Case Report
Progressive Multifocal Leukoencephalopathy (PML)
Presenting as Intractable Dystonia in an HIV-Infected Child

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Summary
Progressive multifocal leukoencephalopathy (PML) has been described in adult immunocompromised patients and has a progressive downhill course. Though dementia and motor disturbances have been described, intractable dystonia is a very unusual manifestation. In children, PML is very rare and often misdiagnosed as other central nervous system (CNS) encephalopathy. No definitive treatment is available.

Introduction
Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease of the central nervous system (CNS) seen in immunocompromised patients. It is caused by primary infection or reactivation of the JC virus.\textsuperscript{1} Mean survival after the onset of symptoms is 6–9 months whereas patients with AIDS on highly active antiretroviral therapy (HAART) may survive upto 2 years.\textsuperscript{2} Brain biopsy remains the definitive way to confirm a diagnosis of PML. However, MRI may help to identify and distinguish PML from other CNS lesions due to its characteristic imaging abnormalities.\textsuperscript{3,4} HAART is currently used to treat HIV-positive patients who develop PML. There is no proven treatment specifically for PML although several drugs have been tested. PML is found in 4–7% of adult patients with AIDS but incidence in HIV-positive children is lacking.\textsuperscript{5} We report a case of PML in an 8½-year-old female child with AIDS who presented with severe dystonia.

Case Report
An 8½-year-old girl was referred to our Pediatric HIV Clinic, Mumbai in August 2003 with severe dystonia on the right side of the body and inability to talk, eat or sit since 15 days.

One year ago, she was admitted in a tertiary general hospital with generalized tonic clonic seizures and loss of consciousness for 3 days. At that time she was diagnosed to be HIV positive by a positive HIV ELISA test and confirmed by a positive Western blot test. Her father had died of AIDS and mother was also HIV positive. Her lumbar puncture was done at that time, which was normal, and showed CSF picture of 5 lymphocytes/cumm, proteins = 36 mg%, sugar = 50 mg/dl and a blood sugar of 70 mg/dl. Her cerebrospinal fluid (CSF) Herpes simplex virus PCR was negative. An MRI of brain was done at the same time, which showed hyperdensities in left occipital lobe, left cerebral peduncle and left lentiform nucleus. She was diagnosed with tuberculous vasculitis, though the MT test was negative and X-ray chest normal. She was treated with anti-tuberculous therapy and discharged. She improved clinically but had right-sided dystonia at that time that was controlled with Benzhexol.

On presentation to us, she had bilateral multiple significant discrete cervical and axillary lymph nodes. She was malnourished with weight being 13 kg.

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Fig. 1. HIV-positive child with PML and intractable dystonia.
Though she was conscious, she was not oriented to time, place or person. She had spasticity in all the four limbs with painful dystonia on the right side (Fig. 1). Her deep tendon reflexes were brisk with positive Babinski’s sign. There was no evidence of meningitis or raised intracranial tension. Apart from a mild hepatomegaly, other systemic examination was normal. MRI brain was repeated, which showed asymmetrical subcortical, right frontoparietal, left occipitoparietal and left basal ganglia lesions hypointense on T1 and hyperintense on T2 weighted images with no post-contrast enhancement suggestive of PML (Fig. 2). CSF JC virus PCR could not be done due to non-availability of the facility. Her CD4 count was 320 cells/cumm with CD8 of 1363 cells/cumm and CD4:CD8 ratio of 0.23 suggestive of severe immune suppression. Her repeat CSF examination was normal. In view of MRI suggestive of PML and immunosuppression, she was started on HAART (AZT + 3TC + EFV + NLF). She was treated with Benzhexol, Baclofen, Tetrabenzene and Diazepam for the dystonia, which has not shown any improvement. On follow-up after a period of 6 months, her CD4 count had increased to 640 cells/cumm, she was able to recognize her mother and eat orally, however, the dystonia has remained the same. She is still unable to sit or turn her body as any movement precipitates a painful dystonia. No adverse effects of antiretroviral therapy have been noted and her biochemistry has remained normal.

**Discussion**

Progressive multifocal leukoencephalopathy caused by group B Human Papovaviruses
(Jacob-Creutzfeldt virus, simian virus 40) results in the destruction of oligodendroglia leading to extensive demyelination. Astrom et al. first described PML in 1958 in association with chronic lymphocytic leukemia and Hodgkin’s disease. Recently, it has been increasingly found in patients with AIDS and has been associated with immunocompromised patients such as patients with lymphoma, leukemia, carcinomatosis and AIDS. The majority of the population is believed to have been exposed to this virus leading to asymptomatic carriage in the kidneys, lymphoid tissue, bone marrow and lymphocytes. In a patient with weakened immune system, the virus may reactivate and spread to the brain by lymphocytes causing neurologic dysfunction and serious and life-threatening disease. 

PML can cause a variety of symptoms such as confusion, disorientation, lack of energy, loss of balance, motor system abnormalities, blurred or double vision, speech difficulties, loss of vision in one eye, dementia and ultimately death. The resulting demyelination is at first patchy involving subcortical regions and then spreads to deep white matter in confluent pattern.

Though brain biopsy remains the confirmative test for diagnosis of PML, brain scans such as MRI or CT scans can reveal the presence of lesions in the brain. An MRI scan depicts lesions of low T1 signal intensity and high proton density on T2 weighted images with absence of edema, mass effect and post-contrast enhancement as was seen in our patient. In AIDS patients, PML increasingly occurs in unusual locations with primary involvement of cortex, basal ganglia, thalamus, cerebellum and brainstem in up to 50% of patients as was seen in our patient. DNA PCR tests to determine the presence of JC virus in CSF specimen are also used, however, the PCR test does not produce a definitive diagnosis because some patients are JC-negative when diagnosed with PML.

Prior to the introduction of HAART, patients with AIDS and PML survived for 6–9 months but HAART may prolong survival depending on their baseline CD4 count as was seen in our patient where her CD4 count did improve but due to irreversible changes in the brain, the dystonia has remained the same. There have been anecdotal reports of use of Cidofovir, cytarabine and interferon alpha as possible treatment for PML but their benefit seems minimal. The overall prognosis is poor.