Case Report

A rare case of Progressive Multifocal Leukoencephalopathy

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Abstract

Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating disease of the central nervous system. It is characterized by widespread lesions caused due to lytic infection of the oligodendrocytes by John Cunningham Virus (JCV), especially in immunocompromised individuals. We report a case of a 36 year old man, a known HIV positive case on Anti-Retroviral Therapy (ART) for 15 years, who was admitted to a tertiary care hospital in Tamil Nadu, South India with history of difficulty in walking, weakness and pain of the lower limbs, involuntary micturition, intermittent altered sensorium, loss of weight and appetite. He was diagnosed to have PML through neuro-imaging studies, serum JC viral antibodies assay and cerebrospinal fluid JCV real time polymerase chain reaction (PCR) assay. We report this rare case of PML in view of its potential interest and we also review literature regarding its etiopathogenesis, diagnosis and management.

Keywords: demyelination, HIV, JC Virus, Progressive Multifocal Leukoencephalopathy

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Introduction

Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating disease of the central nervous system. It is characterized by widespread lesions caused due to lytic infection of the glial cells, especially oligodendrocytes by the JC virus.[1] The JC virus, which was named after a patient John Cunningham, is a human polyomavirus which was formerly known as papovavirus.[1] JCV enters the central nervous system by crossing the blood-brain barrier and infects oligodendrocytes and astrocytes through the $5HT_{2A}$ serotonin receptor.[2] PML is a rare disease that develops in patients with underlying immunosuppressive conditions like Acquired Immunodeficiency Syndrome (AIDS) caused by the Human immunodeficiency virus (HIV), lymphoproliferative diseases, in those undergoing antineoplastic therapy, after stem cell and organ transplantations and in immune-therapies with some monoclonal antibodies.[1,3] This case report briefly highlights the clinical presentation of PML in an HIV patient, the difficulty in diagnosis, the etiopathogenesis and the management.

Case Presentation

A 36 year old man came to the OPD with the complaints of difficulty in walking, weakness and pain of the lower limbs for the past 4 months and involuntary micturition for the past 2 months. He was a known HIV positive case on Anti-Retroviral Therapy (ART) for 15 years. There was a history of intermittent altered sensorium in the past 6 weeks. There was no history of seizures or fever. There was a history of loss of weight and appetite. He was not a diabetic or hypertensive. He was a smoker and an occasional alcoholic.

On clinical examination, there was generalized wasting and the patient was anemic. The vitals were normal. The examination of the cardiovascular system, respiratory system and abdomen were normal. On examination of the central nervous system, there was no sign of neck rigidity. The tone was almost normal in all the 4 limbs. The power was normal in the upper limbs (5/5) whereas it was slightly reduced in the lower limbs (4/5). The deep tendon reflexes were brisk in all the 4 limbs. The cerebellar function tests and the sensory system examination were normal. All the cranial nerves except facial nerve were normal; there was Bell's palsy of the right facial nerve. The speech was normal. There were no involuntary movements and there was an ataxic gait.

The routine investigations were done. The complete hemogram showed a decreased RBC count (3.1 million/mm^3), moderate anemia (Hb = 8.2g/dl) and leukocytosis (13,000/mm^3) whereas the platelet count was normal. The liver function tests and renal function tests were near normal. The C -reactive protein (CRP) level and Erythrocyte Sedimentation Rate (ESR) were elevated. The CD4 counts were 450/mm^3. The urine routine was normal except for occasional pus cells.

The CT brain showed asymmetric focal zones of low attenuation involving the periventricular and subcortical white matter. The MRI brain showed asymmetric diffuse flair/T2 hyperintensity in the bilateral periventricular white matter and subcortical U fibres with diffuse cortical atrophy and prominent sulcal spaces and dilated ventricles, which was reported as being probably due to Progressive Multifocal Leukoencephalopathy. There was no significant abnormality in MR angiography of the circle of Willis and in the cerebral MR Venogram. The serum JC viral antibodies assay and CSF (through Lumbar puncture) JCV Real time PCR assay had given positive results for the presence of JCV.

The patient was started on Highly Active Anti-Retroviral Therapy (HAART) along with supportive treatment and was asked to come for frequent follow-up consultations.

Discussion

The differential diagnoses included - Progressive Multifocal Leukoencephalopathy, HIV Encephalopathy, Atypical Creutzfeldt Jakob Disease, Toxic Leukoencephalopathy and Paraneoplastic Syndromes of the CNS. The CT and, especially MRI findings in this case were more typical of PML which helped in differentiating from the other differential diagnoses. The diagnosis of PML is very difficult due to its vague clinical presentation as seen in this case. The MRI findings, serum JC viral antibodies assay and CSF JCV Real time PCR assay helped in clinching the definitive diagnosis.

JCV is a small non-enveloped double-stranded DNA virus.[1] The promoter sequence of JCV contributes to the aggression of the virus in the CNS and therefore results in the development of PML.[1] 14 subtypes of JCV have been identified specific to different geographical regions.[3] Subtype 2D is found in Indians.[3]

PML is associated with both HIV-1 and HIV-2.[4] HIV infection accounts for around 85% of the total cases.[5] HIV-associated PML also occurs following Highly Active Anti-Retroviral Therapy (HAART) during immune recovery.[6] Majority of patients with HIV infection develop PML in poor immunological status with low CD4 count (<200/µL).[7] There are few reports describing PML in HIV-infected patients with better immunological function (CD4 count >500/µL).[7] In this case, PML had occurred with a relatively high CD4 count (450/µL). A Brain Biopsy depicting characteristic histopathological features of PML like demyelination, enlarged oligodendroglial nuclei and bizarre astrocytes would have been more diagnostic,[8] which could not be done in this case.

As of now, there is no appropriate treatment for PML; however, drugs such as cidofovir, interferons and heparin sulfate have been in trials for treating PML.[9] The multifunctional viral proteins including large T antigen (LT-Ag) and Agnoprotein which are involved in cell cycle progression and viral replication need to get targeted that could lead to novel ways of managing PML.[10]

Conclusion

This case report highlights the clinical presentation, etiopathogenesis and management of Progressive Multifocal Leukoencephalopathy and the need for multidimensional diagnostic methods. Though it is one of the rarest opportunistic infections in HIV patients, considering its fatality, there is an urgent need for the development of new specific drugs for the effective management of PML.

Acknowledgment: Nil

Conflicts of interests: Nil

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