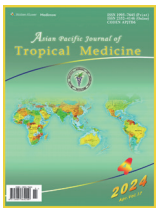

Case Report

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A rare complication of measles infection presented with subacute sclerosing panencephalitis: Report of two cases in India

Razeen Fatima✉, Amir Husain, Iram Tabish

Department of Medicine, JN Medical College, AMU, Aligarh, India

ABSTRACT

Rationale: Subacute sclerosing panencephalitis (SSPE) is a progressive neurological disorder caused by persistent measles virus infection. SSPE predominantly affects children and adolescents. The symptoms usually develop 6-15 years after measles infection and ultimately leading to death in many cases.

Patient concerns: Patient 1 presented with cognitive decline and myoclonus and the Patient 2 presented with diminution of vision with myoclonic jerks.

Diagnosis: Based on the clinical features with a characteristic electroencephalogram pattern and the presence of a high titer of anti-measles IgG in serum and cerebrospinal fluid, these patients were diagnosed as SSPE.

Interventions: Antiepileptics were started for controlling myoclonus along with supportive treatment.

Outcomes: Both patients were discharged on antiepileptics and supportive care.

Lessons: Whenever there are unusual clinical manifestations with unknown vaccination status, SSPE can be suspected and the cerebrospinal fluid should be examined for anti-measles antibodies. Our case study also highlights the importance of universal coverage of measles vaccination. To reduce the incidence of measles and associated deaths, it is important to maintain a high level of immunization coverage for the measles vaccine and to strengthen all the integral components of the national immunization program.

KEYWORDS: Subacute sclerosing panencephalitis; Measles; Myoclonus; Electroencephalogram; Cerebrospinal fluid

1. Introduction

Subacute sclerosing panencephalitis (SSPE) is a progressive neurological disorder caused by persistent measles virus infection. SSPE predominantly affects children and adolescents. The symptoms usually develop 6-15 years after a measles infection[1]. SSPE is characterized by gradual progressive mental decline ultimately leading to death in many cases within 1-3 years[2]. However, the clinical course of the disease tends to vary considerably. The diagnosis is typically based on a characteristic electroencephalogram (EEG) pattern and the presence of a high titer of anti-measles IgG in serum and cerebrospinal fluid (CSF).

Here, we report two cases of SSPE, one presented with cognitive decline and myoclonus, and the other presented with diminution of vision with myoclonus.

2. Case history

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Patient 1 is an 18-year-old female presented with a history

✉To whom correspondence may be addressed. E-mail: razeenfatima@yahoo.co.in

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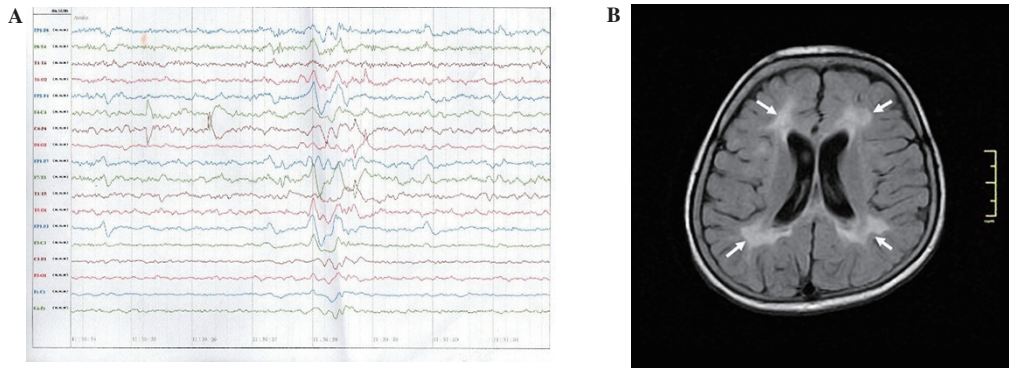

Figure 1. Electroencephalogram showing generalized spike waves and slow waves over both hemispheres of an 18-year-old female (Patient 1) with subacute sclerosing panencephalitis (A); MRI showing T2/FLAIR hyperintensity in periventricular areas and subcortical white matter in a 16-year-old male (Patient 2) with subacute sclerosing panencephalitis (B).

of progressive cognitive decline and decreased attention span. Approximately 7 months ago, the patient was in good health when her parents noticed some behavioral changes such as episodes of irrelevant talking, irritability and disorientation, which gradually progressed over time. Subsequently, jerky movements developed in the left half of the body, predominantly affecting upper limbs for 2 months. Soon the patient was unable to perform any task independently. There was no family history of any psychiatric or neurologic illnesses.

The patient's birth history was uneventful while her developmental milestones were achieved normally. She had not received any vaccinations and her parents were uncertain about whether she had a measles infection in her early childhood. On neurologic examination, she was conscious but disoriented presented with myoclonic jerks involving the head, the shoulders, and the left arm. There were no signs of meningeal irritation. Cranial nerve and fundoscopic examinations were normal. The examination of motor system, tone, power, and reflexes was within normal limits. Laboratory investigations showed normal values of blood counts, chemistry, and electrolytes. CSF examination showed increased levels of anti-measles antibody, but the values of protein, glucose, cell count were within normal limits. Serum IGg measles antibody level was also elevated. EEG showed paroxysmal generalized spike and slow waves over both hemispheres (Figure 1A). MRI brain showed effacement of cortical sulci, basal cisterns and bilateral sylvian fissures, suggestive of diffuse cerebral edema. A diagnosis of subacute sclerosing panencephalitis was made based on the presence of myoclonus, deterioration in cognitive function, elevated cerebrospinal fluid measles antibody levels, and periodic discharges in the EEG. The patient was treated with levetiracetam, clobazam and valproate. She was also given intravenous methyl prednisone for 5 days.

Eventually myoclonus got controlled on the antiepileptics but the level of cognitive impairment remained the same. The patient was put on enteral feeding and proper nutritional and bed care was advised to her guardians. Patient was discharged on antiepileptics and supportive care.

Patient 2 is a 16-year-old male complained of myoclonic jerks for 8 years with increased frequency and a sudden onset diminution of vision 15 days ago. The vision loss was painless and progressive with no reported fever or altered sensorium. The patient had no family history of similar complaints while his birth history was uneventful. The patient took partially immunization and his parents were uncertain about whether he had measles vaccination in childhood. On neurologic examination, he was conscious oriented along with myoclonic jerks involving right arm. There were no signs of meningeal irritation. Visual acuity examination showed the presence of hand movements in both eyes. Fundoscopic examination showed bilateral optic atrophy. The examination of motor system, tone, power, reflexes and sensory examination was within normal limits. Laboratory investigations showed normal values of blood counts, chemistry, and electrolytes. CSF examination showed increased levels of anti-measles antibody, while the values of protein, glucose, cell counts were within normal limits. Serum IgG measles antibody level was also elevated. EEG showed generalized synchronous bursts of spike and slow waves over both hemispheres. MRI brain showed confluencing areas of T2/FLAIR hyperintensities in periventricular region and subcortical white matter, corpus callosum which appear hypointense on T1 (Figure 1B). The patient was given valproate 500 mg *b.i.d.* for myoclonic jerks along with supportive care. The

patient was discharged on antiepileptic treatment. In the follow-up, myoclonus remain controlled on valproate therapy while the visual acuity remained the same.

3. Discussion

SSPE is a rare complication due to persistent measles infection. The worldwide prevalence of SSPE has declined to 1 per 100 000 cases of measles due to higher immunization coverage in developed countries[3]. However, measles remains endemic in many countries with limited access to vaccinations. The clinical features of patients with SSPE include behavioral abnormalities, cognitive decline, myoclonic jerks, seizures, and abnormalities in vision[4].

The symptoms progress through the following 4 stages:

Stage Ⅰ includes behavioral changes (irritability, mood swings, dementia, lethargy, social withdrawal) or cognitive decline.

Stage Ⅱ involves myoclonus, dyskinesia, muscle spasms, seizures, loss of vision.

Stage Ⅲ symptoms have progressed to extrapyramidal symptoms, posturing, and spasticity.

Stage Ⅳ patients may develop akinetic mutism, persistent vegetative state or coma during which breathing, heart rate and blood pressure can be affected[5].

SSPE is difficult to diagnose due to its variable clinical presentation. It is important to consider SSPE in a differential diagnosis in many circumstances. These two cases presented varying clinical symptoms of SSPE. Both patients presented with myoclonic jerks involving half of the body along with other features typical of SSPE. One patient had progressive cognitive decline while the other patient had visual symptoms due to optic atrophy. Although neither patient gave any history of measles infection in childhood but considering their age group, typical clinical manifestations and endemicity of measles in India, these patients were evaluated for SSPE.

According to Dyken's criteria, the diagnosis of SSPE can be established if the patient fulfils any three of the following criteria:

1. Elevated cerebrospinal fluid measles antibody titres
2. Typical or atypical clinical history (typical includes acute rapidly progressive, subacute progressive, chronic progressive, chronic relapsing-remitting while Atypical includes seizures, prolonged stage Ⅰ, unusual age infancy or adult)
3. Typical EEG (periodic complexes)
4. Increased cerebrospinal fluid IgG
5. Brain biopsy
6. Specials: molecular diagnostic test to identify measles virus mutated genome

Usually, two major criteria plus one minor criterion are required; the more atypical the SSPE, the more criteria 5 and/or 6 are needed[3,6].

Both of our patients met the Dyken's criteria on the basis of typical clinical features, typical EEG pattern and increased CSF antibodies. Therefore, whenever there are unusual clinical manifestations along with progressive cognitive decline, SSPE can be suspected and the cerebrospinal fluid should be examined for anti-measles antibodies. There are many differential diagnoses of SSPE which need to be excluded including viral encephalitis, autoimmune encephalitis, atypical multiple sclerosis, Creutzfeldt-Jakob disease, neurometabolic encephalopathies, neoplasms, paraneoplastic syndromes and leukodystrophies[7].

Currently, there is no cure for SSPE, and vaccination program is considered to be the most beneficial and cost-effective way for effective control. Most treatments are aimed at symptom reduction. Supportive treatment including management of seizures and other complications is the mainstay. Divalproate sodium is one of the common antiepileptics used.

Our patients were managed with multiple antiepileptics to control myoclonic jerks along with supportive treatment.

Antiviral drugs and immunomodulators are used in the treatment of SSPE. Among various drugs that have been tried in the treatment of SSPE, inosine pranobex, interferon alfa, ribavirin, and lamivudine are the most commonly used drugs in routine clinical practice. These drugs are used either singly or in combination. Inosine pranobex (Isoprinosine, Inosiplex) is an antiviral drug with immunomodulatory effects given orally in doses of 100 mg/kg/day (with a maximum dose of 3 000 mg/day) in three divided doses to patients with SSPE. Interferon alfa is an immunomodulator drug. It is preferably given *via* the intraventricular route due to its poor blood-brain barrier permeability[8].

Our cases also highlight the importance of universal coverage of measles vaccination. Global measles immunization programmes have focused on increasing routine vaccine coverage in young children through the World Health Organization's Expanded Programme on Immunization[9]. However, measles remains a leading cause of vaccine-preventable death in children below 5 years of age in many regions of the world, particularly in sub-Saharan Africa and South East Asia . The situation remains challenging in India where approximately 50% of the global measles-associated deaths occur. In order to reduce the incidence of measles and associated deaths, the Government of India has adopted various strategies, including expanding coverage with the first dose of the measles vaccine, intensive surveillance activities supported by adequate laboratory support, appropriate case management and implementation of catch-up measles vaccination campaigns for children aged 9 months to 10 years[10].

Hence, it is crucial to maintain a high level of immunization coverage for the measles vaccine and to strengthen all the integral components of the national immunization program to decrease the number of measles related deaths.

Conflict of interest statement

The authors declare there is no conflict of interest.

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Authors' contributions

RF and IT collected the patient data. RF and AH analyzed the data and wrote the manuscript.

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