CHAPTER **43**

BILATERAL ANKLE CLONUS AS INITIAL MANIFESTATION OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY: A Case Report

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INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a rare degenerative disease of the subcortical white matter of the brain seen mostly in immunocompromised hosts. The lesions may also be present in the cerebellum, cortex, and brain stem (1), show early gadolinium enhancement, and may be rarely monofocal (1, 2). There are two subcategories of PML: Human Immunodeficiency Virus- (HIV) related and non-HIV related. The HIV-related group comprises 80-90% of those affected with PML, with the other 10-20% reported in patients treated with immunomodulatory medications for diseases such as multiple sclerosis, rheumatoid arthritis, gastrointestional cancers, and psoriasis (2-4). The incidence of this fatal disease in the HIV population is estimated to be 0.7 cases per 1,000 (3), affecting approximately 5% of HIV patients (2).

The presenting symptoms have been reported as weakness (42%), speech abnormalities (40%), cognitive abnormalities (36%), gait abnormalities (29%), sensory loss (19%), and visual impairment (19%) (1). The most reliable diagnosis is via brain biopsy, although this is rarely done today (1). JCV polymerase chain reaction (PCR) in the cerebral spinal fluid has been reported to have 95% sensitivity and 99% specificity, and is used along with brain magnetic resonance imaging (MRI) and clinical presentation for diagnosis (1). The prognosis has improved since the advancement of highly active anti-retroviral therapy (HAART) with median survival at eleven months (5). Unfortunately, PML continues to have the worst prognosis of any AIDS-related cerebral disorder. The use of HAART has shown a dramatic improvement in long-term survival, to upwards of 50% (2).

CASE REPORT

A 37-year-old man came to the emergency department with a chief complaint of muscle spasms in both of his lower extremities and unsteadiness in his gait for 2 months with worsening over the past 2 weeks. There was no significant past medical, surgical, social, or family history. The patient went to a primary care physician where he received a thorough workup. When he presented to the emergency department he said he was told by his primary care physician that his diagnosis was HIV. The workup in the hospital consisted of a thorough head to toe physical examination, brain, and spine MRI, lumbar puncture (LP), and consults for infectious disease, neurology, and social work. The physical examination showed the following abnormalities: motor examination showed increased tone bilaterally in the lower extremities; muscle stretch reflexes were distinctly hyperactive (3 of 4) in both the upper and lower extremities symmetrically; there was sustained clonus at the ankles, bilaterally; the coordination was moderately impaired in the lower extremities, bilaterally; and a slightly wide-based diparetic gait was exhibited.

MRI of the brain, thoracic, and lumbar spine were normal. MRI of the cervical spine showed early multilevel degenerative disc disease from C2 to T1 with no evidence of nerve root or spinal canal pathology. The lumbar puncture had the following abnormalities: Glucose 37 (normal range 40-70); JC virus PCR detected (normal range not detectable); cell count 31 (normal range 0-10); myelin base protein 2.60 (normal range 0.00-1.10). The serology tests had the following abnormalities: HIV-1 Mutation: L1OI; HIV-1 RNA quant. PCR: 1,690,000. The patient was pancytopenic based on his complete blood count with differential. The T-cell lymphocyte panel had the following abnormalities: % CD3 93 (normal range 62-87); % CD4 3 (normal range 32-64); % CD8 89 (normal range 15-46); CD4/CD8 ratio 0.03 (normal range 0.80-3.90); absolute CD4 count 18 (normal range 430-1,800); absolute CD3 count 538 (normal range 570-2,400).

An absolute CD4 cell count of 18 in a person with HIV changes the diagnosis to full blown AIDS, and increases his/her susceptibility to opportunistic infections and neoplasms. A CD4% below 15% correlates with a high risk of contracting serious infections, and our patient had a CD4%

of 3%. The HIV-1 RNA quantitative polymerase chain reaction measures the viral load of HIV. The CD4 count and viral load have an inverse relationship. Although the brain MRI was negative for any PML-associated lesions, our patient had a positive JCV and clinical neurologic symptoms that correlated with progressive multifocal leukoencephalopathy. JCV is the proven causative agent of PML (3). The patient was treated with Baclofen 5 mg TID, which reduced his spasticity and improved his gait. He was also started on prophylactic doses of Azithromycin and Bactrim DS to prevent pneumocystis jiroveci, toxoplasmosis, and mycobacterium avium complex. He was referred to an HIV/AIDS clinic to continue follow-up and receive his HAART. He was instructed to follow-up with neurology and infectious disease on an outpatient basis.

DISCUSSION

This case is remarkable because the presenting symptoms of PML in a newly diagnosed AIDS patient were bilateral ankle clonus and diparetic gait, which could have easily presented to a foot and ankle surgeon's office. A large percentage of patients with a CD4 cell counts less than 200 present with AIDS-associated dementia or encephalopathy, peripheral neuropathies, polymyositis, vacuolar myelopathies, and/or infections. The presentation of ankle clonus and diparetic gait as the sole symptoms of PML with a CD4+ count of 18 and a viral load of 1,690,000 is very rare.

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