Case Report

Subacute sclerosing panencephalitis in a child with human immunodeficiency virus (HIV) infection on antiretroviral therapy

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Abstract

Subacute Sclerosing Panencephalitis (SSPE) in HIV-infected children is a scarcely reported entity with previous reports describing fulminant course. The impact of highly active antiretroviral therapy (HAART) in altering its course remains unknown. We describe a child with HIV infection, who developed measles at 5 months of age and later developed SSPE at 14 years of age, remaining stable at 7 month follow-up, while on HAART for WHO (World Health Organisation) stage IV disease. The dynamics of HIV-related immunosuppression has an impact on the clinical course of SSPE. Contrary to reported cases of fulminant progression, a classic presentation with slow progression can be expected in children on HAART. We reemphasize the recommendation of "early measles vaccination" to prevent measles infection and subsequent SSPE in these children with an increasingly good life expectancy in the era of HAART.

Key Words

Early measles vaccination in HIV infected children, HAART, SSPE in HIV infected children

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Ann Indian Acad Neurol 2015;18:96-98

Introduction

Subacute Sclerosing Panencephalitis (SSPE) is a slow viral disease caused by altered measles virus with a progressive course leading eventually to mortality. There is scarcity of reports of SSPE in HIV infected children in describing its clinical course and progression. Complex interactions of the altered virus with the deranged immune system and alteration of its course with antiretroviral therapy is still being elucidated. Here we report a case of SSPE in a child with HIV infection on antiretroviral therapy for WHO clinical stage IV HIV disease, with a slowly progressive course like that of classical SSPE, that has not been reported previously in literature.

Case Report

A 14-year-old boy presented with five months history of behavioral changes with declining scholastic performance and three months history of recurrent jerky movements of limbs. He was adopted on day one of life without any legal proceedings, as he was abandoned by his parents. He had normal birth weight and normal developmental milestones. He had an exanthematous fever at 5 months of age, suggestive of measles which resolved without any immediate complications. He was immunized adequately for his age, with measles vaccination been given at tenth month of life.

He developed recurrent respiratory tract infections and loose stools requiring repeated admissions from 7 years of age. He had an episode of epistaxis at 9 years of age, during evaluation of which he was found to be seropositive for HIV I antibodies. He did not have any prior blood product transfusions or sexual abuse to suggest horizontally-acquired HIV infection. Possibility of perinatally-acquired infection was considered as perinatally acquired HIV infection presenting with symptoms only in adolescence and early adulthood has been described in literature.[1] He was lost to follow up then and returned after 3 months with progressive painless visual loss in his left eye that was diagnosed to be CMV retinitis; his concomitant CD4 count was 379 cells per micro liter and CD3 count was 1208 cells per microliter. Since he had WHO clinical stage IV manifestations of HIV disease, he was initiated on highly active antiretroviral therapy (HAART) after treating CMV retinitis. As he developed skin rash to Nevirapine, his initial 3-drug HAART regimen was modified to a combination of Zidovudine, Lamivudine

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DOI: 10.4103/0972-2327.144299

and Efavirenz which was well-tolerated. His CD4 counts improved to 628 cells per micro liter in three months and he was asymptomatic for any other opportunistic infections till 13 years of age.

He was 14-years-old, when he presented to us with five months history of behavioral changes noticed at school in the form of inattention with deteriorating school performance. Within 2 months of onset of behavioral symptoms, he developed recurrent jerky movements of his upper limbs followed by lower limbs with history of dropping objects from his hand while working and recurrent falls. He did not have any loss of consciousness, bladder or bowel symptoms, or visual deterioration. On examination he was well-oriented with recurrent myoclonic jerks involving limbs, axial muscles and face. Ophthalmic examination revealed old healed retinal scars bilaterally. He did not have any pyramidal or extra pyramidal involvement.

His blood counts, renal and liver functions were within normal limits. His CD4 count at presentation with neurological symptoms was 903 cells per micro liter. His MRI Brain [Figure 1] was normal. Electroencephalogram (EEG) [Figure 2] showed paroxysmal slow waves in delta range lasting for 1.5-2 seconds, occurring periodically at 18 seconds interval which had 1:1 relation with myoclonic jerks. CSF analysis showed 5 cells (lymphocytes), with protein of 42 mg % and sugar of 69 mg %. His CSF multiplex polymerase chain reaction (PCR) was negative for EBV, adenovirus, HSV, HZV. Measles serology by standard indirect immunofluorescent assay showed Serum: CSF IgG ratio of 20 (Serum: CSF ratio < 64 is considered positive). CSF oligoclonal banding was positive with IgG index of 0.8 and albumin quotient of 9.72 indicating intrathecal synthesis of antibodies. Hence the clinical picture, EEG and positive serology were diagnostic of SSPE. HAART was continued and he was initiated on Isoprinosine 500 mg four times a day along with antiepileptics. He has been under follow-up for past seven months without any worsening of symptoms and is still independent for his activities of daily living and attending school. His CD 4 counts also have been stable at around 900 cells per μl.

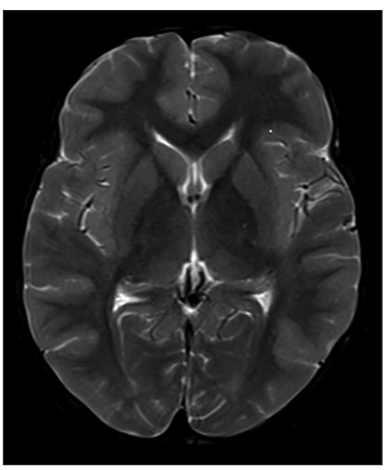

Figure 1: MRI Brain (T2 axial) of the patient done five months after onset of neurological symptoms revealing normal study

Discussion

The neurological complications of measles are acute measles encephalitis, acute disseminated encephalomyelitis, inclusion body encephalitis and subacute sclerosing panencephalitis. Inclusion body encephalitis occurs in immunocompromised individuals, with manifestations occurring within few months of measles infection, with a rapidly progressive course leading to death within a year of onset of the symptoms.[2] Classical SSPE, first described by Dawson in 1934, is caused by latent measles virus 6-8 years after the primary measles infection.[3] However, early-onset SSPE with a fulminant course has been described in children infected with HIV, as well as those perinatally infected with measles virus, probably due to lack of maternal antibodies and impaired host immunity.[4,5] Inclusion body encephalitis has also been reported in a hemophiliac with HIV infection and a child with acute leukemia.[6] Both these cases developed encephalitis 2 and 7 months after uncomplicated measles.

A more recent case reported from our institution was a 17-year old boy with perinatally acquired HIV infection in WHO clinical stage IV disease (extra pulmonary tuberculosis) not on HAART, who had a fulminant course of SSPE and died within 12 weeks of onset of symptoms.[7]

In contrast, our patient with WHO clinical stage IV HIV infection (past CMV retinitis) and SSPE has been stable in clinical Jabbour's stage II[8] for about seven months and so far seems to follow the natural typical course of SSPE, as described in most immunocompetent individuals. The classic periodic complexes as described by Cobb[9] (1966) occurs every 4-15 seconds, although there has been various reports (Westmoreland *et al.*, 1977)[10] where it occur every 1-5 minutes, depending on the stage and progression of disease. Our patients EEG showed periodic complexes, which were occurring every 18 seconds. This electrophysiological correlate again reemphasizes that our patient has a milder disease severity. Normal MRI brain in our patient, five months into the illness, again probably implies a severity of lesser magnitude.

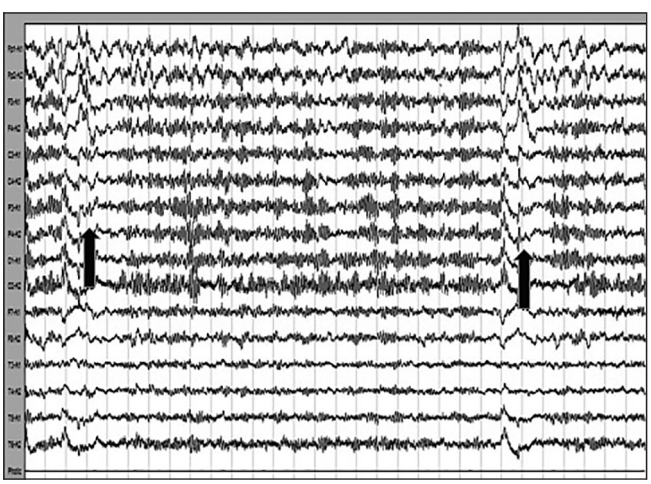

Figure 2: Electroencephalograph of the child (Monopolar montage, Sensitivity of 20 microvolt/mm, Speed 30 sec/page) showing periodic slow wave complexes lasting for 1.5 to 2 seconds occurring at a regular interval of 18 seconds

There are issues regarding the duration of maternal antibodies and seroconversion after vaccination in HIV-infected children. We could not comment about the efficacy of measles vaccination in our patient, since he developed measles infection at 5 months of age prior to measles vaccination, which is routinely given by the end of ninth month of life. Measles vaccination is recommended as early as 6 months of life[11] in HIV infected infants as they are more likely to acquire measles before 9 months of age and may not yet be severely immunocompromised at 6 months.[12]

The defective lymphocyte helper cells TH1 and its cytokines IFN and IL-2 leads to persistence of altered MV virus and subsequent development of SSPE.[13] The level of impairment of TH1 cell function might dictate the clinical course. Hence a classic presentation and slow progression can also be expected, contrary to most reported cases when the primary disease has been stabilized with HAART. However this area needs further research into the complex interaction of the altered virus and the role of HAART in containing the progression of disease.

Conclusion

The occurrence of classic onset and slow progression of SSPE in a child with congenitally acquired HIV infection is described here. The complex interaction of the altered virus with the preexisting immunodeficiency state and the role of drugs in stabilizing and altering its course need further research. We reemphasize the recommendations of early measles vaccination to prevent measles infection and subsequent SSPE in these children who can otherwise look forward to a good life expectancy in the era of HAART.

Acknowledgement

I acknowledge Dr. Ajith Sivadasan, DM, Dr. Anil B Patil, DM and Dr. Prabhakar DM for their help and guidance in preparing this manuscript.

What is known

Subacute Sclerosing Pan Encephalitis with coexisting HIV infection is a scarcely reported entity and the few cases reported so far had a fulminant course resulting in death within few months of onset of the disease manifestation.

What is new

The role of Highly Active Anti Retroviral Therapy (HAART) in containing the progression and altering the course of SSPE remains unknown. Contrary to the reported cases, classic onset and slow progression of SSPE in a HIV infected child can be expected if the primary disease is stabilized by HAART.

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How to cite this article: Muthusamy K, Yoganathan S, Thomas MM, Alexander M, Verghese VP. Subacute sclerosing panencephalitis in a child with human immunodeficiency virus (HIV) infection on antiretroviral therapy. Ann Indian Acad Neurol 2015;18:96-8.
Received: 22-06-14, **Revised:** 06-07-14, **Accepted:** 14-08-14

Source of Support: Nil, **Conflict of Interest:** None declared