PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY – A CASE REPORT

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ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is a progressive demyelinating disease caused by JC virus, occurring in immunocompromised patients. In the HAART era, approximately 5% of the AIDS patients have been reported to develop PML. The clinical presentation of PML is quite variable because lesions may occur anywhere in the CNS white mater; the most common findings are motor weakness, visual defects (e.g. visual blurring, diplopia), and incoordination. The most frequently affected regions are the cerebral hemispheres, followed by subtentorial lesions. The diagnosis of PML in an immunocompromised patient with evocative clinical picture of focal neurologic deficits is made by demonstrating typical findings on brain imaging studies and detection of viral DNA in CSF by PCR examination. Brain biopsy should be reserved for cases with suspicious white matter lesions on CT or MRI in which JC virus is not detected in PCR. Differential diagnosis should consider other primary as well as opportunistic infections of CNS, other demyelinating diseases (such as multiple sclerosis), vascular lesions (e.g. ischemic stroke, HIV vasculopathy), tumors (e.g. lymphoma) and HIV encephalopathy with secondary changes in white matter.

The present paper describes the case of a HIV positive patient with clinical, biological and imaging findings highly suggestive for PML, but negative PCR for JC virus DNA.

Key words: JCV, PML

CASE PRESENTATION

A 19-year-old woman human immunodeficiency virus (HIV) positive presented to the emergency room with headache, gait disturbance, left-side weakness, diplopia and somnolence. Her history revealed that she had a headache that started 2 weeks ago and did not respond to usual analgesics, followed by diplopia and somnolence. The symptoms worsened slightly and she developed left hemiparesis within 10 days.

The past medical history revealed that the patient was known to be HIV positive for 11 years, being treated with highly active antiretroviral therapy (HAART), but she was incompliant and interrupted her medication many times. Currently, she did not take her HAART therapy for 3 months. Her history was also significant for many infections, (being diagnosed with pulmonary tuberculosis 5 years ago and ganglionar tuberculosis 8 months ago, chronic viral B hepatitis), dyslipidemia and lipodistrophy secondary to HAART.

The neurological examination revealed somnolence, fall tendency to left, severe left hemiparesis, left hypotonia, ataxia in the left limbs, brisk left tendon reflexes and Babinski sign on the left. On

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cranial nerves evaluation, there was left palpebral ptosis, limitation of the inward and upward left eye gaze and left lower facial weakness.

The general physical examination was normal, except the presence of lipodistrophy.

DIAGNOSTIC TESTS

Complete blood cell count revealed a white blood cell count of 3600/mm^3, with 75.5% neutrophyls, 11.8% lymphocytes, 9.3% monocytes, 0.4% basophils, 2.6% eosinophils; 3430000/mm^3 erythrocytes with hemoglobin of 9.6 g/dl, mean corpuscular volume 74.2 fL and platelets 290000/mm^3. The erythrocyte sedimentation rate was 80 mm/hr.

Her CD4 count was 9 cells/μL, the CD8 count was 403 cells/ μL and the HIV1 RNA was 38800 copies/ml.

Total cholesterol was 168 mg/dl and triglycerides were 120 mg/dl.

Lumbar puncture retrieved clear, normotensive CSF with 8 white blood cells/mm^3, no blood cells, 0.22 g/l proteins, 51 mg/dl glucose, and absent chlorine.

Chest radiography was without any active lesions.

On cerebral CT scan, there was an area of hypodensity extending from the left pons into the left cerebellum.

MRI scan revealed diffuse lesions up to 1,5 cm situated in the left internal capsula, left pons and midbrain, vermis and left cerebellar hemisphere with minimal gadolinium enhancement, no mass effect and no edema. The lesions were hypointense on T1-weighted images and hyperintense on T2-weighted and fluid attenuated inversion recovery images (see Figure 1).

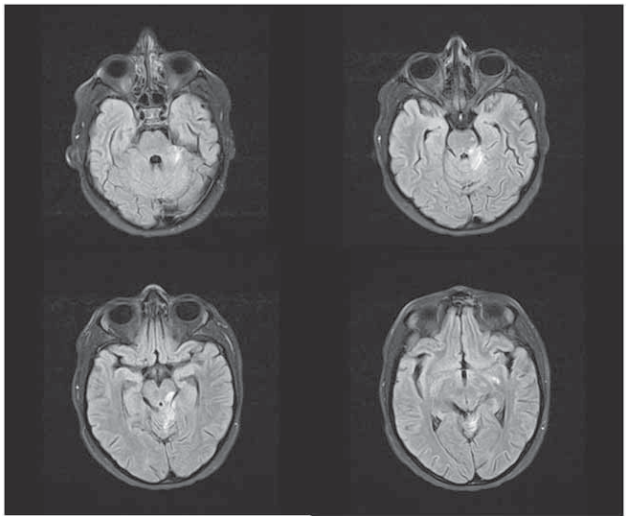

FIGURE 1

OTHER DIAGNOSTIC TESTS

The serology for Cryptococus, Herpes Simplex virus, Varicella-Zoster virus, Cytomegalovirus, Epstein Barr virus, Toxoplasma and Treponema Pallidum was negative.

The CSF cultures for Mycobacterium tuberculosis, bacteria and fungi were negative and the polymerase chain reaction (PCR) for JC virus DNA was negative.

The patient refused brain biopsy.

Clinical course

Initially the patient received HAART and stared an empirical treatment for Toxoplasma encephalitis with Trimetoprim-Sulfametoxazol while CSF studies were pending. The later treatment was discontinued as the studies for Toxoplasma were negative.

One month later, the CD cells count was: CD4 - 38 cells/μL, CD8 – 454 cells/μL, CD4/CD8 = 0.08 and the HIV1 RNA was 468 copies/ml. Clinically, the status of the patient improved, the neurological examination revealing only a mild left hemiparesis, hypotonia in the left upper limb, mild ataxia in the left limbs, brisk tendon reflexes on the left side and left Babinski sign; on cranial nerves examination, there was a mild left palpebral ptosis and the patient complained for intermittent diplopia when watching TV for a long time.

DISCUSSION

Progressive multifocal leukoencephalopathy (PML) is a progressive demyelinating disease caused by JC virus, occurring in immunocompromised patients. In the HAART era, approximately 5% of the AIDS patients have been reported to develop PML (1).

The clinical presentation of PML is quite variable because lesions may occur anywhere in the CNS white mater; the most common findings are visual defects (e.g. visual blurring, diplopia), motor weakness and incoordination (2). The most frequently affected regions are the cerebral hemispheres, followed by subtentorial lesions (in cerebellum and brain stem).

The diagnosis of PML in an immunocompromised patient with evocative clinical picture of focal neurologic deficits is made by demonstrating typical findings on brain imaging studies and detection of viral DNA in CSF by PCR examination (3). Brain biopsy should be reserved for cases with

suspicious white matter lesions on CT or MRI in which JC virus is not detected in PCR (4).

Differential diagnosis should consider other primary as well as opportunistic infections of CNS, other demyelinating diseases (such as multiple sclerosis), vascular lesions (e.g. ischemic stroke, HIV vasculopathy), tumors (e.g. lymphoma) and HIV encephalopathy with secondary changes in white matter.

In our patient, although the clinical picture, the laboratory findings and the imaging studies indicated the diagnosis of PML, the JC virus DNA was not detected in CSF. However, a negative PCR test does not exclude this diagnosis. Before the HAART era, JCV PCR had a sensitivity of 72-92% and a specificity of 92-100% for the diagnosis of PML, but over the past few years it has become more frequent to find negative CSF JCV PCR results in AIDS patients with clinical and radiological presentation indistinguishable from PML (5).

The fact that the patient refused the brain biopsy made the diagnostic more difficult, but excluding other possible causes for her deficit and her good recovery under HAART therapy make PML the most probable underlying condition.

Although numerous drugs have been studied (e.g. Cytarabine, Cidofovir, Topotecan, etc), there is no specific treatment for JCV, the optimization of HAART being the best therapeutic option (5).

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