Fulminant Subacute Sclerosing Panencephalitis in an Individual With a Perinatally Acquired Human Immunodeficiency Virus Infection

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Background: Case reports of subacute sclerosing panencephalitis (SSPE) in individuals with human immunodeficiency virus (HIV) infection are scarce, and the natural history is unclear. To our knowledge, a fulminant presentation has not yet been described.

Objective: To describe a case of fulminant SSPE in an individual with a perinatally acquired HIV infection.

Design: Case report and literature review.

Setting: Christian Medical College Hospital, Vellore, India.

Patient: A 17-year-old boy with a perinatally acquired HIV infection.

Results: The patient presented with subacute-onset cognitive decline and myoclonic jerks with rapid deterioration of health (the patient died within 12 weeks of onset). The findings from magnetic resonance imaging and electroencephalography and the cerebrospinal fluid and serum measles antibody titers were suggestive of SSPE. The fulminant presentation in this case needs to be noted.

Conclusions: Along with the better life expectancy of HIV-infected individuals, there may be an increase in the incidence of SSPE in this population. Fulminant SSPE may be added to the spectrum of measles-associated neurological disorders in HIV.


The implications of the global human immunodeficiency virus (HIV) epidemic for measles-associated neurological disorders, immunological interactions between measles virus (MV) and HIV, and the role of vaccination in prevention are yet to be completely elucidated. To our knowledge, there are scarce reports of subacute sclerosing panencephalitis (SSPE) in HIV-infected individuals, and the natural history remains uncertain.

We present a case of fulminant SSPE in an individual with a perinatally acquired HIV infection. This case is being discussed specifically to highlight the rapid progression of SSPE in an individual with a perinatally acquired HIV infection. To our knowledge, this is the first such reported case in the literature.

REPORT OF A CASE

A 17-year-old boy presented with recent-onset behavioral changes and abnormal involuntary jerky movements of 1-month duration. These movements were noted initially in the left upper limb and in the left half of the face; the jerky movements subsequently spread to the right upper limb and to both lower limbs within 2 weeks of onset. There was also a 1-week history of decreased speech output, withdrawn behavior, and drowsiness. There was no history of fever, headache, vomiting, or seizures. He was detected to be seropositive for HIV infection at birth (perinatal transmission). There was a history of tuberculous uveitis 1 year earlier for which he had received antituberculous therapy for 9 months. There was no history of intake of antiretroviral therapy. The CD4 cell count measured 1 month prior to presentation was 859 cells/µL. There was a history of measles at 1.5 years of age. The child had not been vaccinated for measles.

On examination, the boy’s vital signs were stable. There was no clinically significant lymphadenopathy. He was conscious, oriented to persons but disoriented to time and place. Verbal output was decreased, and speech was slurred. Prominent myoclonic jerks were noted that...
mainly involved the left upper limb and the left side of the face, with dystonic posturing of the left upper limb. There were no signs of meningeal irritation.

A diagnosis of SSPE was considered most likely. Routine blood test results were noncontributory. A magnetic resonance imaging scan of the brain (Figure 1) showed focal asymmetric nonenhancing white matter hyperintensities bilaterally, predominantly in the right frontoparietal region. An electroencephalogram revealed frequent paroxysmal periodic bursts of high-amplitude sharp- and slow-wave complexes seen bilaterally and synchronously, and occurring at intervals of 3 to 4 seconds (Figure 2). Cerebrospinal fluid (CSF) analysis showed minimal pleocytosis (the total white blood cell count was 9 cells/μL [to convert to ×10⁶ per liter, multiply by 0.001], the differential count of lymphocytes was 90% [to convert to proportion of 1.0, multiply by 0.001], and the red blood cell count was 25 cells/μL). The CSF protein and glucose levels were normal (0.033 g/dL [to convert to grams per liter, multiply by 10.0] and 68 mg/dL [to convert to millimoles per liter, multiply by 0.0555], respectively).

Measles antibody titers in both CSF and serum samples were measured using a standard indirect immunofluorescence antibody assay. The in-house indirect immunofluorescence assay is based on the detection of human IgG anti-MV antibodies in paired serum and CSF samples. The serial doubling dilutions of the samples were reacted with MV-infected Vero cells immobilized on glass slides. The presence of intracytoplasmic and intranuclear apple-green fluorescence indicates the presence of anti-MV antibody. The end point was the highest dilution of the sample that showed a more than 2+ fluorescence intensity on a scale of 1+ to 4+. The titer of anti-MV antibodies is the reciprocal of the end-point dilution. A serum titer greater than 40 and a CSF titer of greater than 1 are considered to be significant. The ratio of serum to CSF is considered when making a diagnosis of SSPE. For any patient in whom paired serum and CSF anti-MV antibodies are measured, a serum to CSF ratio of less than 64 is considered to be diagnostic of SSPE. In our patient, the serum measles antibody IgG titer was 40, the CSF IgG titer was 2, and the serum to CSF ratio was 20, which was significant. An analysis for CSF oligoclonal bands was not performed.

A diagnosis of SSPE was made based on the characteristic clinical presentation, the compatible changes in the magnetic resonance imaging scan and the electroencephalogram, and the high titers of measles antibody in blood serum and CSF samples. Valproate sodium and clonazepam were prescribed for the treatment of the myoclonic jerks. Isoprinosine (500 mg 4 times a day) was administered for 6 weeks and subsequently stopped because the patient’s condition continued to worsen. He eventually succumbed to his illness within 12 weeks of onset. An autopsy could not be performed because the patient’s family would not consent to it. The clinical and investigational profiles were consistent with a diagnosis of acute fulminant SSPE.

Figure 1. T2-weighted axial fluid-attenuated inversion recovery sequence showing focal asymmetric nonenhancing subcortical white matter hyperintensities in both frontoparietal regions (right more than left).

**COMMENT**

A classically described spectrum of central nervous system involvement by MV would include acute measles encephalitis, acute disseminating encephalomyelitis, measles inclusion body encephalitis, SSPE, and fulminant SSPE. Measles inclusion body encephalitis is classically described in immunocompromised hosts with a rapidly fatal course, characterized by the presence of viral inclusions on histopathology, minimal inflammation, and the absence of elevated MV antibodies. However, SSPE is usually associated with a progressive, relatively slow neurological deterioration due to a persistent defective MV that escapes the host immune response, inflammation, and highly elevated MV antibodies. Fulminant SSPE, described in 10% of cases of SSPE, has been diagnosed when there is a neurological deficit of 66% within the first 3 months and death within 6 months. Risk factors for fulminant SSPE included exposure to measles at an early age, viral virulence, impaired host defense mechanisms, and concurrent infections with other viruses.

To our knowledge, case reports of SSPE in immunocompromised and HIV-infected persons are scarce. The 2 HIV-infected children with SSPE are unusual because of their young ages (18 and 21 months); these 2 cases could have represented measles inclusion body encephalitis. Our case report describes a young gentleman with a background of perinatally transmitted HIV infection who developed features suggestive of SSPE with fulminant neurological deterioration and death within 12 weeks of presentation. Although the histopathology would be most definitive for differentiating measles inclusion body encephalitis from SSPE, the age of onset, the absence of recent antecedent measles infection, and the high titer of
antimeasles antibody, in particular, support the diagnosis of SSPE in our patient. The characteristic clinical features and the electroencephalographic and magnetic resonance imaging findings support the diagnosis of SSPE. Cerebrospinal fluid pleocytosis is usually absent or minimal in SSPE; a case of rapidly progressive biopsy-proven SSPE, in which the CSF sample showed a white blood cell count of 40 cells/µL, has been reported.2

Under normal circumstances, clinical or subclinical MV infection triggers a cell-mediated immune response that comprises lymphocyte helper T cell 1 (Th1) activation and release of IFNs and IL-2, leading to the eradication of the invasive particle from the infected cells. After the rash phase, a humoral response comprising Th2 and release of IL-4 is mounted to provide long-term protection against future encounters with the virus. An impaired cell-mediated immune response due to genetic polymorphisms or acquired factors like HIV infection can impair the eradication of the MV from the infected cells. This, coupled with a favorable humoral immune response leading to premature antibody production, allows the virus to bypass acute immunological clearance, therefore favoring a chronic intracellular replication.9

Timely immunization is well known to protect against measles and SSPE. However, there have been concerns regarding the protective efficacy and safety of live attenuated vaccine for HIV-infected children. Vaccinated HIV-infected children tend to have lower antibody responses and to show a rapid decline in antibody levels compared with their immunocompetent counterparts.10 Considering adverse events, measles vaccination is not recommended for HIV-infected children with severe immunosuppression, which is defined by their age-specific CD4 counts.11 The impaired placental transfer of antibody from HIV-seropositive mother to child can also predispose infants to measles infection.12 There are also recommendations for early measles vaccination at 6 months because younger HIV-infected infants are not yet immunocompromised.13

With better health care standards and effective antiretroviral therapy, an increasing number of individuals with perinatally acquired HIV infection can survive through adolescence into adulthood. There may be an apparent increase in the incidence and detection of SSPE in HIV-infected persons, especially in developing countries. The natural history of SSPE in HIV-infected persons is currently unclear. Fulminant presentations, as described in the present case, may be related to impaired

Figure 2. Electroencephalogram showing paroxysmal periodic bursts of high-amplitude sharp- and slow-wave complexes seen bilaterally and synchronously at intervals of 3 to 4 seconds.
host defense mechanisms that mainly involve the Th1-derived cytokines like IFN-γ and IL-2. However, there are suggestions that the spectrum of clinical presentation and progression may depend on the dynamics of HIV-related immunosuppression. The expected pattern may be intermediate between measles inclusion body encephalitis (in severely immunocompromised individuals) and chronic SSPE.

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