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Acute HIV infection presenting as fulminant meningoencephalitis with massive CSF viral replication

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A 22-year-old man presented to the emergency department with 10 days of malaise, generalized rash, sore throat, oral ulcers, headache, nausea, and vomiting. On examination he had fever (101.5°F), hepatosplenomegaly, generalized maculopapular rash, and lymphadenopathy. He rapidly became obtunded, requiring intubation. Initial laboratory studies showed mild transaminitis, increased lactate dehydrogenase, and 4,600 leukocytes per μL with 61% bands and 18% lymphocytes. Bacterial and fungal blood cultures were negative as well as a rapid HIV test, additional serologies (including rapid plasma reagin and *Treponema pallidum* particle agglutination), quantitative PCRs (for viruses other than HIV), and urine and blood toxicology. CSF, on hospital day 4, showed a lymphocytic pleocytosis (total leukocytes: 100), high protein, borderline hypoglycorrhachia, and negative Gram stain and culture. Brain MRI revealed no meningeal enhancement or masses. EEG revealed no epileptiform activity. Flow cytometry on bone marrow biopsy and CSF found no evidence of malignancy; neither did an excisional lymph node biopsy (figure 1). An immunofluorescent assay test for HIV returned inconclusive and a Western blot detected HIV gp120/gp160 bands. Quantitative HIV RNA PCR was 1.4×10^6 copies/mL in plasma and in CSF exceeded the upper limit of quantitation (10^7 copies/mL) (figure 2).

The patient's clinical status improved and he was discharged 11 days later with a diagnosis of acute HIV infection with meningoencephalitis. Eighteen days after presentation, darunavir, ritonavir, emtricitabine, and tenofovir were started. A month later, low avidity HIV-1 antibodies were detected and neuropsychological testing revealed mild to moderate impairment in information processing speed, verbal fluency, and motor skills. Neurologic examination showed a mild spastic paraparesis with impaired ambulation. A spinal MRI 2 months later was nondiagnostic. Six months after presentation, his gait was improved, but upper neuron signs remained. Virologic suppression in plasma and CSF was achieved 5 months after initiating antiretroviral therapy (ART) (figure 2).

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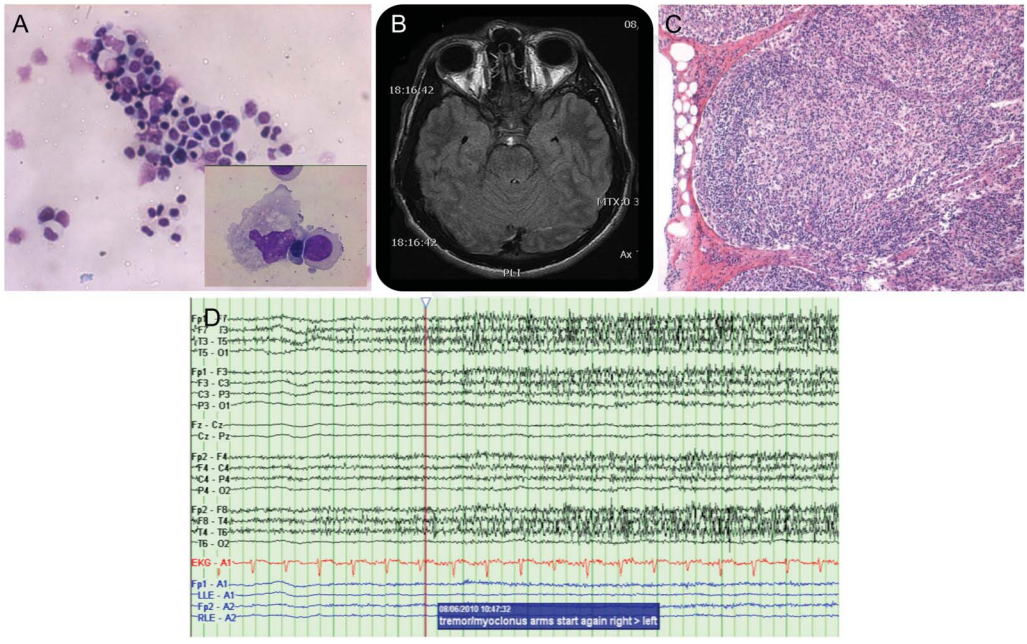
Figure 1 Imaging and biopsy findings



(A) CSF pleocytosis with atypical lymphocytes. (B) MRI brain (fluid-attenuated inversion recovery). (C) Hematoxylin & eosin of lymph node biopsy demonstrates HIV lymphadenitis. (D) EEG during acute episode of tremors shows muscle artifact, generalized reduction in amplitude, and slowing but no epileptiform discharges.

DISCUSSION

We report a case of massive and disproportionately high intrathecal HIV replication during acute HIV infection in a patient with fulminant meningoencephalitis. Acute HIV was diagnosed based on a positive viral RNA, a Western blot with 2 positive bands, no detectable antibody response, and recent sexual exposure to a male partner who reported an illness consistent with acute HIV infection. Meningoencephalitis was attributed to HIV infection, since careful microbiologic and clinical evaluations identified no other cause. Despite pleocytosis, meningismus and meningeal involvement by MRI were lacking. The primary care provider initiated ART 3 weeks after the initial signs of illness, eventually leading to full viral suppression. The patient experienced substantial recovery from the meningoencephalitis, but continued to show mild to moderate impairment on neuropsychological testing and had evidence of bilateral pyramidal tract dysfunction.

Neurologic manifestations of acute HIV are well recognized, though they occur in a minority of cases (17%–24%). The spectrum of neurologic illness is heterogeneous, with aseptic meningitis being most common. Our patient's illness was severe, but even coma and death have been reported.[1,2]

Mounting evidence demonstrates that HIV affects the nervous system at the earliest stages of infection, but early CNS invasion is not well understood. CNS HIV replication may be a critical event, as in the gut. A case of fatal iatrogenic HIV with death 15 days postinoculation has been reported.[2] Autopsy revealed proviral HIV DNA within the cerebral cortex. Such early and extensive CNS invasion might be enabled by the absence of specific neutralizing immune responses in the hyperacute stage, particularly in the CNS.

The higher viral load in CSF than plasma seen in this patient is uncommon, as typically viral loads in plasma exceed CSF at all stages. Early and extensive invasion might lead to chronic CNS inflammation and persistent neurologic deficits. It has been demonstrated that neurocognitive impairment can accompany early HIV.[3] The pathogenesis of these cognitive abnormalities is not completely understood but might be directly related to an overwhelming

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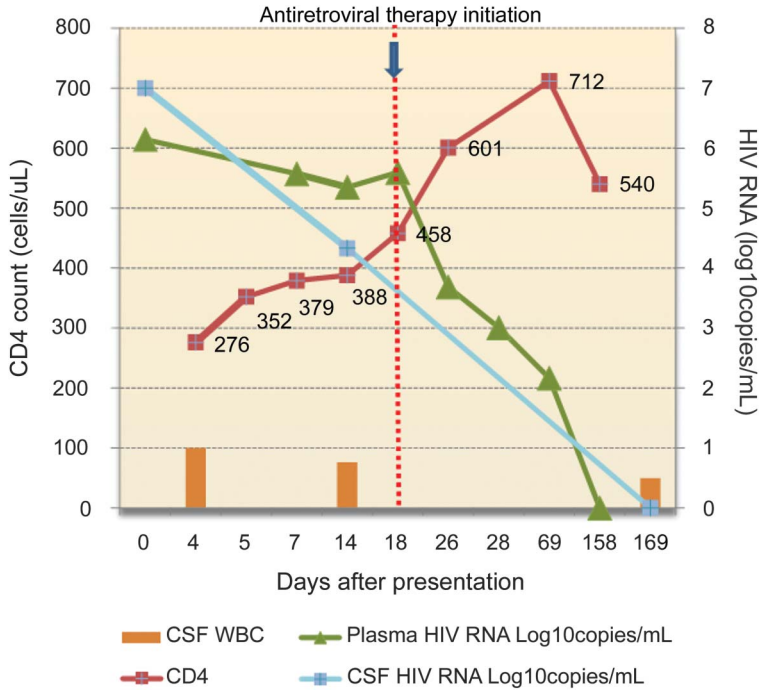
Figure 2 HIV viral load (plasma and CSF), CD4 count, and CSF leukocyte count during the first 6 months since the patient's first hospital admission



ART = antiretroviral therapy.

unspecific inflammatory response during viral invasion. However, neurocognitive improvement can be achieved with prompt ART initiation, and a first regimen with high CNS penetration frequently shows the greatest benefit.[4,5]

Acute HIV infection remains one of the principal factors driving the epidemic because transmission risk is highest in this early phase of the infection. Therefore, initiating ART during this stage reduces transmission risk and long-term complications.[6] However, due to its protean manifestations, only 17% of symptomatic acute cases are accurately diagnosed.[7] Maintaining high vigilance and aggressive testing for acute HIV (such as testing HIV viral loads), especially in high-risk populations, are essential for limiting the spread of the epidemic. Raising awareness among health care providers about the myriad of possible presentations of acute HIV, including unusual ones like this, will contribute to global efforts to combat this epidemic.

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