CASE REPORT

Progressive Multifocal Leukoencephalopathy in an HIV-positive Patient: A Case Report

Abstract

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease that occurs as a complication (4–8%) of the John Cunningham (JC) virus in oligodendritic cells. Progressive multifocal leukoencephalopathy is characterized by focal neurological deficits that usually show insidious onset and steady progression. Since the demyelinating lesions can affect various areas of the brain, specific deficits differ from patient to patient. Patients with PML tend to have a prolonged course with multifocal neurological deficits, such as ataxia, hemiparesis, aphasia, and visual field defects that may occur with or without a change in mental status. Here, we present the case of an human immunodeficiency virus (HIV)-positive patient who initially presented with severe headache, vomiting, and generalized weakness, leading to the diagnosis of PML.

Keywords: AIDS-related progressive multifocal leukoencephalopathy, Antiretroviral therapy, Case report, Human immunodeficiency virus, Immunosuppression, John Cunningham virus.

Introduction

Progressive multifocal leukoencephalopathy (PML) is an infectious disease that affects the central nervous system, caused by the reactivation of the John Cunningham polyomavirus (JCV). The disease is characterized by the destruction of myelin, and if left untreated, can lead to death. John Cunningham polyomavirus is a small, non-enveloped double-stranded DNA virus that was first identified in 1967, and was named after John Cunningham, the person from whom it was first isolated. Progressive multifocal leukoencephalopathy is the only known clinical manifestation of JC virus infection. Before the era of the human immunodeficiency virus (HIV), PML was only seen in severely immunosuppressed patients, such as those with hematological malignancies, organ transplantation, chronic inflammatory conditions, or autoimmune disorders, with an incidence of 4 cases/100,000. However, during the AIDS epidemic, the incidence of PML cases associated with HIV rose dramatically, accounting for 85% of all cases. Progressive multifocal leukoencephalopathy has been diagnosed in 2–4% of HIV-infected patients in developed countries in the pre-highly active antiretroviral therapy (HAART) era. Progressive multifocal leukoencephalopathy cases associated with HIV are often referred to as PML-immune reconstitution inflammatory syndrome (PML-IRIS), due to the immune reconstitution after cART initiation, which can result in paradoxical worsening or the unmasking of an opportunistic infection. This presentation has distinct clinical and radiographic features that differ from classical PML, including lesions with contrast enhancement, edema and mass effect, and a more rapid clinical course. Here, we present a case of PML in an HIV-positive patient who was immediately put on HAART after being diagnosed. While there has been some improvement in the patient's CD4 counts, the prognosis remains poor.

Case Description

A 50-year-old, male patient was admitted to the medical ward with the chief complaint of vomiting for 1 day, severe headache for the last 4 days and generalized weakness for 20 days. There was no history of seizures, fever, head injury, jaundice and ear discharge.

During the clinical examination, the patient displayed slow performance in motor functions and responded slowly to verbal commands. These observations indicate cerebral deficits. The fundus examination did not reveal any abnormalities, and there were no signs of meningeal involvement. The patient also had an unsteady gait, which suggests focal deficits in the brain. However, there were no significant changes in the ECG results. The laboratory tests conducted after the patient's admission showed normal hemogram and biochemistry. The analysis of the cerebrospinal fluid (CSF) showed normal biochemistry. The absolute CD4 count was 54/µL and the CD8 count was 610/µL, resulting in a CD4:CD8 ratio of 0.04. The CSF examination was essentially normal, including a negative polymerase chain reaction (PCR) for JC virus in the CSF. An MRI of the brain revealed a large, ill-defined, subcortical, peripherally enhancing lesion in the right parietooccipital lobe and bilateral cerebellar region without any mass effect, with cortical sparing matter. The lesions were observed to be hypointense on T1-weighted images. Upon conducting histopathological findings, demyelination with bizarre astrocytes and enlarged

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

oligodendrocytes were revealed. Based on the clinical features and investigations, the patient was diagnosed with possible PML, a condition related to AIDS. Other possible differential diagnoses included VZV, CMV, multiple sclerosis, central nervous system (CNS) vasculitis, and acute disseminated encephalomyelitis. Although there is no established cure for PML, the goal is to restore immunity to mount an adequate cytotoxic T lymphocytes (CTL) response against the virus. The patient was started on HAART along with prophylaxis of opportunistic infections.

Discussion

Juvenile-onset cerebellar ataxia with hypomyelination and/or hypoplasia of the cerebellum (JCV) typically presents in childhood as an infection without obvious symptoms. Approximately, two-third of the population harbors a dormant virus that resides in the kidneys and lymphoid organs. When the virus reactivates due to severe immunosuppression, PML can develop. Progressive multifocal leukoencephalopathy can also occur in patients undergoing HAART for HIV, a condition known as immune reconstitution inflammatory syndrome (IRIS) with a poor prognosis. Progressive multifocal leukoencephalopathy has been estimated to occur in 4% of the patients with HIV. With more than 5 million individuals living with HIV/AIDS in India, the incidence of PML in the Indian HIV-infected population is expected to be significant. A study conducted at the All India Institute of Medical Sciences in Delhi found that only 1.2% of patients attending the ART clinic had PML, which is lower than the reported rate of up to 5% in developed countries. Limited access to diagnostic facilities poses a significant challenge to diagnosing PML, resulting in under-diagnosis and under-reporting in resource-constrained settings like India, which could be a contributing factor to the low number of known cases.[1–5]

The symptoms of PML can vary from one patient to another but typically involve progressive neurological dysfunction. This can manifest as clumsiness, weakness, changes in vision, speech, or personality, and signs of raised intracranial pressure or systemic infection. To definitively diagnose PML, doctors will look for three key features in brain lesion biopsies: demyelination, bizarre astrocytes, and enlarged oligodendroglial nuclei. However, this is difficult to do and requires invasive procedures. Instead, doctors may use a combination of clinical features, neuroimaging, and molecular biology testing of CSF to diagnose PML.

There is no specific therapy for PML or the JCV infection that causes it. However, introducing cART (combination antiretroviral therapy) can help improve the prognosis for patients with AIDS-related PML. Protease inhibitor-based ART seems to be especially effective, regardless of the CNS penetration score. After the introduction of HAART, survival rates have improved significantly, with reported 1-year survival rates of 39–56%.

The main approach to treating PML is to use ART to reverse the immunosuppression that interferes with the normal host response to the virus. In a retrospective study of 118 patients with PML who received ART, 63.6% survived for a median of 114 weeks after diagnosis. However, if the diagnosis is delayed, PML can be associated with high morbidity and mortality despite treatment. Unfortunately, in India, patients often present late with advanced immunosuppression, which can result in a poor prognosis. It is crucial to address the lack of diagnostic and management services for these patients in India.[6–9]

Conclusion

Progressive multifocal leukoencephalopathy is a rare disease that requires support from radiography and clinicopathological correlation for proper diagnosis. Early and efficient diagnosis is highly desirable, and the examination of CSF need not be positive. Unfortunately, there is no established cure for PML, so the goal of treatment is to prolong the patient's life. Most cases of PML are found in people who are HIV-positive, so early and effective antiretroviral therapy remains the mainstay of treatment.

Ethics Approval

All the study procedures of this case report were conducted according to the Declaration of Helsinki.

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