

Progressive Multifocal Leukoencephalopathy in HIV as First Presentation: A Case Report

Dr Jingyasa Swain¹, Dr Taranisen Sethi¹, Dr Shradhanjali Pani², Dr Bitan Mohanty²,
Dr Saumya Ranjan Sahoo³

¹Postgraduate Department of General Medicine VIMSAR

²Postgraduate Department of General Medicine VIMSAR

³Postgraduate Department of General Medicine VIMSAR

Abstract: *Progressive multifocal leukoencephalopathy is a rare and late manifestation of AIDS caused by JC virus infection. A 40year old male presented to us with complaints of difficulty in speaking, altered behavior and generalized weakness, he was provisionally diagnosed to be a case of stroke. His laboratory report was positive for HIV. Later imaging as well as laboratory testing was done and he was diagnosed to be a case of progressive multifocal leukoencephalopathy which is the first manifestation in our case rarely reported in Indian literature. This patient unfortunately died after 1month.*

Keywords: PML HIV, PMLE, Progressive multifocal leukoencephalopathy, demyelinating disease in HIV

1. Introduction

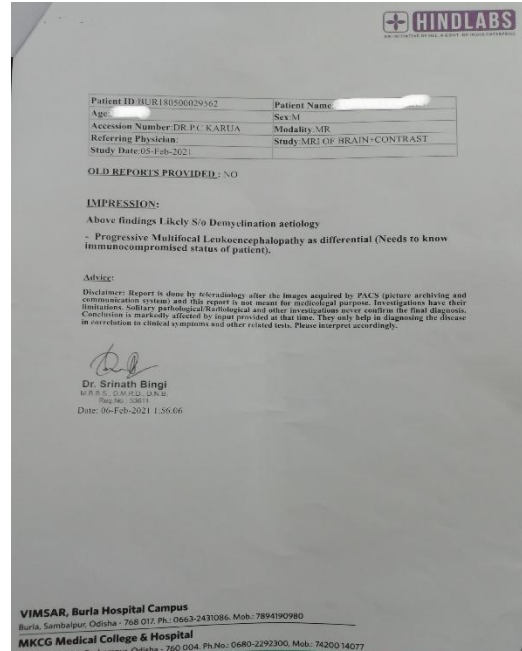
PMLE is a rare disorder caused by JC virus and usually seen in patients with severe deficits in cell mediated immunity. Common cause includes AIDS (82%), followed by hematological malignancies (8%), transplants recipients (3%), chronic inflammatory diseases (2%), and immunosuppressive drugs^{1, 2}. It is pathologically characterized by widespread demyelination of varying size often involving cerebral hemispheres, more than brainstem and cerebellum but sparing the spinal cord and optic nerves. Patients commonly have gradually progressive multifocal neurologic deficits, with or without mental impairment. Typically, patients survive up to 6–9 months from the onset of symptoms, however survival prolongs up to 2 years following institution of HAART³. Brain biopsy remains the gold standard to confirm the diagnosis. However, MRI helps to identify and differentiate PML from similar CNS lesions due to its unique imaging abnormalities^{4, 5}. HAART is recently used to treat PML in HIV patients. However, no treatment has been established for PML in spite of several drug study. It is estimated that PML found in 1-4% patient with HIV AIDS, however as late manifestation¹². Here, we report a case of progressive multifocal leukoencephalopathy as the first manifestation of AIDS which is rare in India.

2. Case Presentation

A 40year male patient presented with complains of altered behavior which was gradually progressive with difficulty in speaking past 20 days associated with gradually progressive generalized weakness and decreased appetite since last 15 days. There was no history of loss of consciousness, headache, seizure, fever, vomiting, visual symptoms, sensory complaints. Patient is a chronic alcoholic. No other relevant personal history was obtained. Patient having average body built with normal vital and general examination.

On neurological examination patient is conscious and inattentive. Mini Mental State Examination score (MMSE) was 20/30 with severely impaired registration,

recall and calculation. Speech is dysarthric and non-fluent with impaired writing and repetition with intact naming, reading and comprehension. Working memory was lost. On lobar function test, there is failed executive function, abstract thinking with intact insight. Agraphia and acalculia is present without left-right confusion or motor apraxia or agnosia. Cranial nerve examination was normal. Motor examination revealed generalized hyperreflexia, Plantar showed extensor response on both sides, tone and power was normal with intact sensory examination. Cerebellar sign was present bilaterally including dysdiadochokinesia, tandem walking. Gait was wide based with difficulty in initiation and turning. Other system examination was normal. An initial diagnosis of stroke was contemplated. Routine investigations revealed an elevated ESR, normal liver enzymes, normal electrolytes, normal renal function test, normal ECG and chest X-ray. His HIV card test came to be positive which was confirmed by ELISA and western blot. The absolute CD4 count was 250/ μ L. His MRI of brain showed multifocal areas of T1 hypointense, T2, FLAIR hyperintense areas involving grey matter and subcortical white matter of bilateral frontal and parietal region without showing postcontrast enhancement or mass effect. Cerebrospinal fluid examination (CSF) was normal. The CSF PCR for JCV could not be done due to non-availability of the facility. Patient was treated with HAART along with other supportive medication, but unfortunately patient's condition deteriorated, and he died after 4weeks of admission to hospital.



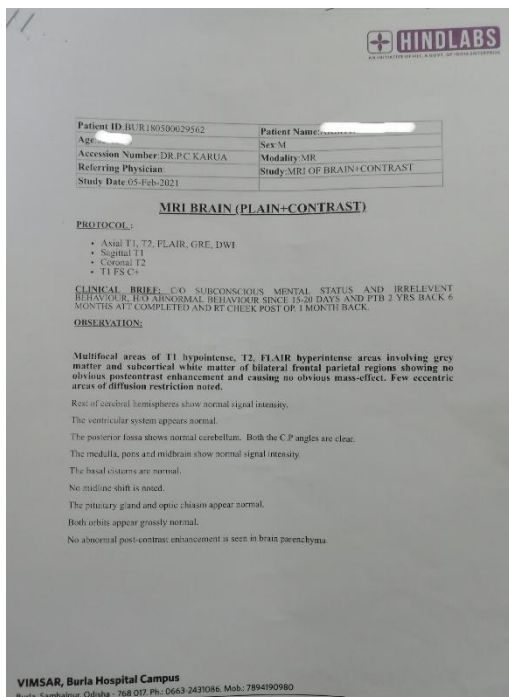
3. Discussion

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease which usually affects the white matter in which infection of astrocytes and oligodendrocyte occurs in forms of lysis^{8, 9}. This is first observed clinically by Adams in 1952, was described morphologically in 1958 by Åstrom and coworkers, and then with a larger body of material by Richardson in 1961. Infection by JCV (John Cunningham virus) is the causative agent of PML. It is assumed to be dormant in the bone marrow or kidney and active replication occurs when immunocompromised state transpires¹³. Through surface receptor virus enters into oligodendrocytes results in enlargement of nuclei of oligodendrocytes and contain abnormal viral inclusion. Leads to cell destruction and resulting in demyelination.

Progressive multifocal leukoencephalopathy is the result of the reactivation of a latent infection rather than of initial infection⁷. PML lesions mostly occur in the subcortical white matter with both hemispheres being affected, the parieto-occipital region being the most common location¹⁰. Lesions also occur in the cerebellum, brain stem, thalamus and in the spinal cord.

Manifestations of the disease includes motor weakness, appendicular ataxia and visual symptoms, altered mental status. Lesions of white matter that corresponds to significant cortical areas sometimes manifests symptoms of a cortical disorder (e. g., agnosia, aphasia)¹¹. Seizures can be present in 18% of patients with PML affecting grey matter cortical area¹¹.

Although diagnosis of PML confirmed by brain biopsy, neuroimaging (MRI or CT scans) of brain can suggest the presence PML lesions in the brain^{3, 4}. MRI scan depicts multifocal areas of T1 hypointense, T2, FLAIR hyperintense lesions involving grey matter and subcortical white matter of bilateral frontal and parietal region without showing postcontrast enhancement or mass effect was



seen in this patient. PCR amplification of JCV DNA from CSF has become an important diagnostic tool, however, the sensitivity of PCR test variable so cannot be used as definitive diagnosis and a negative report does not exclude the diagnosis⁶. If treatment deferred, and immunosuppression not improved, majority of patients dies within 3 to 6 months of onset of symptoms and may be more rapidly in patients with HIV unless treated with cART.

4. Conclusion

In our case PML manifest as first presentation in HIV having limited publication which requires further study and research.

Conflict of Interest: No

References

- [1] Eng PM, Turnbull BR, Cook SF, Davidson JE, Kurth T, Seeger JD. Characteristics and antecedents of progressive multifocal leukoencephalopathy in an insured population. *Neurology* 2006; 67: 884-6.
- [2] Holman RC, Janssen RS, Buehler JW, Zelasky MT, Hooper WC, Epidemiology of progressive multifocal leukoencephalopathy in the United States: analysis of national mortality and AIDS surveillance data. *Neurology* 1991; 41: 1733-6
- [3] Berenguer J, Miralles P, Arrizabalaga J, Ribera E, Drona F, Baraia-Etxaburu J et al. Clinical course and prognostic factors of progressive multifocal leukoencephalopathy in patients treated with highly active antiretroviral therapy. *Clin Infect Dis* 2003; 36: 1047-52.
- [4] Thurnher MM, Donovan Post MJ, Rieger A, Kleible-Popov C, Loewe C, Schindker E. Initial and follow-up MR imaging findings in AIDS-related progressive multifocal leukoencephalopathy treated with highly active antiretroviral therapy. *AJNR Am J Neuroradiol* 2001; 22: 977-84
- [5] Post MJ, Yiannoutsos C, Simpson D, Booss J, Clifford DB, Cohen B, McArthur JC, Hall CD. Progressive multifocal leukoencephalopathy in AIDS: Are there any MR findings useful to patient management and predictive of patient survival? AIDS Clinical Trials Group, 243 Team. *AJNR Am J Neuroradiol* 1999; 20: 1896-906
- [6] Hou J, Major EO. Progressive multifocal leukoencephalopathy: JC virus induced demyelination in the immune compromised host. *J Neurovirol* 2000; 6 (Suppl 2): S98-S100
- [7] Chalkley JJ, Berger JR. Progressive multifocal leukoencephalopathy in multiple sclerosis. *Curr Neurol Neurosci Rep.* 2013; 13 (12): 408. doi: 10.1007/s11910-013-0408-6. [PubMed: 24136456]
- [8] Major EO: Progressive multifocal leukoencephalopathy in patients on immunomodulatory therapies. *Annu Rev Med* 61: 35-47, 2010.
- [9] Wuthrich C, Cheng YM, Joseph JT, Kesari S, Beckwith C, Stopa E, Bell JE and Korolnik IJ: Frequent infection of cerebellar granule cell neurons by polyomavirus JC in progressive multifocal leukoencephalopathy. *J Neuropathol Exp Neurol* 68 (1): 15-25, 2009
- [10] Gray F, DeGirolami U and Poirier J: Escourolle & Poirier's Manual of Basic Neuropathology. 4th ed.: Butterworth Heinemann, 2003.
- [11] Prayson RA: Neuropathology. 1st ed.: Elsevier, Churchill Livingstone, 2005
- [12] Kasper DL, Fauci AS, Hauser S, et al, editors. Harrison's principles of internal medicine, 20th ed. New York: The McGraw-Hill Companies; 2018. 1445p
- [13] Ropper, A. H., Adams, R. D., Victor, M., Brown, R. H., & Victor, M. Adams and Victor's principles of neurology, 11th ed. New York: McGraw-Hill Medical Pub; 2019. 786p