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Case Report

AN INTERESTING CASE OF SSPE WITHOUT PAST MEASLES AND NORMAL VACCINATION

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ABSTRACT
A 12 year normally developed male patient comes with behavioural disturbance, cognitive alteration along with myoclonus. No definite past history of childhood measles. He was properly vaccinated. Examination both physical and csf along with EEG confirmed it as a case of SSPE. The peculiarity is in no past history of measles and development of SSPE even in normally vaccinated child.

INTRODUCTION

SSPE is a chronic complication of measles with a delayed onset and an outcome that is nearly always fatal. It appears to result from a persistent infection with an altered measles virus that is harbored intracellularly in the CNS for several years. After 7–10 yr the virus apparently regains virulence and attacks the cells in the CNS that offered the virus protection. This "slow virus infection" results in inflammation and cell death, leading to an inexorable neurodegenerative process.Virtually all patients eventually succumb to SSPE (Wilbert, 2007).

Key Words: *SSPE, Without Past Measles, Normal Vaccination*

CASES

A previously healthy and developmentally normal twelve- year-old boy presented with history of behavioural disturbances, decreased attention span and headache which started 2 months ago and was followed by myoclonic seizures, progressively worsening behavioural pattern with associated cognitive and locomotor impairment. There was no previous history of exanthematous fever, jaundice or vision abnormality. Immunisation history was normal with no significant family history.Physical examination revealed altered sensorium with Glasgow Coma Scale of 10/15, persistent myoclonic jerks, increased muscular tone, diffuse rigidity . Meningeal signs were absent and cranial nerves were normal. Examination of fundus was normal. Slit-lamp examination excluded the presence of Kayser-Fleischer ring. Our working differential diagnosis was directed to exclude multiple sclerosis, acute demyelinating encephalomyelitis, Hashimoto's encephalopathy, paraneoplastic limbic encephalitis, mitochondrial diseases and other rare neurodegenerative disorders including SSPE. A complete blood count, erythrocyte sedimentation rate, biochemical parameters including blood sugar, urea, creatinine, electrolytes, lipid profile, liver function tests, copper, ceruloplasmin, antinuclear factor, lactic acid, parathyroid and thyroid hormones were all within normal limits; 24-hr urine copper excretion was also in normal range. Abdominal ultrasonography was normal. Cerebro- spinal fluid (CSF) cytology, biochemistry and microbial analysis were normal but with raised titres of measles antibodies in blood and CSF. Scalp electroencephalography (EEG) showed frequent bursts of generalised spikes, polyspikes and sharp wave discharges (rademecker complex). Magnetic resonance imaging (MRI) brain revealed ill- defined irregular areas of altered signal intensity involving white matter of periventricular and subcortical regions. The patient was treated with valproic acid and isoprinosine along with supportive therapy in the form of passive exercises of all four limbs. However the patient succumbed to an episode of cardiorespiratory arrest during a seizure episode.

DISCUSSION

SSPE is a slowly progressive disease characterized by seizures and progressive deterioration of cognitive and motor functions.The diagnosis of SSPE can be reliably established if at least three of the following five criteria are met: (a) progressive sub-acute mental deterioration with typical signs like myoclonus; (b) periodic, stereotyped, high voltage discharges on EEG; (c) CSF globulin levels greater than 20% of total CSF protein; (d) raised titres of measles antibodies in blood and/or CSF in the absence of other antibodies, including against Herpes simplex virus (HSV) and Varicella zoster virus (VZV); and (e) typical histopathological findings on brain biopsy or autopsy. This patient meets criteria a,b and d and so no need for brain biopsy was felt. The pathogenesis of SSPE is related to defective measles virus maturation in neural cells. Aberrant M (matrix) proteins as well as other envelope proteins interfere with assembly and budding of infectious virus. The virus remains in intracellular form and spreads by cell to cell contact.

SSPE has an annual incidence from under 0.1 cases to 5 or 6 cases per million in nonimmunized populations. In areas of high early-life measle attack rates, SSPE accounts for a proportion of childhood neurodegenerative diseases.

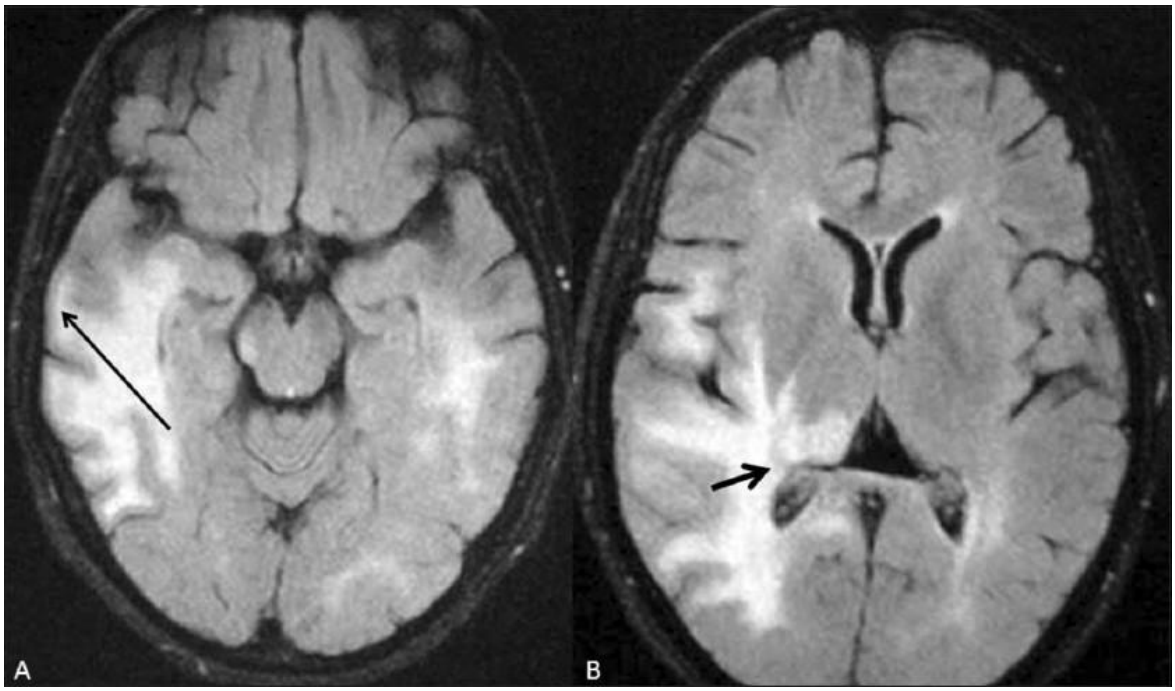

Figure 1: (A and B) Axial FLAIR MRI images of the brain show the T2-hyperintense lesions, seen in Figure 3, more conspicuously, especially in the subcortical (long arrow in A) and periventricular (short arrow in B) regions

Children infected in the first 2 years of life are at greater risk, and case-series consistently show SSPE to be more frequent in boys. The median interval between acute measles infection and SSPE is 8 years, with a range from 2-12 years. The early stage is marked by behavioral or personality changes and declining school performance. Myoclonus, seizures, spasticity, choreoathetoid or ballistic movements, ataxia, and chorioretinitis follow in the second stage, Optic atrophy, quadriparesis, autonomic disability, akinetic mutism and coma occur in the final stage of the disease. Majority of cases follow a progressive downhill course to death within a few years, some temporarily plateau or improve, and possibly 5% remit spontaneously (Garg, 2002).At the time neurological symptoms occur, neurons and glia contain nuclear and cytoplasmic viral inclusion bodies and high titer antimeasles antibody is found in both serum and

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CSF. The CSF/serum antibody ratio is consistent with high levels of intrathecal synthesis of measles antibody. CSF pleocytosis is absent, glucose is normal, and total protein is normal or elevated. Acute symptoms, together with increased intracranial pressure, are poor prognostic signs. The earliest MRI findings are high-signal intensity on T2-weighted images of gray and subcortical white matter in posterior portions of the hemispheres. During the second stage of disease, the EEG shows a pattern of generalized slow-wave complexes with a regular periodicity. The complexes may last up to 3 seconds and occur at regular intervals, between 4 and 14 seconds, against a background of depressed activity.

Some patients have improved or stabilized after one or several 6-week treatments with intraventricular interferon-a through an Ommaya reservoir, starting at 10 U/in2 body surface area per day, with daily increments, up to 106 U/m per day on the fifth day, 5 days per week, combined with oral isoprinosine (Inosiplex), 100 mg/kg per day. There have also been reports of response to intravenous ribavirin in combination with intrathecal interferon-a (Tomoda *et al.*, 200 i). The laboratory endpoint of treatment is the eradication of detectable measles antigen from the CSF. Systemic (subcutaneous) interferon-a, in daily doses of up to 5 million units, has been used with intrathecal interferon-a, to simultaneously treat the peripheral reservoirs of measles virus, lymphoid, and glandular tissue.

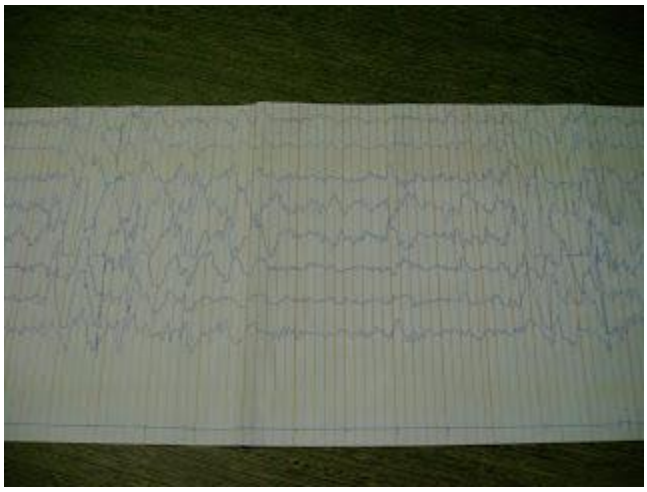

Figure 2: EEG showing characteristic rademecker complex

Prolonged or repeated treatments carry the risks of meningitis, interferon-a induced encephalopathy, and interferon-a upper and lower motor neuron toxicity. Immunization with attenuated live measles vaccine is recommended for infants between 12 and 15 months of age; measles vaccine is one component of the trivalent measles-mumps-rubella (MMR) vaccine. In areas where measles circulates widely, immunization is performed early, at 6 or 9 months. Fatal infection has followed measles vaccine in severely immunocompromised children, but there is no epidemiological evidence that vaccination causes SSPE.

Importance of This Case

This is a case of SSPE gaining an acutely progressive course with no prior history of measles in <2yr or <4yr age group. The patient even took proper vaccination. Prevention of SSPE depends on prevention of primary measles infection through the use of vaccine. SSPE has been described in patients who have no history of measles infection and only exposure to the vaccine virus. However wild-type virus, not vaccine virus, has been found in brain tissue of at least some of these patients, suggesting they had had subclinical measles previously.

SSPE is quite a prevalent condition of such rapid onset behavior disturbance, cognitive decline along with myoclonus in developing countries like ours and needs to be considered in the list of differentials in a child or adolescent with such features.

Table 1: Diagnostic criteria of SSPE [1]

Definitive: criteria 5 with three more criteria; probable: three of the five criteria.	
1. Clinical	Progressive, subacute metal deterioration with typical signs like myoclonus
2. EEG	Periodic, stereotyped, high voltage discharges
3. Cerebrospinal fluid	Raised gammaglobulin or oligoclonal pattern
4. Measles antibodies	Raised titre in serum (≥1:256) and/or cerebrospinal fluid (≥1:4)
5. Brain biopsy	Suggestive of panencephalitis

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