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An IRIS to Remember

To the Editor:

A 48-year-old man with acquired immunodeficiency syndrome presented to our clinic with 6 days of worsening frontal headache, vomiting, diffuse myalgias, and weakness. On examination he had profound lower extremity weakness, increased patellar tendon reflexes, sensory loss in his feet, and Babinski signs present bilaterally. The patient was hospitalized, and a lumbar puncture revealed a cerebral spinal fluid leukocyte count of 4277 cells/uL with 94% atypical lymphocytes, erythrocyte count of 8673 cells/uL, glucose of 63 mg/dL, and protein of 3480 mg/dL. Magnetic resonance imaging (MRI) found diffuse edema of the thoracic spinal cord consistent with meningomyelitis (Figure).

Of note, he had restarted highly active antiretroviral therapy 3 weeks prior. His $CD4^+$ count and human immunodeficiency virus (HIV)-1 viral load at that time were 103 cells/uL and 284,370 copies/mL, respectively. On admission, his $CD4^+$ count was 79 cells/uL and HIV-1 viral load was 606 copies/mL.

The diagnosis of immune reconstitution inflammatory syndrome (IRIS) was made, highly active antiretroviral therapy was discontinued and dexamethasone 10 mg intravenously (IV) every 6 hours was initiated. The patient's strength and sensation improved. Cerebrospinal fluid polymerase chain reaction was positive for varicella zoster virus at day 4 and IV acyclovir was added. Two months after admission, he was able to ambulate with a walker.

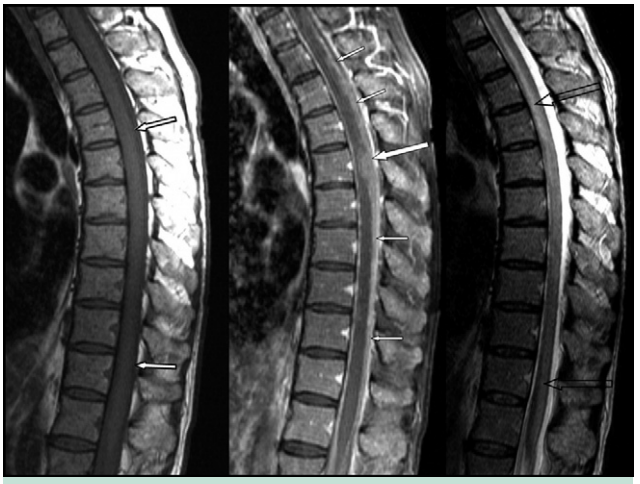

Figure Sagittal magnetic resonance images of the thoracic spine. T1-weighted precontrast image (**left**) shows diffuse swelling (**thick white arrows**) of the spinal cord. T2-weighted image (**right**) demonstrates cord edema (increased signal, **outlined arrows**). Postcontrast T1-weighted fat-suppressed image (**center**) shows extensive leptomeningeal enhancement (**small white arrows**) with nodular intramedullary enhancement at T6 (**large white arrow**).

DISCUSSION

IRIS is a pathologic immune recognition of antigens that occurs after highly active antiretroviral therapy initiation. Although lethal in <10% of AIDS patients,[1] IRIS is an increasingly recognized complication of highly active antiretroviral therapy initiation, with an incidence between 15% and 25%.[2] Risk factors for this syndrome include use of a protease inhibitor, $CD4^+$ nadir <100 cells/uL, and a decrease in the HIV viral load of >2.5 on logarithmic scale.[2] An increase in the total CD4 count may also be seen.[2]

Clinicians should suspect central nervous system IRIS when patients have an unexplained neurological decline accompanied by new or progressive neuroradiological findings, a decrease in plasma viral load of ≥ 1 $\log_{10}$, or histopathology demonstrating T-cell infiltration.[3] Central nervous system IRIS accounts for approximately 75% of deaths from IRIS.[1] There are only 2 prior reports of varicella zoster virus-mediated central nervous system IRIS in the literature.[4,5] Our patient demonstrated neurologic deterioration, transverse myelitis on MRI, and >3 $\log_{10}$ decrease in viral load. His lack of CD4+ recovery is consistent with previous case reports of varicella zoster virus central nervous system IRIS.[4,5]

Although there are no prospective trials to guide the treatment of varicella zoster virus central nervous system IRIS, high dose IV steroids followed by an oral prednisone taper and IV acyclovir have been employed with clinical improvement.[4,5] The decision to discontinue highly active antiretroviral therapy is a difficult one. In mild IRIS, the symptoms are generally self-limited, and

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highly active antiretroviral therapy should be continued.[3] However, interruption of highly active antiretroviral therapy may be necessary in cases of life-threatening IRIS, especially if the patient is unresponsive to corticosteroids.[6] Yet, discontinuing highly active antiretroviral therapy risks life-threatening opportunistic infections, and IRIS may still recur after its re-initiation.[6]

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