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Case Report

A case of Progressive Multifocal Leukoencephalopathy in a HIV patient.

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Abstract

Progressive Multifocal Leukoencephalopathy is a demyelinating disease of the brain which occurs as a result of reactivation of JC (John Cunningham) virus. It is the most common manifestation of JC virus and is typically seen in patients with an immunocompromised status. Here we will be discussing about a 47 years old male patient who presented with altered sensorium and a past history of weakness in the right upper & lower limbs. Also, patient was found to be retropositive recently. He was referred to the department of Radio diagnosis for MRI (Magnetic Resonance Imaging) for further evaluation. The patient had multiple, asymmetric, white matter lesions in bilateral cerebral hemispheres, midbrain and even cerebellum. In the later course of the disease, the patient lost consciousness and ultimately succumbed to death due to multiorgan failure. The typical features of PML, followed by the role of imaging in diagnosis of PML and its peculiar features to differentiate from other similar white matter lesions of the brain are discussed.

Keywords: Progressive Multifocal Leukoencephalopathy, subcortical U-fibers, HIV, Barbell sign.

Introduction

Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating disease, occurring due to reactivation of John Cunningham virus (JCV). PML is most commonly encountered manifestation of JC virus which infects the oligodendrocytes of the immunocompromised patients.[1]

Classically, PML develops when CD4 counts fall below 50-100 cells/µL in AIDS patients and is seen in 5% of autopsies in which patients died from AIDS.[2]

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On imaging, commonest location involved is the supratentorial white matter. The next most common location is the posterior fossa white matter. Involvement of the subcortical U-fibers is typical in later stages of the disease.[3]

In this case report, we evaluated the imaging features of PML in a HIV patient with reduced CD4 counts who presented with altered sensorium.

Case History

A 47 year old male presented to department of Medicine with altered sensorium. There is past history of weakness of upper & lower limbs on right side for 2 months, with a CD4 count level of 350 cells/µL. According to a MRI report from another hospital, corona radiate and centrum semiovale on the left side demonstrated late subacute infarcts.

Motor examination revealed a power of 2/5 in the right upper and lower limbs while the contralateral side was completely normal.

Following altered sensorium, patient was referred to Radio-Diagnosis department for MRI (Magnetic Resonance Imaging) for further evaluation.

Imaging Findings

MRI Brain (Plain & Contrast)

MRI brain demonstrates multifocal T1 hypointense and T2/FLAIR white matter hyperintense areas in bilateral centrum ovale (Figure 1A & 1B) & corona radiata (Figure 2A & 2B); thalamus (Figure 3A & 3B), cerebral peduncle (Figure 4A), thalamus (Figure 4B) on the left side; pons, middle cerebellar peduncle, medulla & right cerebellar hemisphere (Figure 4C).

There is evidence of patchy restricted diffusion in left corona radiata (Figure 5A & 5B), lentiform nucleus and thalamus (Figure 5C & 5D).

The hyperintensities in right frontal region are involving subcortical U-fibers (Figure 6).

There was no evidence of blooming. Also, the lesions did not exhibit post-contrast enhancement.

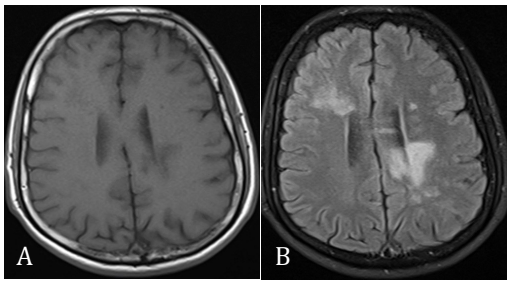

Figure 1 (A & B): MRI brain axial sections demonstrate T1 hypointense & T2 hyperintense lesions in bilateral centrum semiovale.

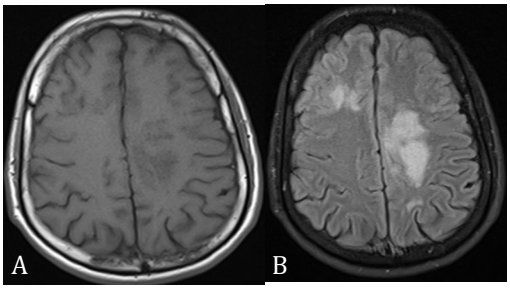

Figure 2 (A & B): MRI brain axial sections demonstrate T1 hypointense & T2 hyperintense lesions in bilateral corona radiata.

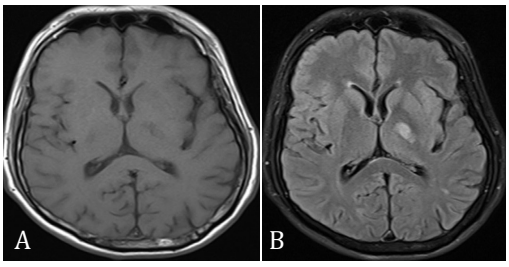

Figure 3 (A & B): MRI brain axial sections demonstrate T1 hypointense & T2 hyperintense lesions in left thalamus.

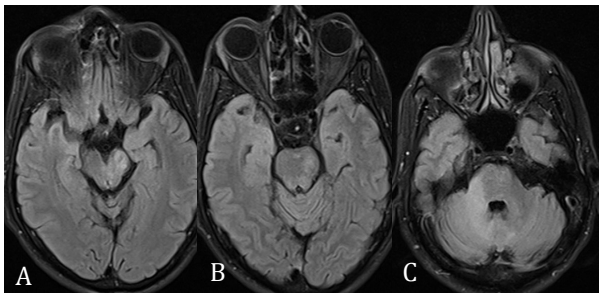

Figure 4 (A, B & C): MRI brain axial sections demonstrate similar T2 hyperintense lesions in left cerebral peduncle, mid-brain, left middle cerebellar peduncle and cerebellar hemisphere.

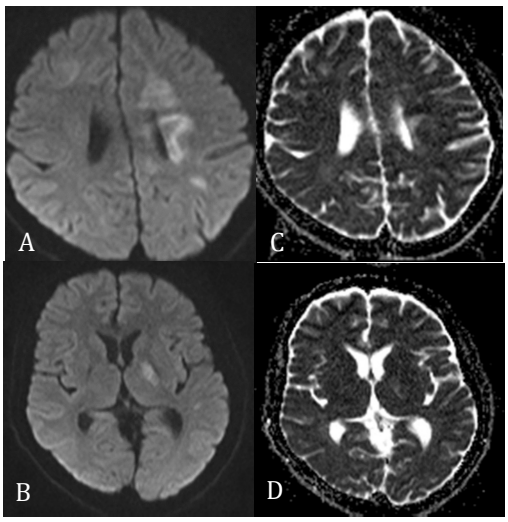

Figure 5 (A, B, C & D): MRI brain axial sections - DWI and ADC images demonstrate subtle areas of restricted diffusion in left corona radiata and thalamus.

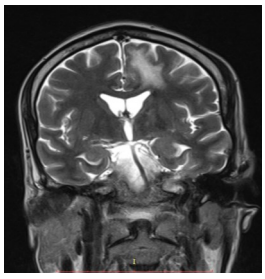

Figure 6: MRI brain T2 weighted image, coronal section demonstrates patchy T2 hyperintensity involving left parietal region & subcortical U-fibers.

Diagnosis

The above features on MRI brain are suggestive of PML (Progressive Multifocal Leukoencephalopathy) involving the white matter and subcortical U-fibers.

Patient had persistent altered sensorium following which he became unconscious and finally died of multi-organ failure few days after MRI was performed.

Discussion

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating and fatal disease of the CNS (central nervous system) that occurs due to reactivation of John Cunningham virus (JCV) and infects the oligodendrocytes.[3] Primary infection is usually asymptomatic but the virus persists in the bone marrow, kidneys and other different sites in the host. The virus is reactivated in immunocompromised patients, especially in cases of profound compromise of cell-mediated immunity. It is usually seen in patients with CD4 counts of 50-100 cells/μL.[2] PML is an AIDS defining illness. HIV (human-immunodeficiency virus), lymphoproliferative disease and MS (multiple sclerosis) together account for majority of the PML cases.[4]

There are 3 distinguished clinical forms of PML:

1. PML due to immunocompromised state.
2. PML-s-IRIS: simultaneous development of Immune Reconstitution Inflammatory Syndrome (IRIS) and PML due to immune reconstitution.
3. PML-d-IRIS: immune reconstitution worsens pre-exiting PML.

Clinical Features

It manifests as small scattered subcortical foci to large bilateral asymmetric confluent lesions that embrace the white matter (most commonly supratentorial region followed by posterior fossa) and subcortical U-fibers.[5] The common clinical manifestations of PML include motor weakness, speech & language disturbances, altered mental status, gait abnormalities, visual abnormalities and seizures.

Imaging Features

CT & MRI play a very crucial role in diagnosing PML. In 90 % of the cases, CT will demonstrate asymmetric, hypodense areas in the subcortical and deep periventricular white matter. The lesions usually do not enhance post-contrast. MRI will demonstrate multi-focal, bilateral, asymmetric and irregular T1 hypointense / T2 hyperintense white matter lesions which typically involve the subcortical U-fibers.[6] Similar to CT, lesions do not show any enhancement on MRI. Restricted diffusion is a positive finding in new active lesions.

As the disease progresses further, the white matter lesions become increasingly confluent in the occipito-parietal and spread across splenium of corpus callosum which gives rise to the characteristic 'Barbell sign'.[7] In contrast to the classical variant, inflammatory form has few distinguishing features. The lesions in the inflammatory form demonstrate mass effect and peripheral enhancement on post-contrast study.

Differential Diagnosis

The list of differentials for PML mainly include HIV encephalitis, Posterior Reversible Encephalopathy Syndrome (PRES) and Acute Disseminated Encephalomyelitis (ADEM).[8] HIV encephalitis characteristically demonstrates symmetric white matter lesions with sparing of subcortical U-fibers. PRES and ADEM can involve both grey & white matter. These entities can be differentiated as they have different history; e.g. hypertension in PRES and recent infection/ vaccination in case of ADEM.

Treatment

PML usually has a poor prognosis with neurological impairment which leads to coma and ultimately death.[6,9] If left untreated, PML will usually have lethal outcomes within a frame of six months. Aim of the treatment should be to strengthen the immune system. HAART (highly active antiretroviral therapy) helps to prolong the survival in many of cases. Other treatment choices include the likes of high dose glucocorticoids in cases of PML-IRIS and cytarabine/mirtazapine in natalizumab associated PML.[10,11]

Conclusion

Attention to characteristic MRI patterns, especially the involvement of subcortical U-fibers and no enhancement on post-contrast imaging is beneficial in screening and early diagnosis of PML in immunocompromised patients.

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