RADIOLOGY CASE OF THE MONTH

Idiopathic CD4 Lymphocytopenia

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A 39 year-old male with a history of diabetes, retinitis pigmentosa, and genital warts presented with intractable occipital headaches accompanied with nausea and vomiting. The patient had markedly depressed CD4 counts. Furthermore the patient tested negative for HIV and HTLV 1/2 and had normal immunoglobulin levels. During hospital course the patient underwent a lumbar puncture and multiple imaging exams, including both CT and MR. Except for occasional nausea and vomiting controlled by therapeutic lumbar punctures, phenergan, and dilaudid the patient's hospital course was uncomplicated.

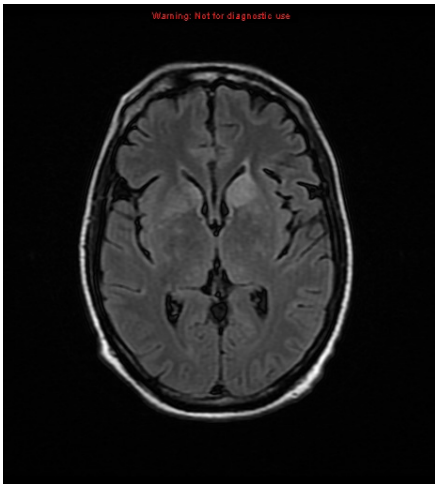

Figure 1a. *Axial FLAIR image*

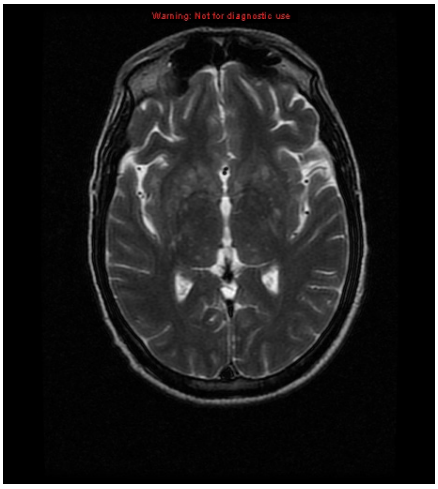

Figure 1b. *Axial T2 Weighted Image*

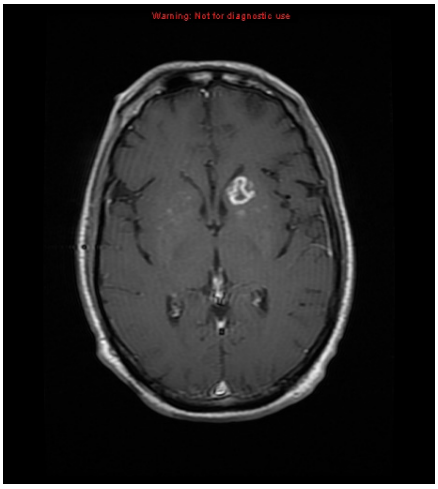

Figure 1c. *Axial T1WI with contrast*

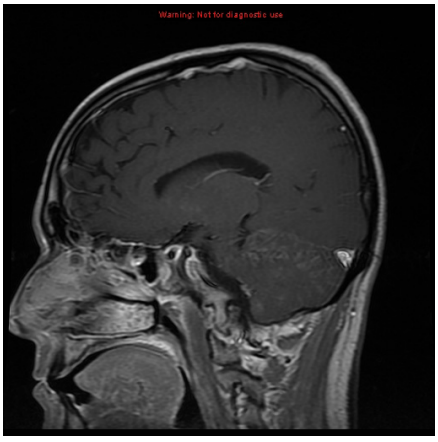

Figure 2a. *Sagittal T1WI with contrast*

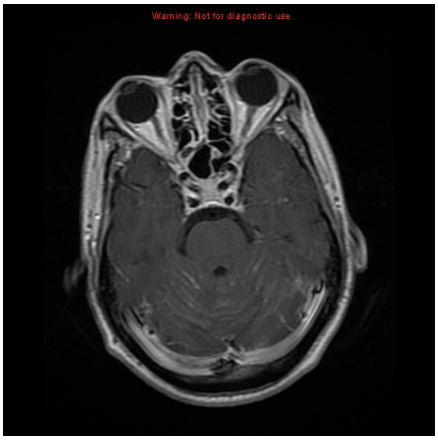

Figure 2b. *Axial T1WI with contrast*

RADIOLOGIC DIAGNOSIS

Idiopathic CD4 Lymphocytopenia with Cryptococcal Meningitis and Cryptococcal Abscess

INTERPRETATION OF IMAGES

MR (Figure 1A) axial FLAIR image demonstrates abnormal signal intensity within the left caudate nucleus. (Figure 1B) axial T2WI demonstrates dilatation of perivascular spaces at the base of the brain. (Figure 1C) axial T1W post contrast demonstrates enhancement of a necrotic lesion involving the head of the caudate nucleus. (Figure 2A) and (Figure 2B) reveal enhancement of the leptomeninges over the cerebellum.

DISCUSSION

Idiopathic CD4 Lymphocytopenia (ICL) is a rare immunodeficiency characterized by low CD4 counts in the absence of human immunodeficiency virus (HIV) and other immunodeficiencies.[1] The most common presenting opportunistic infection in patients with Idiopathic CD4 Lymphocytopenia (ICL) is cryptococcal meningitis followed by persistent genital manifestations of human papilloma virus (HPV).[2] Patients may also suffer from tuberculosis and other atypical mycobacterial infections. Previous cases have shown patients with this disorder suffering from a wide variety of opportunistic infections including Pneumocystis jirovecii pneumonia, aspergillosis, toxoplasmosis, histoplasmosis, hepatitis C, Epstein barr virus (EBV), cytomegalovirus (CMV), John Cunnningham (JC) virus, and Fusobacterium nucleatum. Mainstay therapy includes prophylaxis according to HIV guidelines for certain CD4 count thresholds and treatment of any opportunistic infections.

This condition is defined by the presence of persistent CD4 lymphocytopenia in the absence of HIV infection, and should be considered a diagnosis of exclusion when other conditions leading to depressed CD4 counts are ruled out.[1] Specific criteria for diagnosis include CD4 cell counts below 300 cells/ml or less than 20% of total lymphocytes on at least 2 separate analyses. Any other immune deficiency due to underlying condition or drugs must be excluded. This includes common variable immune immunodeficiency (CVID), which presents with low immunoglobulin levels. Other laboratory findings are variable but may include a slightly elevated or normal CD8 count, CBC differential demonstrating lymphopenia, and normal or slightly low immunoglobulin levels. ICL is distinguished from HIV in that HIV is associated with elevated counts of immunoglobulins and an early elevated CD8 count.[3] Theories behind the pathogenesis include diminished generation of T-cell precursors, increased T-cell apoptosis, alteration of p56 Lck kinase resulting in a defunct CD3 T cell receptor pathway, defective production of cytokines, and circulating CD4 T-cell antibodies.[3]

Cerebrospinal fluid (CSF) in our patient obtained by lumbar puncture from an outside facility grew Cryptococcus neoformans, diagnosing the patient with Cryptococcus meningitis. The patient had CD4 counts of 54 and 72 on two separate measurements during the course of his stay, which fulfilled criteria for diagnosis of Idiopathic CD4+ Lymphocytopenia (ICL). An initial MR of the patient's brain from an outside facility showed an area of abnormal restricted diffusion in the left caudate nucleus on diffuse weighted imaging (DWI) with corresponding abnormality on apparent diffusion coefficient (ADC) map respectively, consistent with a recent vascular insult or inflammatory process. The patient was started on both Amphotericin B at 5 mg/kg and fluconazole 400 mg daily. A repeat lumbar puncture was performed during patient's inpatient treatment, which revealed 48 protein, 87 glucose, 45 WBC (98 lymph, 2 mono), and 3 RBC's. The cerebrospinal fluid obtained (CSF) was positive for India ink stain and showed a cryptococcal antigen titer of 1:512.

In our patient, it appeared that the meningeal component of the Cryptococcal infection involved the perivascular spaces at the base of the brain and cerebellar leptomeninges. On magnetic resonance (MR), there was a focal hyperintensity, with abnormal restricted diffusion indicating acute insult. This was consistent with Cryptococcal involvement of the basal ganglia secondary to Cryptococcal meningitis by way of the perivascular spaces.[7] Patients with AIDS often demonstrate a wide spectrum of cryptococcal manifestation patterns on MR, with dilated perivascular Virchow-Robin spaces.[8-10] As the infection spreads along these perivascular spaces, these spaces may become increasingly dilated and become filled with mucoid and gelatinous material produced by the organism's capsule.[11] In addition, enhancing parenchymal lesions are a sign of further invasion from the CSF spaces forming a granulomatous process as was noted with our patient.[10] Ventricular dilatation, leptomeningeal enhancement, and cryptococcomas are common findings on MR.[8,9] However dilatation of Virchow-Robin spaces tend to be the common finding and should raise concern for cryptococcal infection in any immunocompromised patient.[12]

A follow up with MR of the brain was performed in our patient 18 days after admission, which showed the area of the left caudate nucleus as a ring-enhancing abscess (Figure 1C). The areas of scattered enhancement at the base of the brain and meninges appeared more prominent. As the patient was maintained on Amphotericin B and fluconazole therapy during his treatment period, these areas of abnormal enhancement and rim-enhancing abscess in the left caudate nucleus decreased in size. MR spectroscopy was performed in order to evaluate the area of the left caudate nucleus considered to be a cryptococcal lesion. Elevated levels of lactate and lipids with a relative decrease in the creatine and NAA peak compared to the contralateral normal MR spectroscopy of the right caudate nucleus were noted consistent with necrotic inflammatory process.

Novel therapies for increasing CD4 counts have been studied. Recombinant IL-2 therapy in addition to antifungal agents along with surgical clearance of infection from CNS in ICL patient with Cryptococcus meningitis with subsequent clinical improvement and CD4 increase has been reported.4 IFN-γ has been shown to be therapeutic to an individual with ICL and Cryptococcus meningitis refractory to antifungals.[5] Animal and in-vitro studies have indicated IL-7 as a promising therapy, and recruitment is underway for clinical trials.[6]

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