

Parkinsonian presentation of SSPE: Report of two cases

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Abstract

Subacute sclerosing panencephalitis (SSPE) is a disease caused by defective measles virus. It is usually characterized by progressive dementia; incoordination and generalized myoclonic jerks. Although atypical presentations are known to occur, parkinsonian presentation at the onset is rare. We report two cases of SSPE who developed parkinsonian features before the onset of psychointellectual impairment and myoclonus. We hypothesize that this may indicate upward spread of the virus from the upper brainstem, in contrast to the usual downward spread from the cerebral cortex.

INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) is a delayed form of measles encephalitis, occurring as a sequela to childhood measles infection. It is usually a slowly progressive fatal inflammatory disease of the central nervous system caused by persistent and aberrant measles virus infection.^{1,2} Early diagnosis of SSPE may be difficult since the initial symptoms such as intellectual and behavioral changes may be subtle, and persist for a few weeks to years without florid features of myoclonus. Atypical presentations of SSPE that have been reported include hemiparesis, acute encephalopathy, cerebellar ataxia, visual disturbances, and symptoms suggestive of intracranial space-occupying lesion.³⁻⁵ Thus, SSPE needs to be distinguished from various conditions such as degenerative white matter disease, childhood ataxic disorders and juvenile dementing illnesses.^{2,6} Although extrapyramidal features can occur in SSPE, parkinsonism as an initial presentation is rare.^{7,8} We present two cases of SSPE who presented initially with parkinsonism, and later developed myoclonus and intellectual deterioration, thus raising diagnostic dilemma initially.

CASE REPORT 1

A 13-year-old boy presented with a history of insidious onset, slowly progressive difficulty in standing and walking over two months. This was associated with slowness of limb movement, difficulty turning in bed, rest tremor in the left hand with re-emergence on sustained posture, but no intention tremor. He had difficulty holding objects and performing fine activities with the left hand, and slipping of footwear from the left foot.

His family members had noticed development of progressive slurring of speech with decreased speech volume and output. There was no history of deterioration of scholastic performance, behavioral abnormality, headache, vomiting, loss of consciousness, convulsive seizure, dimness of vision or jaundice. There was no history suggestive of cranial nerve dysfunction, sensory impairment or sphincter disturbance. There was no family history of similar illness. He had no past history of measles. Immunization status was unknown. There was no history of illicit drug intake.

General examination was unremarkable. Neurological examination showed that the patient was cooperative and oriented. Cranial nerve examination revealed normal visual acuity, color vision, fundi, and no evidence of cherry red macula or optic atrophy. He had normal range of vertical and horizontal eye movements, but saccades were slow and pursuit movements were broken. Motor system examination revealed parkinsonian features with mask-like facies, rest and postural tremor in both upper limbs with cogwheel rigidity, bradykinesia, and mild postural instability. There were predominantly left-sided pyramidal signs with exaggerated deep tendon reflexes, weakness of anti-gravity muscles and left extensor plantar response. There were no signs of appendicular and truncal ataxia, sensory or autonomic disturbances.

Three weeks after admission, the patient developed personality and behavioral changes with mental slowness and apathy, and deterioration of intellect followed by action myoclonus and later spontaneous periodic generalized myoclonus. The child was given gradually escalating dose of 300 mg levodopa and 30 mg carbidopa in combination without benefit.

Investigations revealed absent Kayser-Fleischer ring on slit-lamp examination. Blood investigations including red cell morphology, sugar, urea, creatinine, electrolytes (including calcium and phosphate), lipid profile, liver function tests (including ammonia), copper, ceruloplasmin, anti-nuclear factor, parathyroid hormone and lactic acid were all normal. His 24-hour urinary copper excretion was within normal limits. Abdominal ultrasonography showed mild hepatomegaly. Scalp electroencephalography (EEG) was recorded on 16-channels machines using standard procedures. EEG showed paroxysmal generalized bursts of spike and slow wave discharges in a pseudoperiodic pattern (every 8-10 seconds), with generalized background slowing. Nerve conduction studies, electromyography, and plain brain MRI were normal. Axillary skin and muscle biopsies were normal. Cerebrospinal fluid (CSF) study revealed 5 cells per cubic mm and all were lymphocytes, protein 50mg/dl, raised IgG (30 μ gm/dl), positive oligoclonal bands, and elevated anti-measles antibody IgG titer by ELISA.

CASE REPORT 2

A 15-year-old boy presented with insidious onset and progressive tendency to fall while walking associated with slowness of movement over 3 months. He had slurred speech with decreased volume and speed. According to family members, his handwriting deteriorated gradually and at the time of admission, he was unable to write. There was no history of behavioral abnormality, headache, vomiting, loss of consciousness, abnormal hyperkinetic movement, convulsive seizure, dimness of vision, hearing impairment or jaundice. He had no symptom suggestive of cranial nerve dysfunction, sensory impairment or sphincter disturbance. He had no past history of measles and his immunization schedule was complete.

General physical examination was normal. Neurological assessment revealed normal consciousness, but diminished attention span, impaired recent memory, and abnormalities in simple calculation. He had masked facies and normal eye examination except for slow saccades and broken pursuit. He had generalized parkinsonian features with hypophonic speech, cogwheel rigidity, bradykinesia and impaired postural reflexes. There was no resting, postural or intention tremor. He had truncal and gait ataxia without any appendicular ataxia. Sensory examination was normal.

The boy developed generalized myoclonus and intellectual impairment (with decline in scholastic performance) about 8 weeks after illness onset. He was given 300 mg of levodopa and 30mg of caridopa in combination but there was no improvement. There was no Kayser-Fleischer ring on slit lamp examination. Laboratory examinations including hemogram, serum copper and ceruloplasmin, calcium, phosphorous, alkaline phosphatase, and lactic acid were all normal. EEG showed periodic (every 5 seconds) generalized bursts of high-amplitude 2-to-3 Hz slow wave discharges on a slow background. Nerve conduction studies, electromyography and plain MRI of brain were normal. CSF study showed 6 cells per cubic mm (all lymphocytes), protein 60 mg/dl, raised CSF gamma globulin, positive oligoclonal bands of IgG, and elevated anti-measles antibody IgG titer in the serum and CSF. Axillary skin and muscle biopsies were normal.

DISCUSSION

SSPE usually runs a relentlessly progressive clinical course, resulting in death in most cases within 1 to 3 years after diagnosis.¹ The disease characteristically progresses insidiously through the stages of cerebral dysfunction in the form of cognitive impairment and behavioral changes, motor and convulsive phenomena especially stereotyped myoclonic jerks, and deterioration of consciousness (sometimes culminating in coma). Although initially uncertain, the diagnosis of SSPE in both our cases became evident when they developed rapidly progressive cognitive deterioration and myoclonic jerks, with the characteristic EEG changes of periodic complexes, elevated anti-measles serology, and positive CSF oligoclonal bands. Other differential diagnoses of childhood cognitive deterioration and movement disorders such as Wilson's disease, childhood SLE, hypoparathyroidism, Hallervorden-Spatz disease, and progressive myoclonic epilepsy (PME) appear unlikely in view of the lack of corroborative clinical, laboratory, and imaging findings.

Commonly SSPE affects the occipital area initially followed by spread to the anterior portions of the cerebral hemispheres, subcortical structures, brain stem and spinal cord. Clinically the affected patients present in stages characterized by cognitive deterioration, appearance of myoclonus and followed by hypertonic stage.⁹ Patients with SSPE may present initially with atypical symptoms that can cause diagnostic confusion.^{7,10}

We report here 2 cases where parkinsonism was the presenting syndrome, which has rarely been reported in the literature.^{7,8} The first case presented with left upper extremity resting and postural tremor, bradykinesia, hypophonia, and postural instability. The second case presented with bilateral parkinsonian features without rest tremor. Both cases had no myoclonic jerks and cognitive disturbance during the initial phase. The initial manifestation of parkinsonism in our patients suggests an early involvement of the substantia nigra / basal ganglia. Both cases subsequently developed myoclonic jerks. Myoclonic jerks usually represent gray matter involvement, and may be seen in processes affecting various parts of the neuraxis such as the cerebral cortex, thalamus, basal ganglia, dentate nucleus, brainstem or spinal cord.¹¹ In SSPE, there is some evidence to suggest a participation of the cerebral cortex in the generation of generalized myoclonus.¹² Behavioral and personality changes with apathy, depression and psychomotor slowness which subsequently developed in our cases suggest involvement of either the basal ganglia or its

connections with the prefrontal cortex as the possible anatomical substrates.¹³⁻¹⁴ In SSPE, lesions generally initiate from the cerebral cortex and subsequently involve the thalamus, brainstem, cerebellar cortex, and spinal cord.¹⁵ MRI in SSPE typically shows abnormal signal in the junction of gray and white matter of the parieto-occipital cortex. Changes have also been reported in the basal ganglia, similar to other viral affections.¹⁶⁻²⁴ Migratory basal ganglia lesions in SSPE have been reported and axonal spread of virus from the substantia nigra has been implicated in producing parkinsonian symptoms.⁸ Parkinsonian features however have been described at an advanced stage of SSPE.⁸ Our cases developed parkinsonian features as an early manifestation. Possibly, this is due to initial involvement of the substantia nigra, spreading later up the neuraxis to the thalamus, basal ganglia and cerebral cortex by transneuronal spread and thus explaining myoclonus and behavioral changes later in the course of the illness (Figure 1). We acknowledge, however, that our study lacks direct evidence of nigrostriatal pathway involvement. In fact, the lack of response

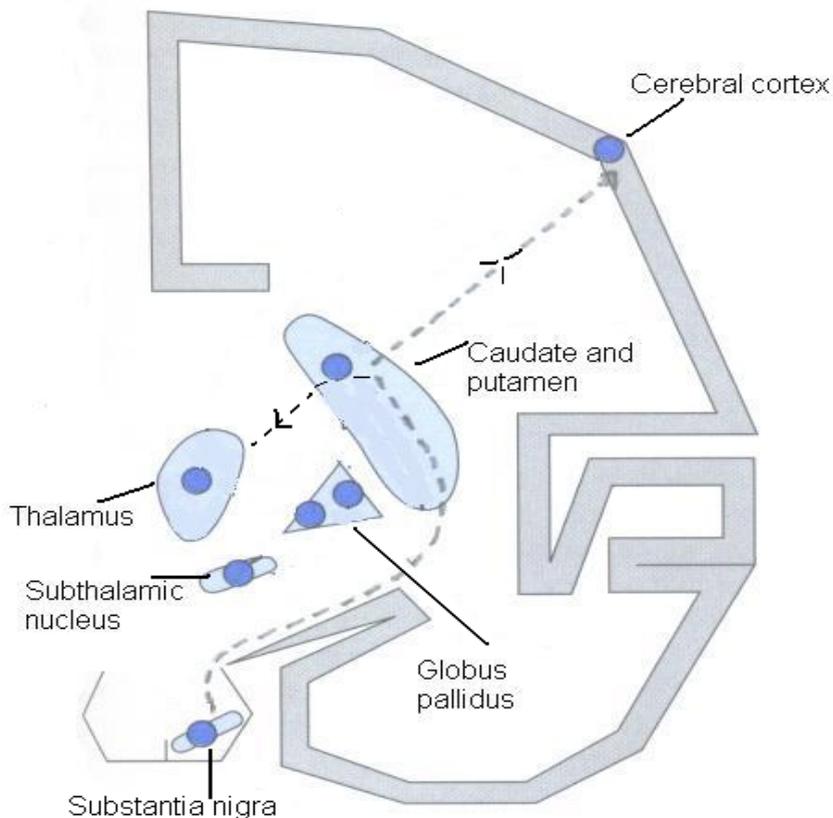


Figure 1. Neuronal circuitry of the basal ganglia and the possible path of spread of SSPE virus (shown by dashed line with arrow).

of the parkinsonian features to adequate doses of levodopa may suggest involvement of extra-nigral structures, such as the putamen, giving rise to a post-synaptic dopamine receptor defect.

In summary, we report on two teenagers with SSPE with parkinsonian features as early manifestations. Our findings suggest that SSPE should be considered in the differential diagnosis of sporadic rapidly-developing parkinsonism in childhood, especially when there is no prior vaccination against measles. We also hypothesize that, in some cases, the viral infection may begin in and then spread upwards from the upper brain stem.

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