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Case Report

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Sudden Dysarthria in a Previously Healthy Individual Unveils Acquired Immunodeficiency Syndrome Diagnosis

Ani Başlangıçlı Dizarti Kliniğiyle Edinilmiş İmmün Yetmezlik Tanısı Alan Öncesinde Sağlıklı Hasta

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ABSTRACT

Progressive Multifocal Leukoencephalopathy (PML), caused by the JC (John Cunningham) virus, is a central nervous system demyelination, usually on an immunosuppressant basis. This report aims to demonstrate that sudden neurological symptoms in patients could result from an immunosuppressive state even if their medical history is unremarkable. A previously healthy, immunocompetent 47-year-old man, diagnosed with PML with sudden dysarthria, was diagnosed with AIDS (Acquired Immunodeficiency Syndrome) and rapidly deteriorated. In conclusion, young, healthy outpatients with sudden neurological symptoms may be diagnosed with complications of acquired immunodeficiency syndrome, even without a history of chronic diseases, malignancies, or immunosuppressant drug use.

Keywords: AIDS; Dysarthria; Progressive multifocal leukoencephalopathy.

ÖZET

JC'den (John Cunningham) kaynaklanan Progresif Multifokal Lökoensefalopati (PML), genellikle immünosupresyon temelinde merkezi sinir sistemi demiyelinizasyonudur. Bu vaka sunumu, hastalardaki ani nörolojik belirtilerin, tıbbi öyküde özellik olmasa bile immünosupresif bir durumdan kaynaklanabileceğini göstermeyi amaçlamaktadır. Bilinen herhangi bir hastalığı olmayan kırk yedi yaşındaki erkek hasta, akut dizartri kliniği ile başvurduktan kısa bir süre sonra PML komplikasyonuyla AIDS (Acquired Immunodeficiency Syndrome) tanısı alarak hızlı bir progresyon gösterdi. Sonuç olarak, ani norolojik semptomları olan ve ayaktan kliniğe başvuran genç hastaların kronik hastalık, malignite veya immunosupresan ilac kullanımı öyküsü olmasa bile; edinilmiş bir immun yetmezlik sendromunun komplikasyonlarına sahip olabileceği ve bu şekilde tanı alabilecekleri akılda tutulmalıdır.

Anahtar sözcükler: AIDS; dizartri; progresif multifokal lökoensefalopati.

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JC (John Cunningham) virus is an agent from the Polyomaviridae family that causes demyelination called progressive multifocal leukoencephalopathy (PML) in the central nervous system on an immunosuppressive basis caused by diseases or drugs.[1] PML has different disease phases; the first phase is the asymptomatic phase in which the virus stays latent in the urinary tract, bone marrow, and spleen. During this phase, an antibodies are detected in most of the population. The reactivation and hematogenous dissemination to the central nervous system of the virus is called the final phase, which generally occurs together with the immunosuppression period.[1] Even if patients do not have a history of infection, malignancy, or immunosuppressive drug usage,

which can create an immunosuppressive environment, they can still present to physicians with PML in different scenarios according to the central nervous system involvement.

Case Report

A 47-year-old man was admitted to the emergency department (ED) with slurred speech for 4 days. His medical and drug history were unremarkable. His physical and neurological examination were normal except for mild dysarthria in long sentences. There were no abnormal skin lesions on inspection. He denied any exposure to chemicals or insects. Cranial computed tomography (CT) and craniocervical CT angiography did not reveal any pathology. Diffusion-weighted magnetic resonance imaging (DW-MRI), Apparent Diffusion Coefficient (ADC) (Figs. 1–2), showed bilaterally but mostly left-sided disseminated hyperintensities in the cerebrum and basal ganglia, Fluid Attenuated Inversion Recovery (FLAIR) sequence was the same.

Blood tests revealed a mildly elevated sedimentation rates and anti-HIV antibody as pathological findings. Other parameters including complete blood count, C-reactive protein, kidney and liver function tests, thyroid panel, B12 vitamin, folate, electrolytes, hepatitis markers, syphilis marker, tuberculosis marker, Lyme disease marker, tumor markers, HbA1c, and vasculitis parameters were normal. The cerebrospinal fluid (CSF) study revealed normal opening pressure, cell count was 105 cells/μL (67% lymph-monocytes), no atypical cells, microprotein level was 59.2 mg/dL, and other CSF parameters were normal. All meningitis panel CSF PCR (polymerase chain reaction) was negative, CSF did not gram stain, and CSF culture was normal. For the differential diagnosis of demyelinating diseases, CSF oligoclonal band screening, aquaporin 4, and anti-MOG (myelin oligodendrocyte glycoprotein) antibodies were negative. Upon double-checking, high titers of anti-HIV antibody; HIV-RNA from blood and JC virus, Acid Fast Bacillus (AFB), and Cryptococcus from CSF were demanded. In the second week of follow-up, fatigue and left-sided hemi-hypoesthesia were added to his neurological examination. Repeated MRI-FLAIR showed enlargement of old lesions bilaterally and a new lesion in the left brain-stem (Fig. 3) and dots-like contrast enhancement (Fig. 4).

After all the results came negative including CSF-AFB and Cryptococcus except blood HIV-RNA; the patient was diagnosed with HIV and dolutegravir treatment was started by the infectious diseases department. Around the 10th day of service follow-up, swallowing difficulty was added to his symptoms but the neurological examination was the same, and repeated MRI didn't show any new lesion. One day later upon the positivity of JC virus DNA-PCR in CSF, the diagnosis of PML secondary to HIV was made. One week later nasogastric tube was inserted because of repeated aspirations, and right-sided hemiparesis was added to his neurological examination. The following day CD4 cell count resulted in 73.8 cells/μL. In the 4th week of outpatient admission to the hospital, after he was diagnosed with AIDS, he died because of respiratory complications.

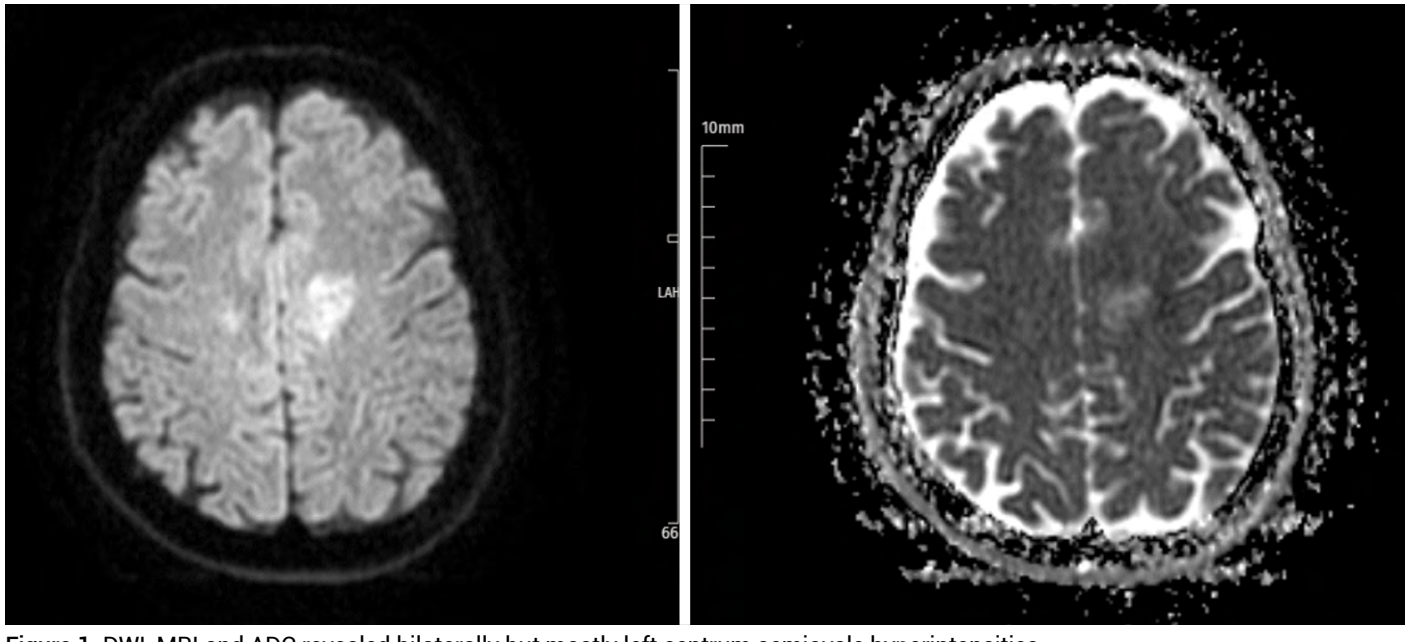

Figure 1. DWI-MRI and ADC revealed bilaterally but mostly left centrum semiovale hyperintensities.

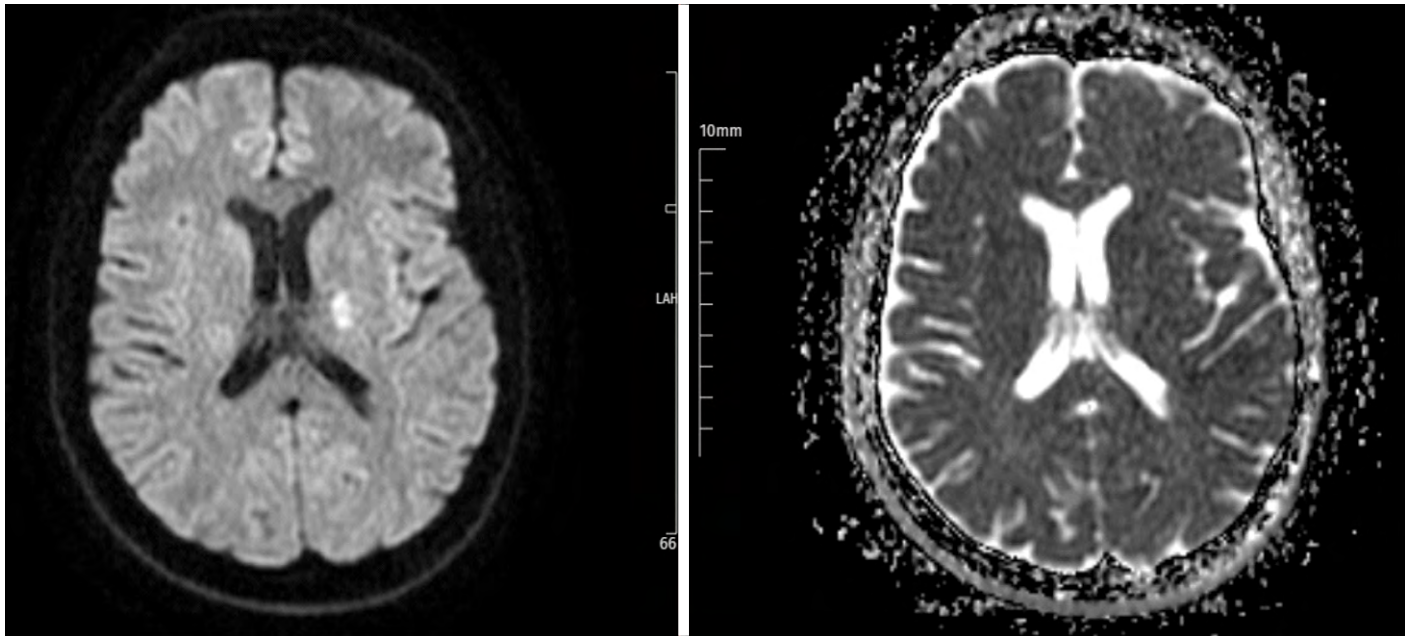

Figure 2. DWI-MRI and ADC revealed left thalamus hyperintensity.

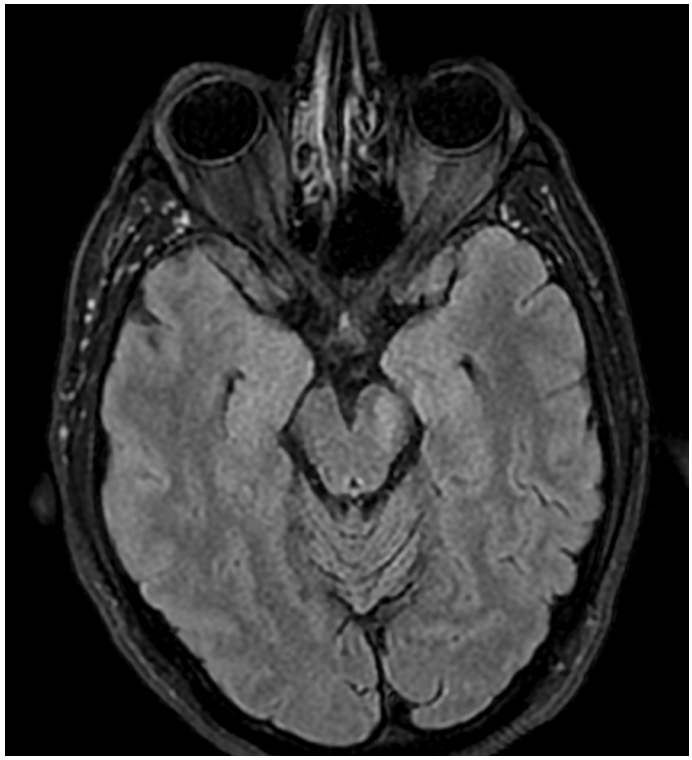

Figure 3. MRI-FLAIR revealed a new lesion in the left brain-stem.

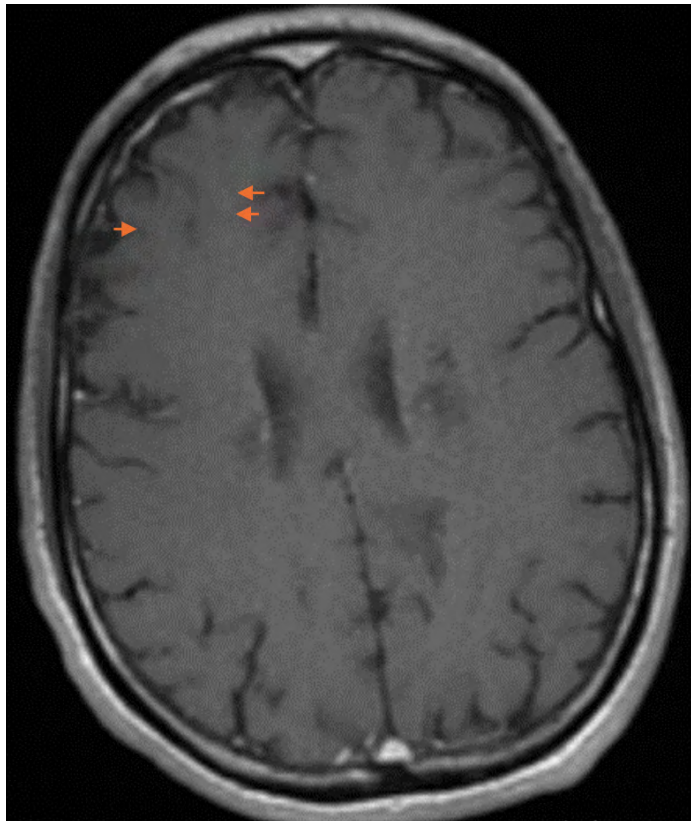

Figure 4. Gadolinium MRI revealed dots like contrast enhancement in the area of the lesions (shown with arrow).

Discussion

PML typically manifests clinically in patients who have reached the immunocompromised stage, and it is not commonly observed in immunocompetent patients. However, in a case presentation published in 2018, it was mentioned that an immunocompetent patient was diagnosed with PML with neurological findings.[2] Classically, PML is frequently observed in AIDS patients with CD4 levels ranging from 50 to 100 cells/μL. However, it can also develop following the use of monoclonal antibodies such as natalizumab and rituximab, in conditions like transplantation, leukemia, solid organ malignancies, lupus, sarcoidosis, or similar diseases, in-

cluding multiple sclerosis. Patients with PML could present to clinics with different symptoms according to the involvement area of the central nervous system. Mostly speech difficulties, including aphasia and dysarthria, motor and sensory deficits, swallowing difficulties, gait or walking ataxias, diplopia, altered mental status, and epileptic seizures could be seen in patients. However, if the patient has no history of any underlying medical condition, the physician could have trouble making a differential diagnosis. The differential diagnoses are multiple sclerosis, posterior reversible encephalopathy syndrome (PRES), vascular diseases, malignancies like lymphoma or infectious and non-infectious encephalitis. PML lesions in MRI tend to confluence and could be in bilateral white matter tracts asymmetrical also thalamic involvements could be seen often.[3] Also, involvements of the brain stem and cerebellum are shown in cases.[4] Unique dots-like contrast enhancements could be seen in the lesion called the Milky Way sign. While brain biopsy remains the gold standard diagnostic technique for PML diagnosis, when clinical and neuroradiological findings are sufficient, the presence of JC virus DNA PCR positivity in the cerebrospinal fluid examination can also be adequate for making the diagnosis.[5] Usually, routine CSF parameter studies yield results within normal limits when diagnosing PML. However, in a multicenter cohort study conducted in Germany in 2020, comparing the CSF results of 108 patients diagnosed with PML, it was mentioned that HIV-associated PML-complicated patients might have increased cell and protein values in their CSF results and these findings would not exclude the diagnosis of PML. Also, oligoclonal bands positivity could be seen due to potentially leading to an increase in intrathecal IgG synthesis.[6]

Conclusion

In cases where patients present with different neurological examination findings and atypical hyperintense lesions on neuroimaging, it's important not to consider typical demyelinating diseases solely. It should be kept in mind that patients may present with complications of acquired immunodeficiency syndromes, even if they don't have a history of chronic diseases, malignancies, or immunosuppressive drug use. In light of current data, there is no specific treatment for the JC virus. However, it is essential to recognize patients during the process leading to PML and implement the necessary treatment steps. Due to their potential for rapid progression, patients should undergo relevant investigations with a multidisciplinary approach to avoid delays in diagnosis and treatment.

Disclosures

Informed consent: An informed consent form was taken from the subject's brother.

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