Case Report

Progressive Multifocal Leucoencephalopathy: An Unusual Presentation

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Abstract

Progressive multifocal leucoencephalopathy (PML) is a rarely occurring demyelinating disease of the central nervous system caused by a neurotropic papovirus named JC virus (JCV). The most frequently affected areas are the cerebral hemispheres, especially the parieto-occipital region, followed by the cerebellum and brain stem. The disease occurs predominantly in individuals with an immunocompromised state and impaired cellular mediated immunity (CMI) due to other underlying illness. The course of the disease is still most often rapidly progressive and fatal. Suspicion of PML should lead to an extensive immunological investigation before considering of brain biopsy, which is still the only specific test.

Key words; Progressive multifocal leucoencephalopathy, JC virus, Cell mediated immunity.

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Case Report

A 56 years old male, non-smoker, non-alcoholic, non-diabetic presented with complaints of forgetfulness especially of more recent memory than remote memory since last 4 months. It was associated with headache and recurrent cough which was not associated with sputum for which he was taking treatment from local practitioner but symptoms were not relieved. On examination he was conscious and oriented with normal cardiovascular, respiratory and abdominal examination. Neurological examination revealed mini mental scoring of 19/30 with deficit of recall and rest of the neurological examination was normal. Laboratory investigations revealed pancytopenia, but liver, renal and lipid profiles were within normal limits. HIV serology was negative. MRI brain revealed demylination in parietal and occipital areas (Figure-1) suggestive of progressive multifocal leucoencephalopathy (PML). He was treated with steroids as prednisolone at 1 mg/kg/day with gradual improvement in the symptoms as well as correction of pancytopenia.

Figure 1. MRI brain of the patient

Discussion

The term "progressive" in PML means that the disease continues to get worse and often leads to serious brain damage. The term "leukoencephalopathy" means that

the disease affects mainly the white matter of the brain or myelin. Progressive multifocal leukoencephalopathy (PML) is a neurological disorder characterized by destruction of cells that produce the myelin, an oily substance that helps protect nerve cells in the brain and spinal cord, also known as central nervous system (CNS) white matter. It is caused by a virus called JC virus (JCV), named after the initials of the patient in whom it was first discovered. The virus is widespread, found in at least 85% of the general adult population. It remains inactive in healthy individuals and causes disease only when the immune system has been severely weakened, such as in people with HIV/AIDS, or hematological malignancies, and in organ transplant recipients who receive immunosuppressant medications to avoid rejection of the transplanted organ. Mechanism of demyelination in progressive multifocal leukoencephalopathy (PML) was elucidated by demonstrating ultrastructurally the relationship between the affected glial cells and myelin sheaths. The myelinating cells in the central nervous system, namely ollgodendroglias, were specifically attacked by PML-virus, with eventual primary destruction of myelin sheaths.[1]

PML may be caused by pharmacological agents, like efalizumab, belatacept, rituximab, natalizumab, infliximab chemotherapy,
corticosteroids and various transplant drugs such as tacrolimus.[2,3]

Patient may manifest as headaches, loss of coordination, clumsiness, loss of language ability (aphasia), memory loss, vision problems, weakness of the legs and arms that gets worsened. The lesions affecting the parietal and occipital lobes can lead to a phenomenon known as alien hand syndrome.[4]A partial differential diagnosis includes the CNS lymphoma, toxoplasmosis, HIV encephalopathy, HIV dementia, other (non-HIV) forms of dementia, cerebrovascular disease, neurosyphilis, CNS opportunistic infections(e.g., tuberculosis, cryptococcosis, and cytomegalovirus), multiple sclerosis[5]. Definitive diagnosis requires a brain biopsy and identification of characteristic pathological changes, or detection of JC virus DNA in CSF of patients with radiographic and clinical findings consistent with PML.

Presumptive diagnosis of PML often is made on the basis of clinical presentation, brain imaging, and laboratory tests. A brain biopsy should be considered with patients for whom a diagnosis is unclear.CNS imaging may reveal changes typical of PML, but is nonspecific. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) for detecting PML. Classic PML presents as single or multiple hypodense lesions in the subcortical white matter, with no surrounding edema. On MRI, lesions show increased T2 signal and little or no enhancement with gadolinium. On CT, PML lesions typically are nonenhancing. In some patients, and particularly in patients taking ART, PML lesions may show inflammatory changes, such as enhancement, and there may be cerebral edema. CSF evaluation include CSF cell count, protein and glucose levels which generally are normal or show mild pleocytosis and slightly elevated protein. JC virus PCR assays are approximately 75-85% sensitive.[6]

There is no specific treatment for JC virus. Initiate ART for patients who are not already receiving treatment. If symptoms are caused by immune reconstitution, consider adding corticosteroids (e.g., dexamethasone) to help decrease inflammation. Possible treatments for PML include cidofovir and interleukin-2. Mefloquine is an antimalarial drug that can also act against the JC virus. Administration of mefloquine seemed to eliminate the virus from the patient's body and prevented further neurological deterioration. [7-9]

Conclusion

Progressive multifocal leukoencephalopathy (PML) is a neurological disorder characterized by destruction of cells that produce the myelin. It is caused by a virus called JC virus (JCV). PML was elucidated by demonstrating ultra-structurally the relationship between the affected glial cells and myelin sheaths. Definitive diagnosis requires a brain biopsy and identification of characteristic pathological changes, or detection of JC virus DNA in CSF of patients with radiographic and clinical findings consistent with PML. There is no specific treatment for JC virus.

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