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Case Report

A rare case of progressive multifocal leukoencephalopathy ☆

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ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease of the central nervous system (CNS) due to John Cunningham (JC) virus reactivation most often in immunocompromised patients. The brainstem and the anterior corpus callosum are uncommon locations for white matter lesions. We present a case of PML in a 40-year-old female presenting to the emergency department for a tonic seizure with transient postictal confusion. The inpatient workup revealed low cluster of differentiation cell counts (CD3 and CD4), transaminitis, positive drug screen, and abnormal electroencephalogram (EEG). The computed tomogram (CT) of the head and magnetic resonance image (MRI or MR) of the brain showed evidence of subcortical and periventricular white matter lesions in the right hemisphere extending into the brainstem and the left frontal lobe. The hospital course consisted of supportive measures, seizure treatment along with prophylaxis, and human immunodeficiency virus (HIV) management along with prophylactic antibiotics. The patient was discharged with appropriate medications and outpatient referrals. Overall, this case describes some key points. It highlights particular imaging characteristics of PML in the setting of inadequately treated HIV. For example, white matter lesions cross the anterior corpus callosum rather than the splenium, as in the "barbell" sign. In addition, the lesions extend inferiorly along the ipsilateral corticospinal tract into the midbrain and pons. This could be one of the first cases to capture both of these features given the rarity of their concomitant occurrence.

Introduction

Progressive multifocal leukoencephalopathy is a progressively demyelinating CNS condition associated with immunosuppression with CD4 counts <200 cells/μL (i.e. HIV, post-transplant, cancer, medications) due reactivation of the JC virus reactivation commonly within oligodendrocytes, astrocytes, and cerebellar granule cells [1,2]. Rarely, PML can appear in certain immunocompetent states (i.e. sarcoidosis) [3]. Clinical features of PML include hemiparesis, ataxia, aphasia, hemianopsia, diplopia, seizures, inattentiveness, and

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encephalopathy [4]. PML manifests as multiple bilateral asymmetric patchy lesions mostly in the supratentorial space and rarely in the posterior cranial fossa or brainstem [5,6]. CT typically shows hypodense lesions in the periventricular and subcortical white matter [7]. MRI is more sensitive in detecting features like laminar necrosis and specific signs, especially at an earlier stage [8,9]. Usually, PML lesions neither enhance nor exhibit mass effect, but enhancement can indicate improved immunity [10]. Cerebrospinal fluid (CSF) analysis and brain biopsy confirms diagnosis [11,12]. Management involves strategic improvement of immunity (i.e. antiretroviral therapy for HIV, discontinuation of immunosuppressants) to avoid immune reconstitution inflammatory syndrome (IRIS) [13]. Serial imaging with worsening cortical atrophy, lesion size, convergence of lesions, or signal intensity suggests poor prognosis [8]. Most cases lead to coma or death despite treatment [2].

Case presentation

A 40-year-old female with a past medical history of diffuse astrocytoma, epilepsy, intravenous (IV) drug use, HIV, chronic hepatitis C virus infection, cirrhosis, bacterial endocarditis, cerebrovascular accident (CVA) presented to our emergency department for a witnessed tonic seizure lasting about 1 to 2 minutes. She experienced postictal confusion for about 15 minutes before returning to her normal baseline mentation without any additional symptoms. Physical examination revealed mild right upper quadrant tenderness to palpation, left upper and lower extremity hemiparesis, and left lower extremity Babinski sign. The initial vitals and electrocardiogram (EKG) were insignificant. Initial labs were significant for low CD3 and CD4 T-lymphocyte counts, elevated liver function tests, and urine drug screening positive for opioids, amphetamines, and tetrahydrocannabinol (THC). EEG showed slowing of right-sided wave activity suggesting underlying pathology. The CT head without contrast showed hypoattenuation of a large area of subcortical white matter in the right frontal lobe with preservation of gray-white matter interface. The MRI brain with and without contrast showed right-sided subcortical and periventricular lesions extending along the ipsilateral corticospinal tract into the brainstem and across the corpus callosum into the left periventricular white matter. PML was the highest on our list of differential diagnoses given the imaging features. HIV encephalopathy and multiple sclerosis (MS) were next on the list given that they can have similar signal intensity and enhancement patterns on imaging and that they also commonly involve the periventricular areas. Other conditions lower on the list included CVA and tumor. However, imaging helped rule out other conditions and PML was favored over HIV encephalopathy and MS given that lesions of PML are more likely to present subcortically and asymmetrically. Hence, a presumptive diagnosis of PML was made given the clinical and radiological features. Confirmation of diagnosis was performed via CSF analysis. Management consisted of IV lorazepam for seizure treatment, medications to treat pain and anxiety, fall precautions, and seizure precautions. Neurology recommended levetiracetam for seizure prophylaxis. Infectious disease recommended highly active antiretroviral therapy (HAART) for HIV and prophylactic antibiotics. The patient was discharged with outpatient referrals for neurology and infectious disease after clinical improvement.

Discussion

We have presented a case of PML in the setting of inadequately treated HIV. Initial evaluation revealed findings suspicious for intracranial lesions despite no further seizures, possibly indicating a CNS infection. The CT head without contrast shows findings initially suspicious for vasogenic edema but more so indicative of PML given the involvement of periventricular and subcortical white matter and the lack of mass effect (Fig. 1)

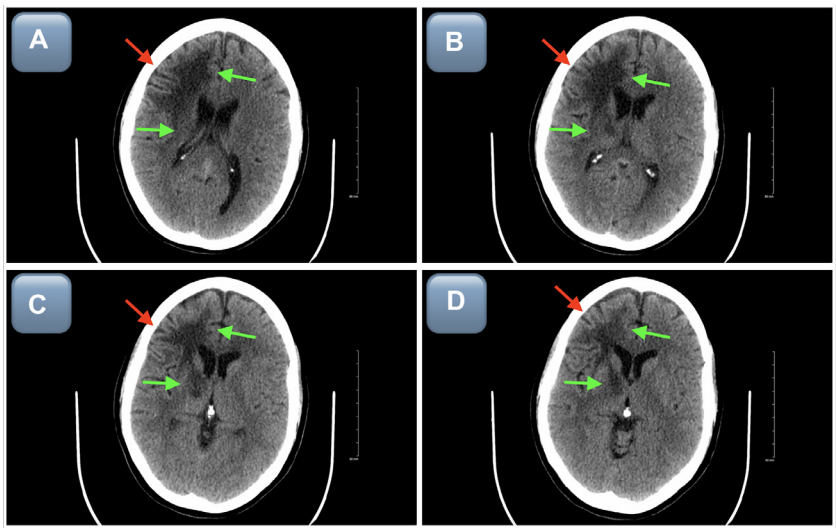

Fig. 1 – Axial noncontrast CT head in a 40-year-old female from most superior (A) to most inferior (D) showing subcortical and periventricular white matter hypoattenuation in the right frontal lobe (green arrows) with intact gray-white matter interface (red arrows) and no mass effect. These findings are suspicious for PML.

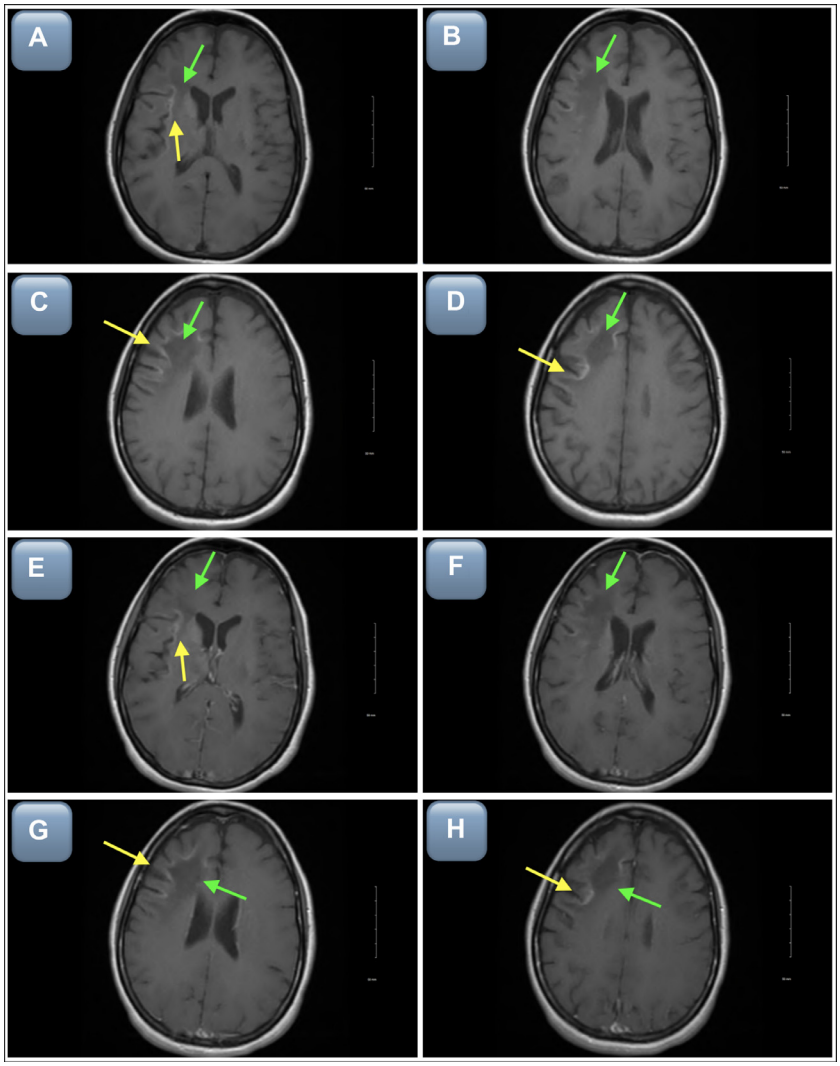

Fig. 2 – Axial noncontrast T1-weighted (A-D) and post-contrast T1 (E-H) MRI brain in a 40-year-old female showing hypointense subcortical and periventricular white matter in the right frontal and parietal lobes with defined margins (green arrows), partly hyperintense right frontal cortex and insula (yellow arrows), and no significant contrast enhancement. These findings are significant for PML with laminar necrosis.

[7]. However, there is no scalloping on the lateral margin of the hypodensity, likely meaning no extension into subcortical U-fibers (Fig. 1) [5]. The MRI brain captures the abnormalities with higher quality. The T1-weighted sequence echoes similar features observed on the CT head (i.e. hypointensity, margins) and shows no significant enhancement with contrast, which is typical of PML and likely means an insufficient immune response (Fig. 2) [7,9]. Moreover, the right frontal cortex and insula appear hyperintense on T1, suggesting laminar necrosis, which is a unique characteristic of PML (Fig. 2) [9]. Conversely, the noncontrast T2-weighted and T2 FLAIR sequences portray the white matter lesions as hyperintense (involving the right frontal, parietal, temporal, insular, basal ganglia, and thalamic regions), which is also consistent with PML (Fig. 3) [8,9]. The "milky way" sign describes additional punctate lesions surrounding a main lesion [6]. The "barbell" sign shows parieto-occipital hyperintensities crossing the splenium into the contralateral hemisphere [14]. The "shrimp" sign shows increased signal in the cerebellar white matter sparing the dentate nucleus [15]. No particular signs (i.e. "milky way", "barbell", and "shrimp") are observed in this case (Fig. 3) [15]. However, the lesions cross the anterior segment (i.e. rostrum and genu) of the corpus callosum into the left frontal lobe whereas the "barbell" sign involves parieto-occipital lesions crossing the splenium (Fig. 3) [14]. Another uncommon feature is the extension of the lesions along the right corticospinal tract through the posterior limb of the internal capsule into the midbrain and pons (Fig. 3) [6]. Diffusion-weighted imaging (DWI) usually portrays restricted diffusion but can also show centrally hypointense and peripherally hyperintense signals [8]. In our case, DWI shows central hypointensity and posteromedial hyperintensity, which can be seen in PML despite no restricted diffusion (Fig. 4). The aforementioned features are all potential characteristics of PML, showing patchy lesions bilaterally

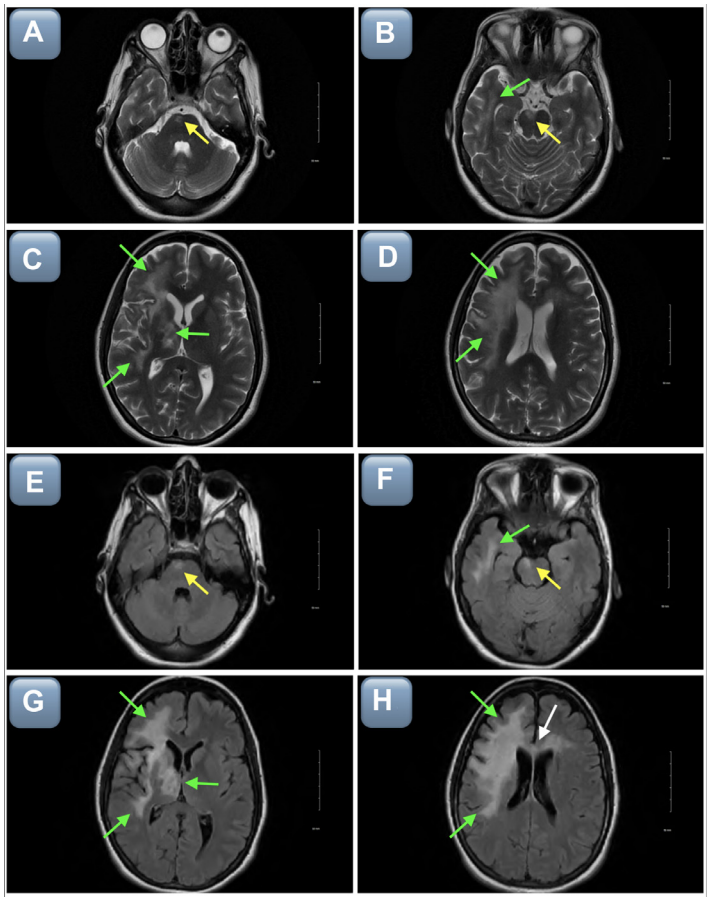

Fig. 3 – Axial noncontrast T2-weighted (A-D) and T2 FLAIR (E-H) MRI brain in a 40-year-old female showing hyperintense white matter lesions in the right frontal, parietal, temporal, insular, basal ganglia, and thalamic regions (green arrows) with no mass effect; they extend into the midbrain and pons via the ipsilateral corticospinal tract (yellow arrows) and the left frontal lobe via the anterior portion of the corpus callosum (white arrow). These findings are uncommon but consistent with PML.

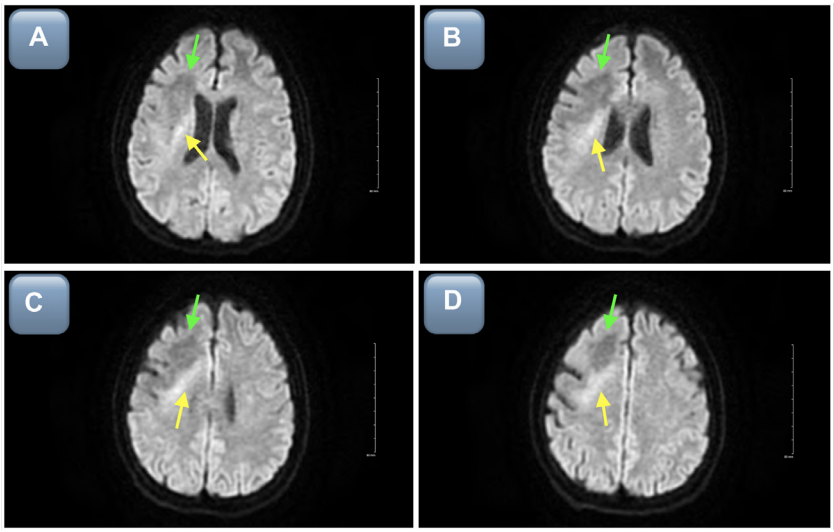

Fig. 4 – Axial diffusion-weighted MRI brain in a 40-year-old female from most inferior (A) to most superior (D) showing centrally hypointense (green arrows) and peripherally (posteromedially) hyperintense (yellow arrows) signals in the right frontal lobe but no evidence of restricted diffusion or mass effect. These findings are indicative of PML.

and asymmetrically overall. MR perfusion typically shows increased signal, especially near the leading edge [7]. MR spectroscopy can show low creatine and N-acetylaspartate (NAA) (due to neuronal loss) but high choline (due to lysis of cells) and lipids (due to myelin breakdown) in the early phase [7]. However, MR spectroscopy and MR perfusion were not used in our case. No additional rare findings, such as posterior cranial fossa lesions and extension into gray matter, were noted [6].

Conclusion

Our patient, a middle-aged female, had a nonspecific clinical presentation with a seizure in the setting of untreated HIV, which led to particular imaging findings. Most imaging features associated with PML are observed in this case. However, this may be the first instance to capture white matter lesions extending into the ipsilateral (right) corticospinal tract and across the anterior corpus callosum into the contralateral (left) hemisphere, in contrast to the "barbell" sign, which involves the posterior corpus callosum. Other rare locations like the posterior cranial fossa and gray matter did not have lesions. Modalities like MR perfusion and MR spectroscopy may have uncovered additional findings if performed.

Patient consent

Written informed consent for publication was obtained from the patient.

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