

Akinetic rigid syndrome as a presenting feature of subacute sclerosing pan encephalitis

Leema P Cornelius MD DM (Neuro), Neeraj Elango MD DM (Neuro), Venkateswaran Kuttava Jeyaram MD DM (Neuro)

Department of Paediatric Neurology, Institute of Child Health & Hospital for Children, Madras Medical College, Chennai, India

Abstract

Atypical presentations of subacute sclerosing panencephalitis include hemiparesis, acute disseminated encephalomyelitis, cerebellar ataxia, visual disturbances, symptoms suggestive of the intracranial space-occupying lesion, and extrapyramidal movement disorders. Parkinsonism as the presenting feature of subacute sclerosing panencephalitis is a rare occurrence. Here we report a child who presented with bradykinesia and rigidity, underwent extensive investigations, finally turned out to be subacute sclerosis panencephalitis.

Keywords: Subacute sclerosing panencephalitis, bradykinesia, rigidity

INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a slowly progressive fatal inflammatory disease of the central nervous system caused by persistent and aberrant measles virus infection.¹ It is characterized by an insidious onset of cognitive decline, behavioral problems, myoclonic jerks, and eventually complete neurologic deterioration. Though extrapyramidal symptoms can occur in the later stages of the disease, akinetic rigid syndrome as an initial presentation is rare.² Herewith we report a case of SSPE presenting as an akinetic rigid syndrome.

CASE REPORT

A ten-year-old healthy female child got admitted with progressive difficulty in walking and standing, associated with the slowness of limb movements over the past three months. There was slowness of voluntary movements in the limbs in carrying out the day-to-day activities such as eating, brushing, combing, rising from bed, and walking. She had developed tremors in both hands affecting her day-to-day activities, frequent backward falls while walking, slurring of speech with reduced speech output in the last month. The child did not have visual disturbances, behavioral issues, or sleep problems. There was no history of fever, headache, vomiting, seizures,

or altered sensorium. No history of drug intake, exanthem, vaccination, head trauma, or jaundice either. She was immunized up to age.

On examination, she was conscious, oriented, had poor attention span, and had difficulty in doing simple arithmetic calculations. She had an expressionless face and her speech was slow, monotonous with reduced word output. Cranial nerve examination showed slow saccades and broken pursuit eye movements. Her vision and fundus examination were normal. Motor system examination revealed lead pipe rigidity in all four limbs, normal power with brisk deep tendon reflexes, and extensor plantars. Rest and postural tremors were noticed in both upper limbs. There were no cerebellar signs. During walking, the patient had difficulty maintaining her balance by swaying backward. Other system examination was normal.

On the basis of history, physical examination showing bradykinesia, rigidity, rest and postural tremors, mask-like facies - a clinical diagnosis of akinetic rigid syndrome was made. Wilson disease, childhood Huntington disease, juvenile parkinsonism, dopa responsive dystonia (DRD), pantothenate kinase-associated neurodegeneration (PKAN), autoimmune encephalitis were considered as differential diagnosis, and investigations were planned.

Complete blood count, blood sugar, serum

Address correspondence to: Dr. Leema Pauline, Dept. of Paediatric Neurology, Institute of Child Health & Hospital for Children, Egmore, Chennai, Tamilnadu, India. E-mail : leema_pauline@rediffmail.com

Date of Submission: 18 October 2021; Date of Acceptance: 3 December 2021

<https://doi.org/10.54029/2022ipn>

calcium, renal and liver function tests, lipid profile, serum ceruloplasmin, and copper were normal. The slit-lamp examination did not show Kayser-Fleischer ring. Peripheral smear was negative for acanthocytes. The child was started on levodopa-carbidopa combination (to start with 1mg/kg/day and increased up to 7mg/kg/day) and trihexyphenidyl (1mg/day in divided doses and increased to 6mg/day). MRI brain showed hyperintense signals in both putamen and subcortical frontal white matter in T2W and FLAIR sequences with diffusion restriction (Figure 1).

In view of bilateral basal ganglia involvement, mitochondrial etiology, organic acidemias were also considered and mitochondrial cocktail consisting of carnitine, thiamine, riboflavin, biotin was added. Serum lactate was normal. The electroencephalogram was normal. Tandem mass spectrometry and urine organic acids were negative. Cerebrospinal fluid analysis showed no cells, normal biochemistry, and sterile culture. CSF lactate was normal.

As there was no improvement in the clinical status, pulse methylprednisolone and intravenous immunoglobulin were given considering a possibility of autoimmune etiology. Repeat EEG showed diffuse background slowing. CSF virology was negative for Japanese encephalitis, Herpes, West Nile, enterovirus, varicella-zoster, Epstein bar, and cytomegalo viruses. CSF autoimmune panel including antibodies to DR2 receptors turned out to be negative. Thyroid profile and serum parathormone levels were within normal limits. Antinuclear antibodies were negative. The retroviral screening was negative. There was no significant improvement in the clinical picture. Meanwhile, during the third week of hospital

stay, the child developed myoclonic seizures, and the third EEG revealed periodic complexes suggestive of SSPE. A second CSF examination was done and sent for measles IgG antibodies, which showed elevated measles-specific IgG (1:625) levels confirming the diagnosis of SSPE. Sodium valproate and clonazepam were added. The historical review did not yield a prior history of measles. Mitochondrial cocktail, levodopa were withdrawn. Over the next one month child progressively deteriorated and succumbed.

DISCUSSION

Extrapyramidal signs such as rigidity, chorea, and dystonia are usually observed in the later stages of SSPE, and finally, the patient goes into a vegetative state. Initial presentation with predominant extrapyramidal features is uncommon. Only a few cases have been reported in the literature.³⁻⁶ Neuro Wilson was excluded in our case by normal ceruloplasmin and absent KF ring. The absence of diurnal variations and no response to L-dopa made dopa-responsive dystonia a distant possibility. Neuroimaging did not show the typical findings of PKAN (eye of tiger sign) or childhood Huntington disease (caudate atrophy). Normal serum, CSF lactate, and absence of optic atrophy, ophthalmoplegia made mitochondrial disorder less likely. Juvenile parkinsonism usually presents as dystonia and responds to L-dopa clinically, whereas our patient had bradykinesia, rigidity and did not respond to L-dopa.

Magnetic resonance imaging (MRI) findings in SSPE patients are usually nonspecific. The findings include ill-defined high signal intensity areas on T2-weighted images, commonly seen in the occipital subcortical white matter than in the

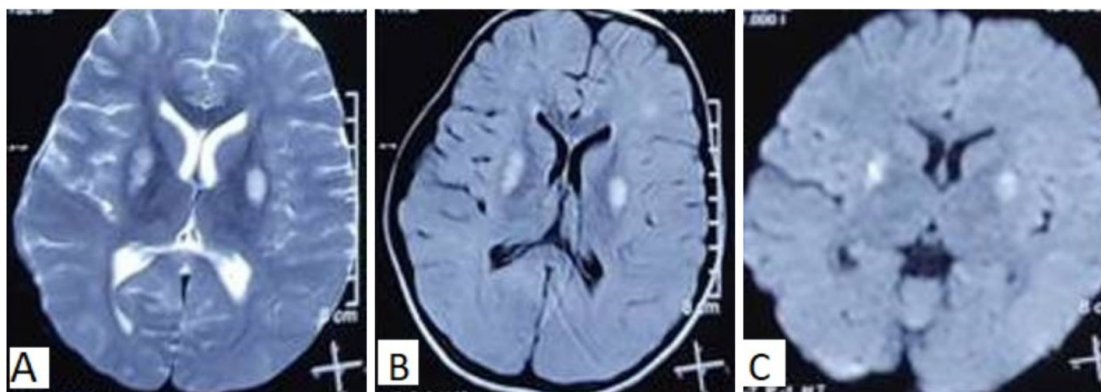


Figure 1. (A) MRI brain T2W image showing hyperintense signals in both putamina, and left frontal cortex. (B) FLAIR sequence showing hyperintense lesions are not suppressed. (C) Diffusion Weighted Imaging showing diffusion restriction

frontal region.⁷ The brainstem, cerebellum, and corpus callosum are less commonly involved. Basal ganglia involvement is not infrequent.⁸ Migratory basal ganglia lesions in SSPE have been reported and axonal spread of the virus from the substantia nigra has been implicated in producing parkinsonian symptoms.⁹ Diffusion restriction is not a common finding in SSPE, though it is a widely documented finding in measles encephalitis. Only a few reports cite diffusion restriction. Diffusion restriction could be due to cytotoxic or intramyelinic edema secondary to the necrotizing leucoencephalopathy. Though SSPE is classically described as a chronic encephalitis, the fulminant form can have acute necrotizing encephalitis like presentation.^{10,11}

Early in the course of the disease, the electroencephalogram (EEG) may be normal or show only moderate, non-specific generalized slowing.⁷ The first two EEGs of our patient did not show the classical periodic discharges.

Diagnosis of SSPE can be very challenging particularly in atypical cases when myoclonus is absent or subtle.¹² We did find our case challenging as she presented with parkinsonian features, basal ganglia hyperintensities, absent myoclonus, and a normal EEG at admission. The disease progressed rapidly and she succumbed within a month of diagnosis suggesting a fulminant course. Genetically determined immune dysfunction preventing a successful cell-mediated immune clearance of measles virus before two years of age had been implicated in the fulminant course of the disease. Steroid therapy would have led to further worsening. Autopsy examination of the brain could not be conducted as the parents were unwilling is the limitation.

SSPE is a progressive disorder and death usually occurs in 1–3 years. Approximately 5% of the patients can have substantial spontaneous long term improvement. A fulminant presentation with death within 6 months of the onset can be seen in around 10% of patients. A protracted course with the survival of >3 years after onset is seen in 5%–6%.¹³ Older age of onset was found to be associated with a better prognosis.¹⁴

Anti-viral drugs and immunomodulators have been used singly or in combination to slow down the progression of the disease. Intra ventricular or intra thecal Interferon alpha, an immuno modulator and oral Isoprinosine in the dose of 100mg/kg/day in three divided doses (maximum 3000mg /day) are considered to be the way forward. If there is improvement or stabilization, then combined therapy for life long

or at least six months, and isolated isoprinosine for rest of life. Symptomatic therapy for myoclonic jerks include sodium valproate, clonazepam and levetiracetam.¹²

In conclusion, parkinsonism can be an initial manifestation of SSPE. Hence CSF measles antibody testing should be considered in a child presenting with akinetic rigid syndrome and altered mentality. A high index of suspicion and knowledge about atypical presentations would avoid unnecessary investigations.

DISCLOSURE

Financial support: None

Conflict of interest: None

REFERENCES

1. Dyken PR. Subacute sclerosing panencephalitis. *Neurol Clin* 1985; 3:179-95. PMID: 2581121.
2. Prasanth LK, Taly AB, Sinha S, Ravi V. Subacute sclerosing panencephalitis (SSPE): an insight into the diagnostic errors from a tertiary care university hospital. *J Child Neurol* 2007; 22: 638-8. DOI: 10.1177/0883073807303999.
3. Misra AK, Roy A, Das SK. Parkinsonian presentation of SSPE: Report of two cases. *Neurol Asia* 2008;13:117-20.
4. Bozlu G, Cobanogullari Direk M, Okuyaz C. Subacute sclerosing panencephalitis with parkinsonian features in a child: A case report. *Brain Dev* 2015;37(9):901-3. DOI: 10.1016/j.braindev.2015.02.008.
5. Garg D, Reddy V, Singh RK, Dash D, Bhatia R, Tripathi M. Neuroleptic malignant syndrome as a presenting feature of subacute sclerosing panencephalitis. *J Neurovirology* 2018;24(1):128-31. DOI: 10.1007/s13365-017-0602-4.
6. Serin HM, Bilen S, Cans A. Subacute sclerosing panencephalitis presenting as hemidystonia. *Med Bull Haseki* 2014;52:137-9. DOI: 10.4274/haseki.1451
7. Garg RK. Subacute sclerosing panencephalitis. *Postgrad Med J* 2002;78:63-70. DOI: 10.1136/pmj.78.916.63.
8. Akdal G, Baklan B, Cakmakçi H, Kovanlikaya A. MRI follow-up of basal ganglia involvement in subacute sclerosing panencephalitis. *Pediatr Neurol* 2001;24:393-5. DOI: 10.1016/s0887-8994(01)00267-3.
9. Sawaishi Y, Yano T, Watanabe Y, Takada G. Migratory basal ganglia lesions in subacute sclerosing panencephalitis (SSPE). Clinical implications of axonal spread. *J Neurol Sci* 1999; 168: 137-40. DOI: 10.1016/s0022-510x(99)00177-x.
10. Oguz KK, Celebi A, Anlar B. MR imaging, diffusion-weighted imaging and MR spectroscopy findings in acute rapidly progressive subacute sclerosing panencephalitis. *Brain Dev* 2007; 29 (5):306-11.
11. Shah D, Srinivasan K, Sakale T, Sajith S, Kesavadas C. Diffusion restriction in fulminant

- subacute sclerosing panencephalitis: Report of an unusual finding. *Neurol India* 2015;63:452-6. DOI: 10.4103/0028-3886.158268.
12. Saurabh K, Singh VK, Pathak A, Chaurasia RN. Subacute sclerosing panencephalitis: An update. *J Clin Sci Res* 2021;10:35-42.
 13. Prashanth LK, Taly AB, Ravi V, Sinha S, Rao S. Long term survival in subacute sclerosing panencephalitis: An enigma. *Brain Dev* 2006;28:447-52. DOI: 10.1016/j.braindev.2006.01.008.
 14. Guler S, Kucukkoc M, Iscan A. Prognosis and demographic characteristics of SSPE patients in Istanbul, Turkey. *Brain Dev* 2015;37:612-17. DOI: 10.1016/j.braindev.2014.09.006.