis, abscess, or tuberculoma are known to occur frequently in patients with AIDS.[4]

TB meningitis typically evolves over 1-2 weeks but may present acutely with headache, mental changes (confusion/lethargy), neck rigidity, low-grade fever, malaise, anorexia, irritability, and paresis of cranial nerves. Involvement of cerebral arteries may produce focal ischaemia, coma with hydrocephalus and intracranial hypertension. Tuberculoma is uncommon and presents with seizures and focal signs. Although toxoplasma encephalitis and CNS lymphoma are more commonly encountered in HIV-infected patients, CNS TB is a significant cause of cerebral infection.

Lumbar puncture is the cornerstone for diagnosis of TB meningitis. Computed tomography (CT) or magnetic resonance imaging (MRI) brain may show hydrocephalus and abnormal enhancement of basal cisterns or ependyma. Whereas, in CNS tuberculoma CT or MRI reveals contrast-enhanced ring lesions. A biopsy is necessary to establish diagnosis.

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PCNSL is defined as lymphoma limited to the brain and spinal cord without systemic disease. As with other AIDS related lymphomas, these are also aggressive B-cell neoplasms, either diffuse large cell or diffuse immunoblastic non-Hodgkin's lymphoma. However, unlike AIDS related systemic lymphomas where only 30%-50% of tumours are associated with Epstein-Barr virus (EBV) infection, AIDS related PCNSL has a 100% association with EBV.[5]

Clinical features range from focal seizures to rapidly growing mass lesion in the oral mucosa to persistent unexplained fever. It can present with B-grade symptoms of fever, night sweats, weight loss and focal neurological deficits, headache, seizures. MRI or CT may reveal a few 3 to 5 cm lesions. These lesions often show ring-enhancement on contrast administration and may occur in any location, the most common locations being deep white matter.[4]

In clinical practice the presentation of CNS TB is not always classical. Very often there is a dilemma between CNS lymphoma and TB which have very similar clinical and radiological characteristics especially in the setting of AIDS. Often biopsy and histopathological, microbiological examination is required to confirm the diagnosis.

CASE REPORT

A 42-year-old male presented to our emergency medicine department with a history of fever and vomiting of 5 days duration. Physical examination was unremarkable. On evaluation he was found to be reactive for human immunodeficiency virus1 (HIV1) infection with CD4+ count of 63 cells/mm^3 and a viral load of 1,260,779 copies/mL. Upper gastrointestinal endoscopy, barium swallow and CT brain were normal. He was treated with supportive care and started on highly active antiretroviral therapy (HAART) with tenofovir, emtricitabine, efavirenz, *Pneumocystis jiroveci* prophylaxis and was discharged in a stable condition.

After 5 months he was again brought to emergency medicine department with complaints of aggressive behaviour, irrelevant talking and memory loss. On physical examination, he was irritable with memory disturbances; no focal neurological signs were evident.

Laboratory testing revealed an erythrocyte sedimentation rate of 48 mm at the end of first hour. Liver and renal function tests were normal. Chest radiograph showed no obvious radiological abnormality. Mantoux test was negative. Serological tests for hepatitis B surface antigen (HBsAg) and hepatitis C virus (HCV) were negative. MRI brain (Figure 1) showed a large heterogeneous peripherally enhancing ill-defined lesion in left parieto-occipital lobe. Cerebrospinal fluid (CSF) examination revealed glucose 33mg/dL, protein 120 mg/dL; 40 cells (all lymphocytes) and adenosine deaminase (ADA) 40 U/L. CSF cytology was negative; for malignant cells; Gram's stain was negative, Zeihl-Neelsen stain did not reveal acid fast bacilli. CSF serology for toxoplasma and herpes simplex virus, as also the cryptococcal antigen test were negative. CT of chest revealed a fibrotic lesion in the right upper zone. EBV

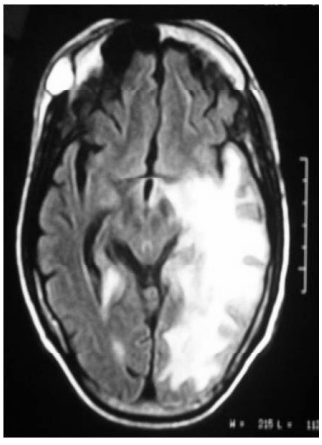

Figure 1: MRI brain axial FLAIR imaging showing ill-defined heterogeneous, hyperintensity noted involving left parieto-occipital region and also involving the splenium of corpus callosum with extension of contralateral lobe, with extensive perilesional oedema noted, lesion also involving the occipital horn of left lateral ventricle

polymerase chain reaction (PCR) was done to rule out PCNSL and was negative. Stereotactic biopsy of the lesion in the brain was considered. Magnetic resonance spectroscopy (MRS) showed on elevated lipid lactate peak (Figures 2A and 2B) and a reduced N-acetylaspartate (NAA) and creatine suggestive of infective aetiology.

Given the above clinical scenario, CSF examination findings, negative EBV PCR, MR Spectroscopy suggesting infective aetiology and also given that tuberculosis is the most common opportunistic infection in HIV/AIDS patient, CNS tuberculoma was considered. The patient was started on daily self-supervised antituberculosis treatment (ATT) and corticosteroids. Patient showed remarkable improvement clinically. MRI showed significant reduction in the size of the lesion at three months of follow up (Figure 3).

DISCUSSION

In the background of immunocompromised host the most common differential diagnosis for a CNS mass lesion include primary CNS lymphoma, toxoplasmosis and tuberculoma. While less common lesions are pyogenic abscess, cysticercosis, and syphilitic gummas. In our case we had a very large lesion in the brain parenchyma with a CD4+ count of 63 cells/µL. We initially suspected PCNSL, following which we have done EBV PCR which was negative. Then we considered second differential diagnosis of tuberculoma. This patient had features common to PCNSL and tuberculoma, namely, altered sensorium, memory disturbance, irrelevant talk, raised ESR, heterogeneous peripherally enhancing ill defined lesion and lymphocytic predominance in CSF.

Though sterotactic brain biopsy would confirm the tissue diagnosis, due to risks associated with doing the procedure we did MR spectroscopy to identify an infective lesion. MRS done at the site of lesions showed a increased lipid peak and a decreased NAA peak with increased choline/creatine ratio[6]. MRS helps to identify lipids within the tuberculoma that are considered characteristic for TB. The characteristic MRS findings in tuberculomas also help in ruling out primary CNS lymphomas. However, the appli-

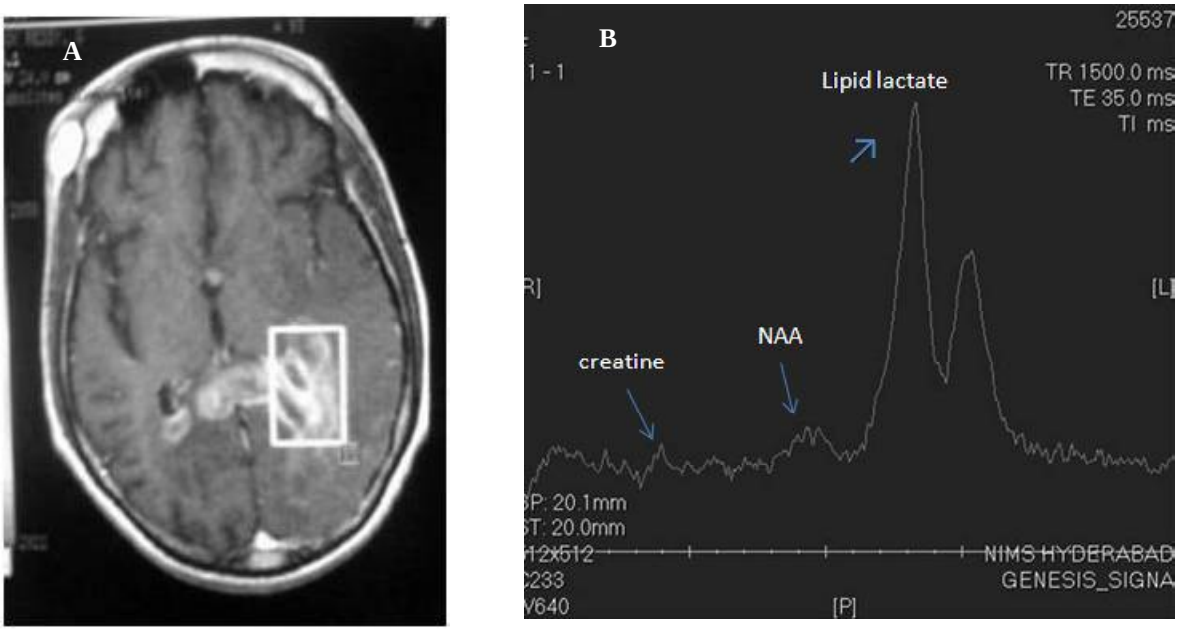

Figure 2: Singal voxel localizer (rectangle) placed on the lesion involving corpus callosum and periventricular white matter (A). Single voxel MRS reveals lipid-lactate peak (short arrow), reduced NAA and creatine (long arrows) and absence of choline typical for tuberculoma (B)
MRS= magnetic resonance spectroscopy; NAA=N-acetyl aspartate

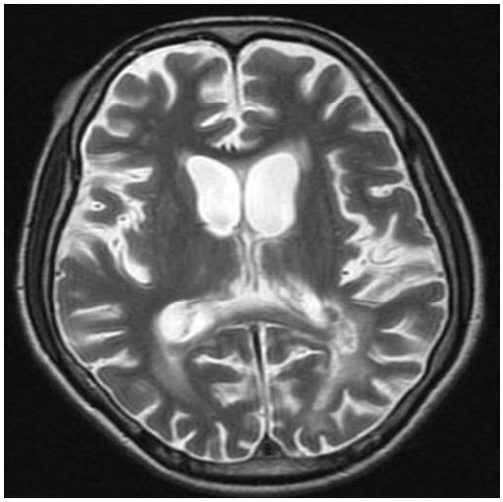

Figure 3: Follow up MRI at 3 months showing significant reduction in the size of the lesion

cation of MRS in the diagnosis of tuberculomas in HIV-TB co-infected patients merits further detailed study. In vivo and in vitro MRS has shown elevated lipid peaks within the TB lesions.[7] MRS study safely avoids the need of brain biopsy to confirm the nature of lesion. Moreover CNS biopsy is invasive and in 5%-33% of cases no diagnosis can be reached due to sampling problems or tissue non-viability.[8,9] MRS may prove a useful non-invasive investigational tool to differentiate tuberculoma and CNS lymphoma which are often confused.

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