Case Report

Neurocognitive Presentation of HIV: HIV-associated Progressive Encephalopathy

A case report and review of the literature explores HIV presenting as a syndrome complex with cognitive, motor, and behavioral features.

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Acute HIV infection often involves neurological symptoms in which patients present with an encephalopathic syndrome with no clear history that might otherwise raise a high index of suspicion for HIV. These patients, during the initial infectious phase, may not have yet underwent seroconversion and so routine HIV antibody testing may not be positive leading to a lost opportunity for treatment as anti-retroviral therapy is most effective in this acute phase of HIV infection. The phenomenon has been previously well-described but remains an under-recognized and under-appreciated presentation of HIV infection.

Case Report

A 60-year-old man was admitted to the Loyola University Medical Center in November 2009 because of headache, neck pain, and fever. One week before admission, the patient went on a ship cruise to Puerto Rico. On the first day of the trip, he became ill with development of a headache accompanied by fever and chills. He was evaluated by the cruise physician and prescribed azithromycin. He was also advised to take ibuprofen. The patient continued this treatment for five days without improvement; his fever continued, the headache worsened, and he developed neck pain. He became progressively fatigued, weak, and
also developed mild confusion. He returned from the cruise and was brought to our emergency department by concerned family members.

The patient lived at home with his family in another state and was an owner of several restaurants. He had traveled to Chicago two weeks prior to join his family on the aforementioned cruise, and was planning on returning home after the vacation. The patient’s admission medical history included borderline hypertension, and admission medications were only acetaminophen. He provided no history of alcohol, tobacco, or illicit drug use. He denied any nausea, vomiting, vision changes, focal neurological symptoms, or loss of consciousness.

On initial examination the patient appeared in mild distress due to the headache. The axillary temperature was 37.1°C. The pulse was regular at 89 beats per minute, the blood pressure was 137/81mm Hg, and the respiratory rate was 20 breaths per minute.

The general examination showed no abnormalities. On neurological examination, however, he was inattentive and distractible; he had difficulty following two-step commands and recalled 2/3 words at five minutes. His speech was fluent. The cranial-nerve examination was normal. He had some difficulty cooperating with the motor examination due to neck pain, but strength and coordination were otherwise normal. He was not able to stand with both eyes closed, but his gait otherwise appeared to be steady. The sensory and reflex examinations were also normal. The Brudzinski sign was negative, but the Kerning sign was positive.

Laboratory investigations included a normal complete blood count and a complete metabolic panel. The C-reactive protein was elevated at 2.8, and the sedimentation rate was increased at 58. A chest radiograph was also normal except for an old clavicular fracture. Magnetic resonance imaging of the brain, with special attention given to the temporal area, with and without gadolinium contrast, did not reveal any abnormalities. An electroencephalogram showed diffused slowing consistent with encephalopathy but no epileptiform activity. A lumbar puncture demonstrated mild lymphocytic pleocytosis: white blood cell count was 40 with 81 lymphocytes and elevated CSF protein at 63.

Because of the altered mental status and abnormal CSF findings, the possibility of viral encephalitis led to initiation of acyclovir 1000mg twice a day at admission. The HSV CSF titer drawn at admission was 3.01, and the patient was continued on acyclovir for a total of six days, until the HSHV PCR results came back negative. Multiple additional CSF studies were obtained, including West Nile Virus IgM, Varicella Zoster Virus, Cytomegalovirus, fungal cultures, CSF cultures, and Acid Fast Bacilli; these all returned negative.

Additional serum studies were sent for HIV 1 and 2 antibodies, influenza A and B, respiratory syncytial virus assay, blood cultures, Epstein Barr Virus and mononucleosis screen. All of these tests were also negative. A CT of the chest and thorax was obtained to investigate for any infectious or neoplastic process and was also normal.

Throughout the hospitalization, the patient continued to complain of neck pain that later developed into a back and shoulder discomfort, especially on the right side. It was thought that the discomfort might be attributable to muscle spasm, so a trial of cyclobenzaprine, and then low dose diazepam, was attempted without providing relief to the patient. Due to the continued significant pain in the neck, back, and shoulder, an MRI of the cervical spine and brachial plexus was obtained. The images from the initial MRI were suboptimal and the study was repeated again with sedation. The repeat study revealed no cervical spine or brachial plexus etiologies, but demonstrated a bursal surface tear of the right anterior supraspinatus tendon. Orthopedic consultants recommended conservative therapy and the patient was started on a flexor patch and a steroid taper for the rotator cuff injury.

Ultimately, the patient’s family arrived from out of state and he was discharged with plan to travel back home and follow up with his primary care physician. It was not until two weeks after dis-
charge that the HIV viral load returned at over 500,000 and the patient’s primary physician was subsequently contacted, and retroviral therapy was initiated. Of note, neither the patient nor the family had ever provided a history of HIV risk factors.

Discussion
Human immunodeficiency virus (HIV) has infected approximately 33 million individuals worldwide, and the virus is rapidly becoming a world pandemic. Initial presentation of an acute infection often involves neurological symptoms. These individuals present with an encephalopathic syndrome, but no prior suspicion for HIV diagnosis and insufficient HIV antibodies to produce a positive HIV enzyme immunoassay. They present at a crucial time: at initial phase of the infection, and prior to seroconversion, when antiretroviral therapy has been shown to be most effective in reducing mortality and morbidity. HIV infection of the CNS is especially problematic; it causes a barrier to management and eradication of the virus because of the incomplete impermeability to antiretroviral drugs, resulting in sub-therapeutic levels within the CNS. As a result, while the HIV infection goes undiagnosed, the CNS ends up being a reservoir for the virus, providing a safe environment where the virus can replicate and mutate. Early treatment with antiretroviral therapy targets the virus before it has the advantage of sequestration in the CNS. Considering the crucial importance of prompt and accurate diagnosis of an acute HIV infection, it is troublesome that guidelines for management of acute HIV aseptic meningitis are limited to case reports. The need for increased awareness of neurological presentation of acute HIV infection is evident.

On admission to the hospital, our patient was thought to have an acute change in mental status accompanied by headache, neck pain and fever along with CSF lymphocytosis and elevated CSF protein. In this patient, the absence of clinical and laboratory evidence of electrolyte or organ function abnormalities ruled out metabolic or toxicologic etiologies. Instead, given the abnormal cerebrospinal fluid findings, the focus was redirected at infectious causes of meningitis and encephalitis. While the patient was treated with an antiviral agent (acyclovir) because of appropriate concerns of HSV encephalitis, retroviral therapies were not initiated early in the course of therapy. All other tests for viral, bacterial, and fungal pathogens were negative, and symptomatic treatment was ineffective except for a transient improvement in headache that may have been related to the administration of pain medications. It was not until after discharge that the HIV viral load was found to be significantly elevated; previously obtained HIV antibody testing was negative. As such, a missed opportunity for early intervention in HIV infection resulted.

In this context, the diagnostic evaluation was disappointingly inconclusive as to the etiology; it was not until after the patient had been discharged that an HIV viral load of over 500,000 was discovered. While the patient did not disclose any risk factors for HIV infection, his presentation was consistent with acute encephalitis likely due to a recent HIV infection. Unfortunately, it is often difficult to identify patients with primary HIV infection when they fail to disclose risk factors for acquiring the virus and there are no clinical findings indicative of immunosuppression. The presentation is depressingly common. Similarly, in other reports, patients with an underlying diagnosis of primary HIV infection were not initially identified, which resulted in a delay of diagnosis.

Successful identification of a primary HIV infection is fundamental; it offers the patient the opportunity to receive potent antiretroviral therapy prior to the time of virus seroconversion, when one can favorably affect the prognosis of the disease.

Neurological symptoms can occur before HIV diagnosis is suspected, before there are sufficient HIV antibodies to produce a positive HIV enzyme immunoassay. Neurological features of an acute HIV virus infection include aseptic meningitis, meningoencephalitis and encephalitis that can occur in up to 17 percent of patients. These individuals present with fever, headache, stiff neck,
photophobia, CSF with mild lymphocytic pleocytosis and slightly elevated protein, but normal glucose. Approximately 40-90 percent of patients with an acute HIV infection present with physical symptoms similar to influenza or mononucleosis. Primary HIV infection is characterized by fever, lethargy, and headache and generalized flu-like symptoms. The HIV virus does not directly invade nerve cells, but rather causes inflammation. It is this persistent infection and inflammation that results in breakdown of the blood-brain barrier, neuronal and axonal injury, neurotoxicity, and clinical symptom such as confusion, forgetfulness, headache and even changes in behavior and cognition.

Unfortunately the management of acute HIV aseptic meningitis is limited to case reports. Our case is consistent with other reports in the literature. One case report described a patient that presented with mild confusion and was not able to follow commands. Another case described a patient that had been well until 13 days prior to presentation, at which time he began having bi-frontal headaches, low-grade fever and began experiencing changes in behavior. Interestingly, another very similar report described a 31 year-old male, which presented with one week of confusion and fever after having returned from a trip to the Caribbean; this patient’s provisional diagnosis was viral encephalitis, based on lymphocytic fluid obtained via a lumbar puncture and he was treated with intravenous acyclovir.

It is evident that accurate diagnosis of HIV infection is crucial at time of acute onset. In acute presentation, when suspicion is high, the need for thorough history-taking cannot be forgotten. But patients can fail to disclose risk factors for HIV infection; hence, proper testing is crucial. It is important to remember that a viral load can detect the virus a few days after HIV infection, while a standard HIV antibody test can remain negative for months after the HIV infection.

While starting acyclovir in patients with a clinical picture of meningoencephalitis until an HSV PCR returns negative is an accepted clinical practice, a parallel approach is not considered for acute HIV infection. We suggest therefore, in cases of meningoencephalitis of unclear etiology, where the HIV antibodies are negative and the HIV viral load has been sent but remains pending, it may be reasonable to initiate a short course of retroviral drugs until return of the HIV viral load assay results. Thus, with awareness of the neurological presentations of an acute HIV infection, diligent history taking, proper laboratory testing, and rapid initiation of therapy, failure to identify primary infection can be minimized and crucial delays in antiretroviral therapy can be eliminated.

The author(s) declare that they have no competing interests.

An attempt was made to contact the patient, but this unsuccessful. However we have taken adequate steps to keep his identity safe and in no way have we revealed any personal information about the patient in the case report.


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