Progressive Multifocal Leucoencephalopathy: Report of Two Diverse Cases

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Abstract:
Progressive Multifocal Leucoencephalopathy (PML) is a rare neurological disorder. The clinical suspicion about this disease in the setting of an immunosuppressive patient even in presence of vague neurological symptoms has to be very high . We describe here two cases of PML a post renal transplant patient and second elderly patient with no underlying immunosuppression.

Keywords: PML, JC virus, Renal transplant.

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Introduction

PML is a progressive disorder characterized by multifocal areas of demyelination. It is a rare and fatal disease. Pathologically there is inflammation of the white matter of brain at multiple locations. With demyelination, the axons of the nerve cells are destroyed, impairing the transmission of nerve impulses. Symptoms include weakness, paralysis, vision less, impaired speech and cognitive deficits. It is different from MS in that it destroys the cells producing myelin unlike MS which attacks myelin only. As such it progresses rapidly. Diagnosis is made by MRI, CSF PCR for JC virus and Brain Biopsy. No cure is known. Disease may stop with improvement in immune system

Case Scenario 1

A 40 year old male who had undergone kidney transplant 3 months prior to for end stage renal failure and was on immunosuppressive therapy in the form of Azathioprine 50mg twice daily presented to our Out patient dept .with chief complaints of Headache of one week duration. It was more on right side, throbbing, present throughout the day and even woke him up during night. There was associated history of one episode of generalized seizure. There was no history of vomiting, nausea, trauma, fever, rash. Weakness of any side or cranial nerve dysfunction Patient had taken analgesics with partial relief. Systemic examination including neurological examination .was normal. Investigations revealed a normal CT scan (Fig.1). CSF showed raised proteins with no cells and negative gram/AFB/India ink .MRI Brain showed a demyelinating lesions in the right parietal lobe and left occipital suggestive of PML (Fig 2 and 3). CSF PCR for JC virus could have aided in the diagnosis but the facility is not available in INDIA The immunosuppresents were stopped and patient was put on anti convulsants The patient had initial improvement but succumbed to his illness after 4 months.

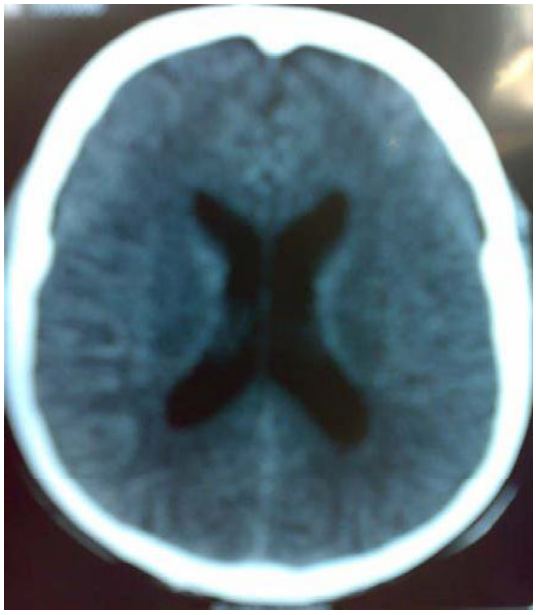

Fig. (1). of Case 1: Normal CT of patient.

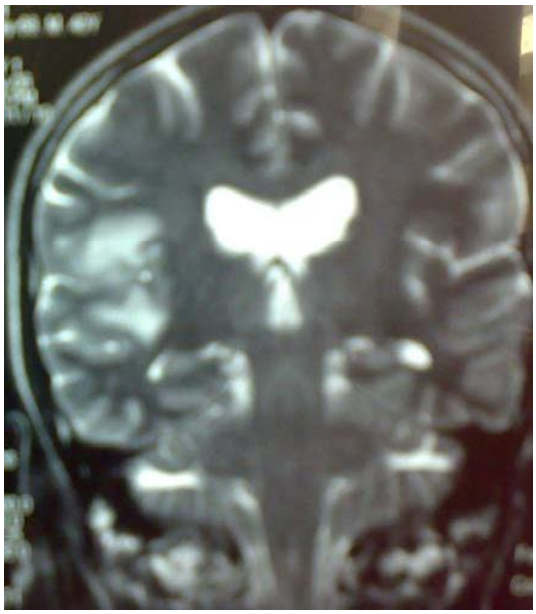

Fig. (2). MRI T2 image of Right Temporal Hyperintense image.

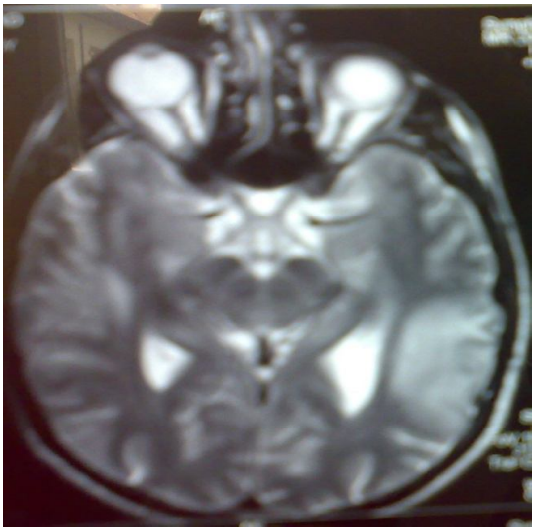

Fig. (3). Case 1: T2 w image Left Parieto-occipital hyperintense image.

Case Scenario 2

A 65 years old male presented to us with the history of forgetfulness (more for recent memory than remote memory) for the last six months. There was associated history of occasional headaches and recurrent chest infections. Examination revealed a conscious, cooperative, oriented patient with normal systemic examination. Neurological examination revealed mini mental scoring (MMSE) of 20 with deficits in recall. Rest of the neurological examination was normal. Investigations revealed pancytopenia with normal renal., Liver function tests & lipid profile. HIV serology was negative .NCCT Head was normal . MRI brain revealed demyelination in parietal area and occipital area suggestive of PML(Figs.4,5 and 6) .PCR for JC virus couldn't be done as the facility isn't available in the country. Patient was managed with steroids for pancytopenia (on hematologist advice).There was marginal improvement in CBC but the memory deficit worsened. The patient is surviving despite of persisting disease for more than 9 months now.

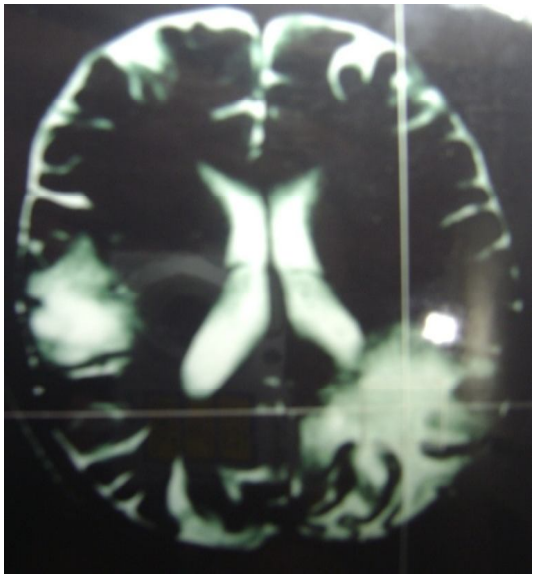

Fig. (4). Case 2: MRI T2 image Paieto occipital hyperintense image.

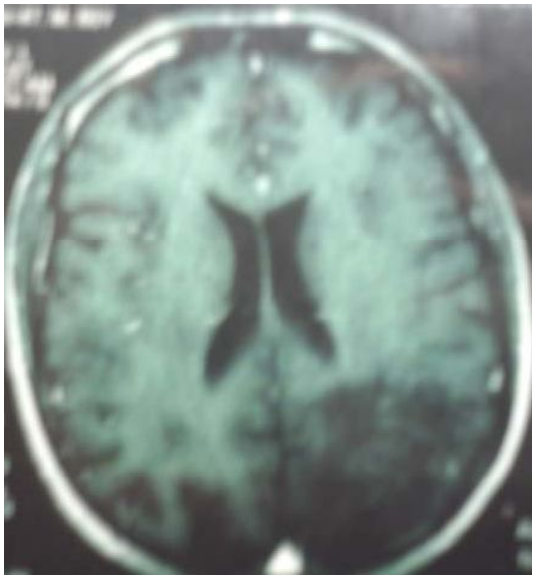

Fig. (5). Case 2, T1: Hypointense lesion in left occipital area Non-enhancing lesion.

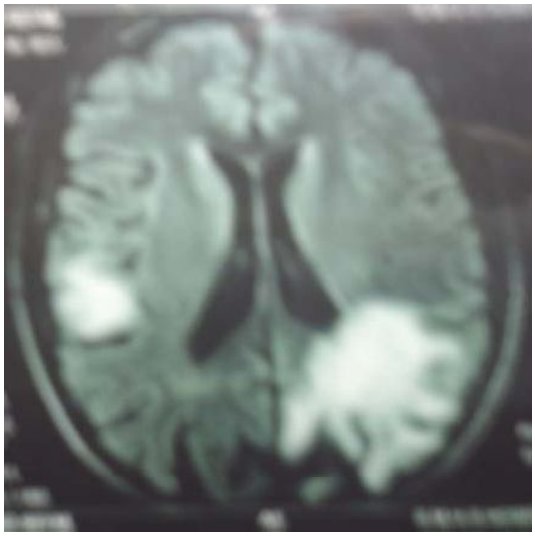

Fig. (6). Case 2: Proton Density image shown in Right Paieto area and in left occipital area.

Discussion

Most of the cases of PML reported in literature show a linear correlation with immunosupression and limited data is existing when PML has been reported in the immunocompetant individuals . The frequency of PML has been estimated at 1 for 5000 kidney transplantation, 1 for 2000 chronic lymphoid leukemia and 1 for 10,000 Hodgkin's disease[1] Although there is no treatment of PML but successful resolution of symptoms is reported in a post renal transplant patient by stoppage of immunosuppresssants and restart of hemodialysis[2] There are reports of PML with autoimmune disorders .Nived et al reported PML with SLE , Rheumatoid arthritis and with immunosuppressants treatment[3] Autoimmune disorders especially SLE needs special attention especially when such disorders have neuropsychiatric manifestation .Scprecher et al reported PML in SLE and authors emphasized that PML should be considered in neuropsychiatric SLE before empiric therapy with immunosuppressants[4] PML has also been reported also after bone marrow transplantation and after lymphoproliferative disorders Some research is suggesting a link between HIV and JC viruses.

It is quite possible that our second patient had neurotoxicity mimicking PML, however, classical MRI findings of PML with some alternative diagnosis can not be ruled out Brain biopsy and JC virus serology could have been contributory to document PML but the facility doesn't exist Further it is difficult to explain continued survival in our second patient. A Neurotoxicty mimicking PML was reported by Matijaca et al in a post renal transplant patient with chronic hepatitis B and authors postulated that the concomitant use of cyclosporin with mycophenolate mofetil and lamivudine, despite normal concentrations of cyclosporin, might cause the accumulation of toxic metabolites and lead to neurotoxicity that mimics PML in a chronic viral environment[(5)]

There are reports of PML occurrence after chemotherapy .Yokoyama et al described PML in a 48 year old female with rituximab based chemotherapy who had significantly low CD 4 count .Authors observed that while giving rituximab based chemotherapy attention must be paid to the potential occurrence of PML ,particularly in patients with low CD4 (+) T –cell counts[6.]Among other drugs infleximab, Natulizumab, chemotherapy, steroids and tacrolimus have been implicated[7,8.]Growing interest in rheumatology has arisen from reports of patients with rheumatic diseases suffering from PML. A direct relationship to rheumatologic disease itself, for example systemic lupus erythematosus, or to immunosuppressive therapy, is debated. Therefore, PML should be included in the differential diagnosis of non-specific neurologic symptoms and, if suspected, relevant diagnostic procedures (MRI, CSF analysis including virus-specific PCR, and possibly brain biopsy) need to be performed

We conclude that in the setting of immunosupression there should be high index of suspicion to consider PML as differential diagnosis when patient has any neurological impairment .

References

1. Progressive mutifocal leukoencephalopathy after renal transplant , Report of two cases Reznik M , Halleux J Urbain E et al Acta Neurol Beig 1981 Jul-Aug;81(4):205-14
2. Crowder CD, Gyure KA ,Drachenberg CB Werner J et al Successful outcome of progressive mutifocal leukoencephalopathy in a renal transplant patient .Am J Transplant 2005 May :5(5):1151 -8

3. Nived O Bengtsson A, Jonsen A Sturfelt G Progressive multifocal leukoencephalopathy –the impotance of early diagnosis illustrated in four cases. Lupus 2008:17(11) :1036-41
4. Shprecher D , Frech T , Chin S Eskandari R et al Progressive multifocal leukoencephalopathy associated with lupus and methotrexate overdose. Lupus ,2008:17(11):1029-32
5. Matijaca M , vlasic –Matas J ,jankovic S et al Neurotoxicity that mimic progressive mutifocal leukoencephalopathy in patient with transplant kidney CollAntropol . 2007 Mar;31(1):349-53.
6. YokoyamaH ,Watanabe T ,Maruyama D , KimSW et al Progressive multifocal leukoencephalopathy in a patient with B-cell Lymphoma during rituximab containing chemotherapy : case report and review of the literature. IntJ Hematol 2008 oct 15 Epub ahead of print
7. Ahsonit AJ. Treatment of non-AIDS progressive ML with cytosive Arabimurich. J Neurovisc 7 (4): 386-90, 2001.
8. Villar JF, Lazan E et al. Impress in PML after cidofovin. Infectin 35(1): 33—40, 2007.