COMMENT & CRITIQUE

Subacute sclerosing panencephalitis presenting as schizophreniform disorder

Subacute sclerosing panencephalitis (SSPE) is a slow progressive and mostly fatal neurological disorder caused by the measles virus typically affecting children and young adults. SSPE is characterised by progressive mental deterioration, recurrent myoclonic jerks and distinctive periodic complexes on the electroencephalogram (EEG). Diagnostic laboratory findings include immunoglobulin G (IgG) measles antibodies in the cerebrospinal fluid (CSF) (1). In developed countries where there is high population coverage for the measles vaccination, very low rates of SSPE have been reported. However, in developing countries such as India or Papua New Guinea where the vaccination coverage is inadequate, there is a high prevalence of SSPE (2,3). Behavioural abnormalities are the common early clinical presentations of patients with SSPE before the distinctive neurological features emerge. Sometimes, adolescents may present to psychiatrists with overt psychotic features. The case described below is such a presentation.

A 15 year-old tenth-grade student was brought by his parents to a board-certified psychiatrist with paranoid and self-referential delusions of several months duration. There was no family history of psychosis or any precipitating life events prior to the onset of psychotic symptoms. Based on a history and mental status examination, he was diagnosed with first-episode schizophreniform disorder (International Classification of Diseases (ICD) F20.8). It was unclear whether this patient was tested for known causes of psychotic symptoms at this age, such as illicit drug use, or autoimmune disorders such as central nervous system lupus, Huntington's disorder or Wilson's disease etc. Nonetheless, he was treated with a first-generation antipsychotic medication, the duration of which was not clear. He then started to experience recurrent falls for which he was referred to the Department of Neurology. At this point, positive psychotic symptoms were no longer evident, but what was evident instead was apathy and mostly negative symptoms. In reviewing his history, it was noted that he had suffered from measles exanthemata at 8 months of age and that he had not received the measles vaccine.

On neurological examination, he had bilateral upper and lower extremity cog-wheel rigidity and axial myoclonic jerks with delayed relaxation. It was surmised that these axial myoclonic jerks were the cause of the patient's falls. A tentative diagnosis of SSPE, stage 2, was made based on a history of measles in infancy, altered behaviour, recurrent falls, myoclonic jerks and extra pyramidal involvement (4). On investigation, the patient had the following findings: the EEG showed distinctive Raeder-Mecker complexes (Fig. 1) consisting of periodic high-amplitude slow-wave complexes, which were synchronous with the myoclonic jerks. The CSF analysis was positive for IgG measles antibodies with a titre of 3.65 relative fluorescence values (RFV) units. These findings confirmed a diagnosis of SSPE, and the antipsychotic medication was stopped. The parents of the patient were advised about the option of starting isoprinosine and intraventricular alpha-interferon treatment, but they were not able afford this treatment. He received sodium valproate for the myoclonic jerks. Following discharge from the hospital, the patient could not be contacted for follow-up.

SSPE has been reported from all parts of the world, but in the developed countries, it is considered a rare disease with lesser than 10 cases per year reported in the United States (5). However, in developing countries like India, SSPE continues to be highly prevalent with rates as high as 21 per million population (6). The most effective way to reduce the incidence of SSPE is to reduce the cases of measles in the community. Since the introduction and broad use of the measles vaccine, there has been a decrease in the incidence of measles and consequently of SSPE in most of the developed world (7). The World Health Organisation indicates that if $\geq$95% of the susceptible population is immunised, then it is possible to eliminate measles in the community (8). In countries such as the United States, Measles, Mumps and Rubella vaccine coverage has remained consistent, ranging from 91 to 93% since 2001 (9). However, in developing countries like India, the coverage of measles vaccine is still around 65% as per a survey performed in 2001 (10).

The behavioural symptoms of SSPE usually start in the teenage years, and this coincides with the first-episode presentations of either a schizophreniform disorder or a manic episode associated with bipolar disorder. As behavioural abnormalities are a common first presentation of SSPE, psychiatrists working in developing countries should consider SSPE in the differential diagnosis of first episodes of psychoses. There have been case reports of SSPE patients presenting with psychotic features. Jahnel reported a case of 19 year-old man who initially presented with hallucinations and negative symptoms and was diagnosed with schizophrenia. Later, when the full-blown neurological symptoms set in, the patient was diagnosed to have SSPE. The author noted that there were only four case reports in the literature about patients with SSPE presenting with psychosis (11). In reviewing the details of the six previously reported patients in the literature, one striking feature common in all the patients was the absence of a positive family history of psychosis. Three patients were diagnosed with childhood-onset schizophrenia and two were diagnosed with schizophreniform disorder. Delusions, especially of paranoia and persecution, were noted in four patients. Speech

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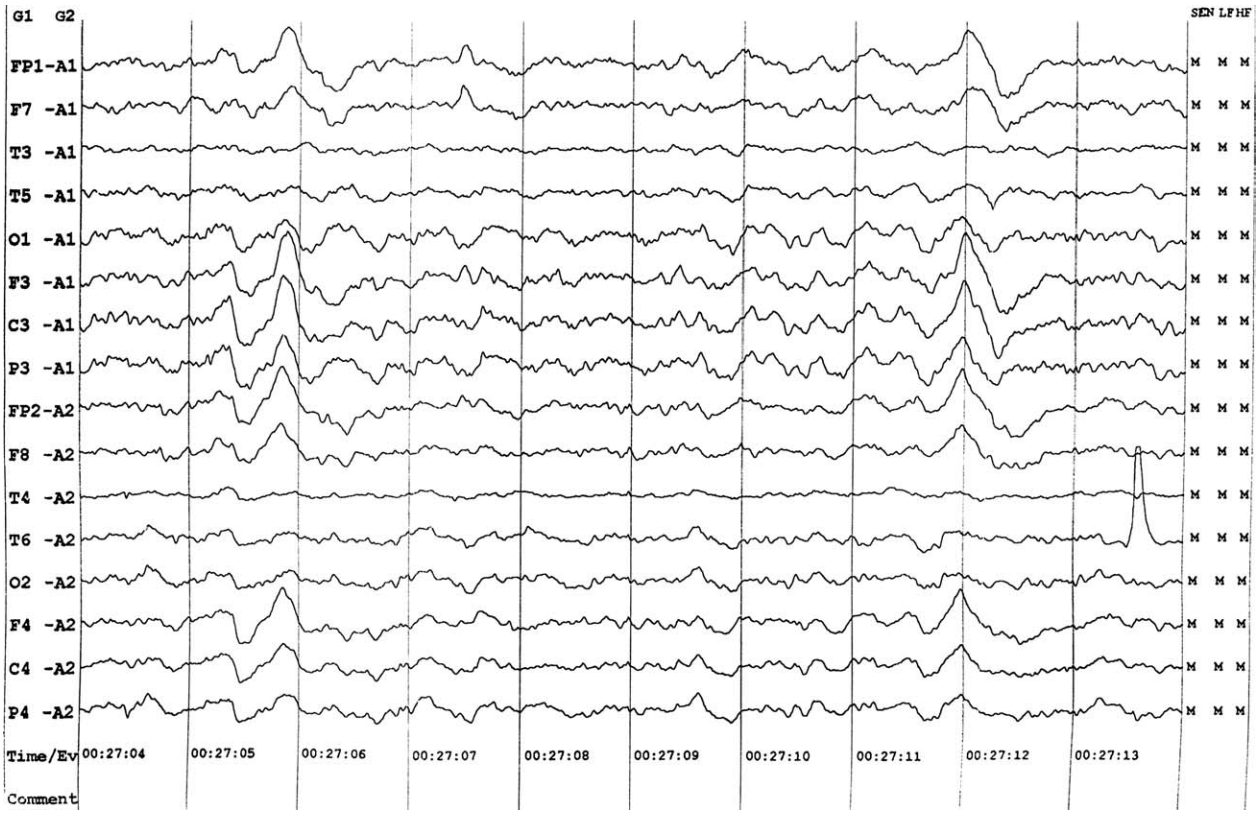

Fig. 1. Typical EEG of a patient with SSPE showing periodic complexes (Raeder-Mecker complexes) on a slow background.

disturbances were noted in three patients – echolalia, perseveration and incoherence being reported in these three patients (12–14).

In patients with SSPE, the parietooccipital region of the brain is most severely affected subsequently; pathological involvement spreads to the anterior portions of cerebral hemispheres, subcortical structures, brainstem and spinal cord. To explain the occurrence of schizophrenia-like symptoms together with coprolalia and involuntary vocalisation in the cases described by Caplan et al., the authors postulated that the involvement of the basal ganglia, limbic and mesencephalic grey areas of the brain very early in the disease process may explain the psychiatric symptoms in contrast to the initial posterior involvement seen in the usual presentations of SSPE. This rare occurrence of early subcortical and anterior cortical grey matter involvement may explain why psychosis is an infrequent and atypical presentation of SSPE (12,15).

In young adolescents presenting with psychotic symptoms, especially if such symptoms are accompanied by extra pyramidal rigidity and/or myoclonic jerks, psychiatrists working in the developing world or those in the developed world working with young migrants from the developing countries should consider SSPE in the differential diagnoses. Other possible neurological causes in such presentations could include neuroleptic-induced parkinsonism, juvenile Huntington's disease and Wilson's disease. An EEG and diagnostic titres of CSF IgG antibodies to the measles virus can confirm the diagnosis of SSPE.

Highly effective therapy for SSPE has not yet been developed, but immunomodulators such as alpha- and beta-interferon or isoprinosine are promising. The intraventricular administration of alpha-interferon in combination with oral isoprinosine is currently the most effective treatment, resulting in the stabilisation and improvement of neurological disability in 30% of treated patients (16). In developing countries like India, the cost of this treatment runs into hundreds of thousands of rupees, which may not be affordable by many. Symptomatically, patients are started on sodium valproate or clonazepam for the myoclonic jerks as was performed in this patient (17).

Even though SSPE is a mostly progressive and fatal disorder, a few instances of prolonged remission have been described in literature, suggesting that the prognosis may not be uniformly bad for a few patients, and hence, it is important to diagnose this condition accurately and early. It is expected that most cases of psychotic symptom presentations of SSPE would be seen in stage 1 of the disease. Behavioural changes are most frequent in stage 1 and can be misconstrued as a first episode of psychosis. So, it is critical to perform a careful neurological examination at stage 1, especially in patients with no positive family history, extremely disinhibited behaviour, rapid onset psychosis, seizure-like activity and vague neurological symptoms(13,14).

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