Bilateral Ankle Clonus as Initial Manifestation of Progressive Multifocal Leukoencephalopathy

A Case Report

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We report on a rare case of foot and ankle clonus as the initial presentation of progressive multifocal leukoencephalopathy in a young patient with no known history of HIV or AIDS and no significant past medical or social history. The patient came to the emergency department with a chief complaint of muscle spasms in his lower extremities and unsteadiness in gait. The patient was diagnosed as having bilateral ankle clonus. Work-up revealed an absolute lymphocyte CD4+ count of 18, an HIV viral load of 1,690,000, and a positive John Cunningham virus polymerase chain reaction in the cerebral spinal fluid, indicating that the patient had progressive multifocal leukoencephalopathy and AIDS. The diagnosis of progressive multifocal leukoencephalopathy should be in the foot and ankle surgeon's differential diagnosis when a patient presents with neurological symptoms in the lower extremities. (J Am Podiatr Med Assoc 104(5): 548-549, 2014)

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; show early gadolinium enhancement; and may be rarely monofocal.[1,2] There are two subcategories of PML: HIV-related and non-HIV related. The HIV-related group comprises 80% to 90% of those affected with PML, with the other 10% to 20% reported in patients treated with immunomodulatory medications for diseases such as multiple sclerosis, rheumatoid arthritis, gastrointestinal cancers, and psoriasis.[2-4] The incidence of this fatal disease in those with HIV is estimated to be 0.7 cases per 1,000,[5] affecting approximately 5% of HIV patients.[2] The presenting symptoms have been reported as 42% weakness, 40% speech abnormalities, 36% cognitive abnormalities, 29% gait abnormalities, 19% sensory loss, and 19% visual impairement.[1] The most reliable diagnosis is via brain biopsy, although this is rarely done today.[1] John Cunningham virus (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 and clinical presentation for diagnoses.[1] The prognosis has improved since the advancement of highly active anti-retroviral therapy (HAART) with median survival at 11 months.[1] Of patients treated with HAART, 0.6% will develop PML.[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]

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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 during the previous 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 work-up. When he presented to the emergency department he said he was told by his primary-care physician that his diagnosis was HIV. The work-up in the hospital consisted of a thorough head-to-toe physical exam, brain and

spine magnetic resonance imaging (MRI), lumbar puncture (LP), and consultations for infectious disease, neurology, and social work. The physical exam showed the following abnormalities: motor-increased tone bilateral lower extremities; muscle stretch reflexes-distinctly hyperactive 3/4 in both upper and lower extremities symmetrically with sustained clonus at ankles, bilaterally; coordination-rapid alternating movements moderately impaired bilateral lower extremities; gait-slightly wide-based diparetic.

Brain, thoracic, and lumbar spine MRI were normal. A cervical spine MRI showed early multilevel degenerative disc disease from C2-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 (normally not detectable); cell count 31 (normal range, 0–10); and 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. Based on his CBC with differential, the patient was pancytopenic. The T-cell lymphocyte panel had the following abnormalities: percentage CD3: 93 (normal range, 62–87); percentage CD4: 3 (nomal range, 32–64); percentage CD8: 89 (normal range, 15–46); CD4/CD8 ratio: 0.03 (normal range, 0.80-3.90); absolute CD4 count: 18 (normal range, 430-1800); and absolute CD3 count: 538 (normal range, 570-2400). 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 percentage below 15% correlates with a high risk of contracting serious infections, and our patient had a CD4 percentage 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 neurological symptoms that correlated with progressive multifocal leukoencephalopathy. JCV is the proven causative agent of PML.[4] The patient was treated with baclofen 5 mg three times daily, which reduced his spasticity and improved his gait. He was also started on prophylactic doses of azithromycin and sulfamethoxazole/trimethoprim to prevent pneumocystis jiroveci, toxoplasmosis, and mycobacterium avium complex. He was referred to an HIV/AIDS clinic in San Diego to continue follow-up and receive 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 count less than 200 present with AIDS-associated dementia or encephalopathy, peripheral neuropathies, polymyositis, vacuolar myelopathies, and/or infections. The presentation of ankle clonus and di-paretic 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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Conflict of Interest: None reported.

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