ISSN - 2394-7721

American Journal of Oral Medicine and Radiology

Journal homepage: www.mcmed.us/journal/ajomr

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY – A CASE REPORT

Guru T. Arun[1], Deivam S[2], Prabhu N[3*]

Department of Radiodiagnosis[1], Skin and STD[2], Microbiology[3], Chennai Medical College Hospital and Research Centre (SRM Group), Tiruchirapalli, India.

Article Info

Received 23/01/2015
Revised 16/02/2015
Accepted 19/03/2015

Key words:- PML, AIDS patients, MRI, temporoparietal subcortical white matter.

ABSTRACT

Progressive multifocal leucoencephalopathy (PML) is a demyelinating disease of the central nervous system which affects the white matter and cause by the reactivation of HIV. We report the case of 55 year old man with HIV for 14 years and have increasing left sided hemiparestesia to coordination disorder. While he underwent radiodiagnosis, MRI showed asymmetrical areas of high signal intensity on T2 and FLAIR weighted sequences on pons, dorsal midbrain, bilateral frontal and right temporoparietal subcortical white matter without mass effect and contrast enhancement. Retrospectively, patient was examined for JC-virus and was found to be positive. The epidemiology of the disease has changed and the majority of cases now occur in association with acquired immunodeficiency syndrome (AIDS). MR imaging is the preferred imaging method for diagnosis of PML. Typically, PML appears as widespread, asymmetric lesions in the white matter. The lesions are focal, discrete and asymmetrical. HAART at present is the most effective treatment for PML. It is postulated that HAART reduces the viral load and thus improving the immune function.

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a rare and usually fatal viral disease characterized by progressive damage or inflammation of the white matter of the brain at multiple locations [1,2]. PML has since been reported in patients with other hematological malignancies (such as lymphomas) or connective tissue diseases and in transplant patients and patients receiving long-term treatment with immunosuppressive agents [3]. The complication of various conditions which result in impaired cellular immunity are lymphoproliferative disorders, chronic granulomatous disorders such as sarcoidosis, iatrogenic immunosuppression, cancer chemotherapy and autoimmune disorders [4]. In general, PML has a mortality rate of 30-50 percent in the first few months and those who survive can be left with varying degrees of neurological disabilities. PML occurs almost exclusively in patients with severe immune deficiency, most commonly among patients with acquired immune deficiency syndrome (AIDS), but people on chronic immunosuppressive medications including chemotherapy are also at increased risk of PML, such as patients with transplants, Hodgkin's Lymphoma, multiple sclerosis, psoriasis and other autoimmune diseases.

The occurrence of PML in persons without known immunosuppression is exceedingly rare. Although traditionally associated with conditions of cellular immunocompromized the concept that profound cellular immunosuppression is required for the reactivation of the JC virus has recently been challenged [5,6]. HIV-associated PML also occurs during immune recovery following the initiation of highly active antiretroviral therapy (HAART). Such cases are associated with an inflammatory reaction in brain lesions and contrast enhancement on neuroimaging studies [7,8]. The outcome

Corresponding Author

Prabhu N
Email: - leptoprabhu@gmail.com

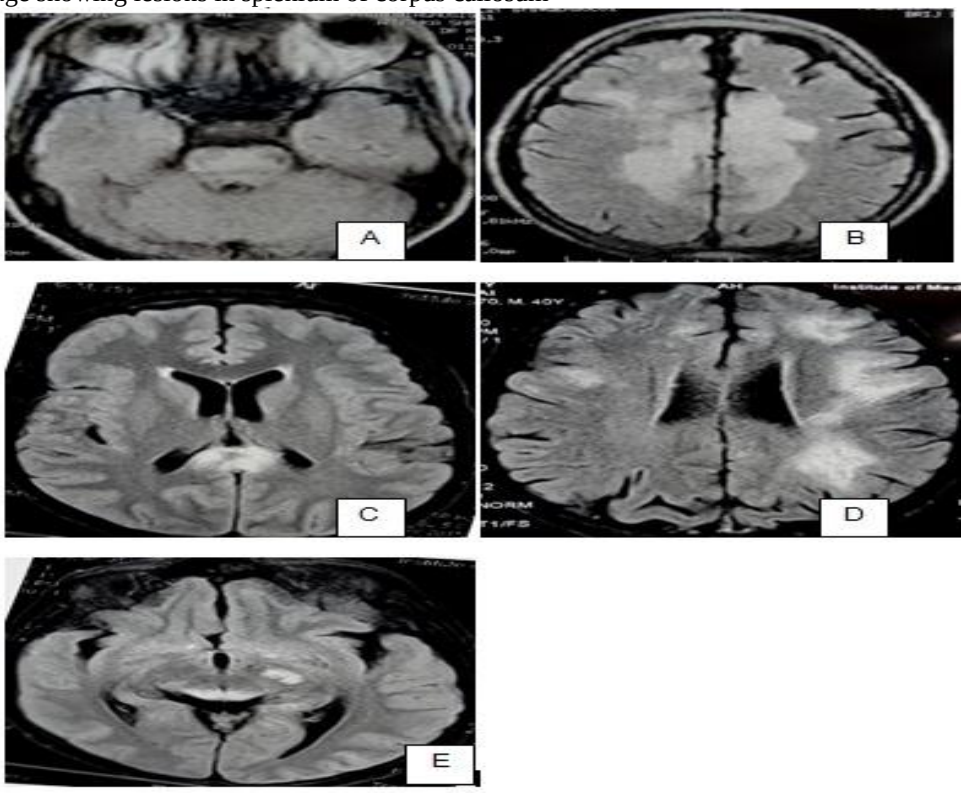
of inflammatory PML is more variable than that of PML in end-stage AIDS. Most patients with HIV infection develop PML in the setting of a poor immunological status expressed by a low CD4 cell count (<200/µL). Very few reports have described of PML in HIV-infected patients in the setting of better immunological function (ie, CD4 counts >500/µL) [9].

By observing this case, we review the clinical presentation, diagnosis including radiology, current treatment options and the outcome of progressive multifocal leukoencephalopathy in HIV patients with involvement of white matter and possible affecting regions are the cerebral hemispheres followed by subtentorial lesions.

Case report

A 55 year old male with human immunodeficiency virus (HIV) for 14 years had a 4 week history of increasing left sided hemiparestesia, ataxic gait, dysarthric speech and coordination disorder. His history revealed that he had a headache that started 4 weeks ago and did not respond to usual analgesics. The symptoms worsened slightly and he developed left hemiparesis. The past history revealed that the patient is undergone highly active antiretroviral therapy (HAART), during interview it was noted that he was incomplaint and interrupted his medications many times. He did not take HAART therapy and the general physical examination was normal except the presence of lipidystrophy. Physical examination revealed ataxic gait and no other motor or sensory deficit. The CD4+ count was 140 cells/ mm3 at the time of PML diagnosis. MR imaging was performed. MRI showed asymmetrical areas of high signal intensity on T2 and FLAIR -weighted sequences on pons, dorsal midbrain, bilateral frontal and right temporoparietal subcortical white matter without mass effect and contrast enhancement (Figs. 1 – A,B,C,D,E). Deep gray matter structures were spared. Retrospectively, patient was examined for JC-virus and was found to be positive.

Progressive Multifocal Leukencephalopathy in patients with acquired immuno deficiency syndrome (PML)
Fig A & E: White matter lesions seen on pons & dorsal midbrain shown on FLAIR image.
Fig B & D: FLAIR image showing Predilection for subcortical white matter lesions
Fig C: FLAIR image showing lesions in splenium of corpus callosum



DISCUSSION

Progressive multifocal leucoencephalopathy (PML) was first diagnosed by a German neuropathologist, Hallervorden in 1930. It was described as a syndrome in 1958 by Astrom and Richardson and identified as a viral disease in 1965 by ZU-Rhein. The JC virus was isolated in 1971 by Padgett and Walker which is a DNA containing Polyomavirus [10]. Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating

infection of the CNS caused by a polyomavirus, the JC virus and it usually occurs in immunodeficient patients, caused by the JC papovavirus, a DNA virus, has been shown to persist in the kidneys and is shed in the urine. More than 80% of the human adult population is seropositive for JC virus specific IgG antibodies. It typically has caused death within 2½ to 4 months of diagnosis [11].

Originally, over 60% of cases of PML occurred in the setting of immunologic compromise from lymphoproliferative or myeloproliferative disorders [10,11]. In the past two decades the epidemiology of the disease has changed and the majority of cases now occur in association with acquired immunodeficiency syndrome (AIDS) [1]. The incidence of PML has increased significantly and now HIV associated cases account for upto 85% of all cases of PML [12]. PML has been estimated to affect 4% of patients with HIV infection and it is associated with AIDS has dramatically increased the frequency of and death rate from PML [1,7,8].

The clinical features are of progressive focal neurological dysfunction. Commonly aphasia/dysathria, monoparesis, hemiparesis, ataxia, cortical blindness or visual field defects are reported. Mental status changes like confusion, dementia and even coma are seen. Seizures are infrequent (<10%). There are no clinical features of raised intracranial pressure or of systemic infection [12]. Clinically, it presents as relentlessly progressive focal central nervous system dysfunction, such as hemiparesis, aphasia, cortical blindness, or altered mental states [10].

This virus causes extensive myelin breakdown and white matter destruction, because of its targeting of the oligodendrocytes in severely altered cellular immunity [7]. The CSF biochemistry and cytology is normal. In CSF, detection of JC virus by PCR is diagnostic. The sensitivity and specificity are 70% and 90-100% respectively. In negative PCR for JC virus repeat CSF examination or brain biopsy [8] which is confirmatory for diagnosis. The recent improvements in newer imaging techniques like MR spectroscopy are replacing the older invasive methods for diagnosing PML [9]. The MR imaging is the preferred imaging method for diagnosis of PML [12]. Typically, PML appears as widespread, asymmetric lesions in the white matter. The lesions are focal, discrete and asymmetrical if bilateral [7]. They are predominantly subcortical white matter lesions involving arcuate (U) fibres. The lesions spare periventricular regions and are dominantly located in parieto-occipital lobes. The lesions are hypointense on T1W and hyperintense on T2W and FLAIR images. Typically no mass effect is seen and contrast enhancement is rare. Both cortical and subcortical atrophy is not seen. Contrast enhancement may be seen in some cases, particularly with techniques such as magnetization transfer contrast that suppress the background signal intensity of white matter.

The absence of mass effect and enhancement has been used to distinguish PML from other entities that occur frequently in the immunocompromised host, such as lymphoma and toxoplasmosis. The partial resolution may occur spontaneously or, more commonly, after chemotherapy. In MR Spectroscopy, there is decreased N-acetylaspartate (NAA) with significantly decreased NAA/ Creatine ratio with increased choline and increased lactate peak. It has been suggested that such imaging features as increasing atrophy, confluence of lesions and increasing hypointensity on T1-weighted images and increasing high signal intensity on subsequent T2-weighted and fast-FLAIR images could be used as indicators of a poor prognosis in AIDS patients with PML [3,4,12].

CONCLUSION

The common differential diagnoses of PML are Toxoplasmosis, Cryptococcus, AIDS Dementia Complex, CNS Lymphoma and CNS Tuberculosis. Currently there is no proven therapy for AIDS related PML. Cidofovir (an antiviral agent with activity against JC Virus) appears to have no additional benefit over HAART administration alone. HAART at present is the most effective treatment for PML [12,13]. It is postulated that HAART reduces the viral load and thus improving the immune function. Further investigation required to confirm the PML stages.

REFERENCES

1. Berger J. (2003). Progressive multifocal leukoencephalopathy in acquired immunodeficiency syndrome: explaining high incidence and disproportionate frequency of the illness relative to other immunosuppressive conditions. *J Neurovirol*, 9, 38-41.
2. McCalmont V, Bennett K. (2007). Progressive multifocal leucoencephalopathy: a case study. *Prog Transplant*, 17, 157-160.
3. Haider S, Nafziger D, Gutierrerz JA, Brar I, Mateo N, Fogle J. (2003). Progressive multifocal leukiencephalopathy and idiopathic CD4+ lymphocytopenia: a case report and review of reported cases. *Clin Infect Dis*, 31, 20-22.
4. Sharma SK, Soneja M, Ranjan S, Miglani S, Hari S, Sinha S, Wig N. (2013). Progressive multifocal leucoencephalopathy in HIV/ AIDS: observational study from a tertiary care centre in Northern India. *Ind J Med Res*, 138, 72-77.
5. Vaklavas C, Rafiq EPS, Lovy J, Escobar MA, Tsimberidou M. (2010). Progressive multifocal leucoencephalopathy in a patient without apparent immunosuppression. *Vir J*, 7, 256-260.
6. Smolle E, Trojan A, Schuster SJ, Haybaeck J. (2014). Progressive multifocal leucoencephalopathy – a case report and review of the literature. *In vivo*, 28, 941-948.

7. Vendrely A, Bienvenu B, Gasnault J. (2005). Fulminant inflammatory leukoencephalopathy associated with HAART-induced immune restoration in AIDS-related progressive multifocal leukoencephalopathy. *Acta Neuropathol (Berl)*, 109, 449-455.
8. Weissert R. (2011). Progressive multifocal leukoencephalopathy. *J Neuroimmunol*, 231, 73-77.
9. Delobel P, Brassat D, Delisle MB, Scaravilli F, Clanet M. (2004). Progressive multifocal leukoencephalopathy in an HIV patient with normal CD4 T-cell count and magnetic resonance imaging. *AIDS*, 18, 702-704.
10. Cinque P, Koralnik I, Clifford D. (2003). The evolving face of human immune deficiency virus related progressive multifocal leukoencephalopathy: a defining a consensus terminology. *J Neurovirol*, 9, 88-92.
11. Sacktor N. (2002). The epidemiology of human immunodeficiency virus associated neurological disease in the era of highly active antiretroviral therapy. *J Neurovirol*, 8, 115-121.
12. Rosca O, Rosca EC, Negrutiu L. (2011). Progressive multifocal leukoencephalopathy – a case report. *Rev Rom De Boli Infect*, 14, 95-97.
13. Koralnik IL. (2006). Progressive multifocal leucoencephalopathy revised: has the disease outgrown its name. *Ann Neurol*, 60, 162-173.