Brainstem involvement in subacute sclerosing panencephalitis

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Subacute sclerosing panencephalitis (SSPE), which usually develops 2-10 years after measles infection, is a progressive neurologic disorder with an insidious onset. The neurologic dysfunctions associated with SSPE include generalized myoclonic jerks and seizure activity, and progression of the disease usually results in coma and death within one to two years after onset. Most of the cerebral lesions in SSPE are observed in the periventricular and subcortical white matter. Brainstem involvement in SSPE is very rare. In this paper, we report two cases with brainstem involvement in SSPE that was accompanied by other intracranial lesions with magnetic resonance imaging (MRI). These two patients died in a short time. Thus, brainstem involvement should be considered in patients with SSPE.

Key words: subacute sclerosing panencephalitis, brainstem, children.

Subacute sclerosing panencephalitis (SSPE) is caused by an unusual response to measles virus infection and is commonly characterized by behavioral changes followed by ataxia, myoclonic jerks and other focal neurologic signs. The diagnosis is based on history, typical electroencephalography (EEG) findings, elevated serum and cerebrospinal fluid (CSF) anti-measles antibody titers, and typical clinical findings[1].

Magnetic resonance imaging (MRI) is not necessary for diagnosis but may be helpful in the differential diagnosis[1,2]. In SSPE, the usual MRI manifestation is the presence of bilateral asymmetric lesions in the cerebral hemispheres. The basal ganglia, cerebellum, spinal cord, and corpus callosum are less commonly involved[2,3]. Brainstem involvement is very rare, with only a few cases reported previously, particularly in the Turkish series[4–7].

This report summarizes the unusual pattern of brainstem involvement in two children with SSPE.

Case Reports

Case 1

A 12-year-old boy was referred to our clinic because of drop attacks. The drop attacks were first noted two weeks before admission to the hospital. There was no history of problems at birth or with neuromotor development. Although he was immunized against measles at the age of 9 months, he had suffered from measles at the age of 10 months. He had exhibited mood changes, hyperactivity and aggression toward his sister during the three months before his admission. Slowed speech and impaired school performance were noted by teachers before the evaluation. Three months after admission, he had several attacks of myoclonic jerks, seizures and vomiting.

On admission, neurologic examination revealed an alert, cooperative boy with unprovoked drop attacks. Cranial nerves were intact, deep tendon reflexes were normoactive and plantar response was bilateral flexor. He admitted to our clinic in stage J:1 according to Jabbour staging[8].

Urinalysis, hemogram, CSF and routine biochemical analysis were normal. The patient's serum and CSF anti-measles IgG index were consistent with SSPE diagnosis (Table I).

His EEG revealed 1–3 Hz periodic and bilateral high amplitude sharp and slow-wave complexes. His cranial MRI scan on admission showed no lesion. The patient was prescribed inosiplex (inosine pranobex) (100 mg/kg/day) and interferon alpha 3 million units subcutaneous

Table I. CSF and Serum Anti-Measles IgG Index in the Patients

Index	SSPE	Case 1	Case 2
CSF measles IgG/CSF total IgG Serum measles IgG/serum total IgG	>10	63	143

SSPE: Subacute sclerosing panencephalitis. CSF: Cerebrospinal fluid. Ig: Immunoglobulin.

twice a week and carbamazepine for myoclonic seizures.

Myoclonic seizures disappeared in the first week of treatment. The patient was symptom-free for a period of five months after initial treatment, until he became bedridden within a week. MRI obtained during this period revealed high signals in the pons, which extended to the middle cerebellar peduncles, right temporal lobe and mesencephalon on T2-weighted images. High signal activity was more pronounced on the right hemisphere in the centrum semiovale (Fig. 1). His disease progressed to deep coma within one month and he eventually died.

Case 2

A seven-year-old boy was referred to our hospital for assessment of epilepsy and was admitted to the clinic with drop attacks, ataxia, silence, meaningless conversation, and dullness, which had developed in the last 15 days.

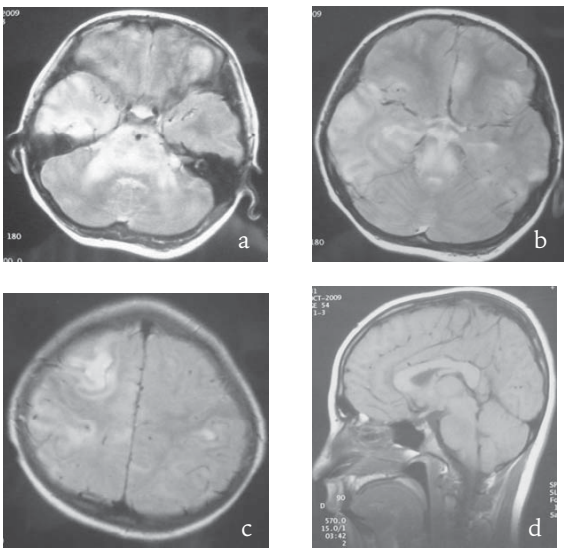

Fig. 1. Axial T2-weighted magnetic resonance images show high signal in the pons extending to middle cerebellar peduncles and right temporal lobe **(a)** and mesencephalon **(b)**, and more pronounced on the right hemisphere, in the cortical and subcortical white matter in the cerebrum **(c)**. Sagittal T1-weighted image shows low signal in the pons **(d)**.

He was not immunized against measles and had suffered from measles at about nine months of age. On examination at admission, he was a well-nourished child with a normal body weight (25–50 p) and height (25–50 p).

On neurologic examination, the patient was mute and had intense myoclonic jerks in his body. He could not walk unaided. Deep tendon reflexes and plantar responses were brisk and extensor symmetrical, respectively. His clinical stage was J:II according to Jabbour staging[8].

Hemogram, routine blood chemistry and urinalysis were normal. CSF investigation showed elevated titers of the measles antibody (Table I). In EEG examination, 1–1.5 Hz periodic high amplitude sharp and slow-wave complexes were detected. His MRI scan revealed hyperintense lesions in the pons and middle cerebellar peduncles (Fig. 2).

The patient was prescribed inosiplex and carbamazepine for myoclonic seizure and intravenous immunoglobulin, considered a fast course. However, his disease was unresponsive to therapy and he died within one month.

Discussion

Subacute sclerosing panencephalitis (SSPE) is an infrequent inflammation of the central nervous system, which has been advocated to develop due to a persistent measles infection. Most of the patients with SSPE survive for 1–3 years after diagnosis, with a mean survival of about 18 months[9].

The diagnosis of SSPE is based on the presence of characteristic clinical manifestations, electroencephalogram changes (a pattern of periodic complexes) and elevated antibody titers against measles in plasma and CSF[10].

Neuroimaging procedures are not necessary for diagnosis but may provide important clues in the clinical assessment and differential

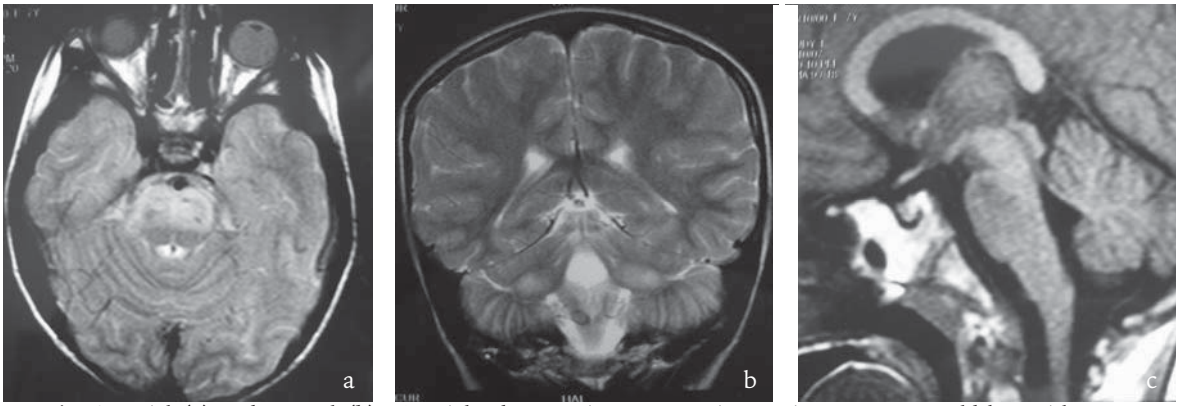

Fig. 2. Axial **(a)** and coronal **(b)** T2-weighted magnetic resonance images in a seven-year-old boy with SSPE show hyperintense lesions in the pons **(a)** and middle cerebellar peduncles **(b)**. Sagittal T1-weighted image shows hypointense lesion in the pons **(c)**.

diagnosis of SSPE[4]. MRI findings in a patient with SSPE may be normal in the early periods. With progression of the disease, MRI usually demonstrates several changes, such as increased white matter signal intensity and cerebral atrophy.

The presence of bilateral asymmetric lesions in the cerebral hemispheres, especially in the parietal and temporal lobes, has been reported. In patients with advanced disease, lesions have been reported to develop in the periventricular white matter, corpus callosum and basal ganglia. In the chronic stage, encephalomalacia and atrophy have been observed[2,3]. Brainstem lesions are very rare and are usually accompanied by other intracranial lesions[3-7].

Brismar et al.[3] reported that only one of 44 patients with SSPE had a cranial MRI scan that detected extensive increased-T2-intensity white matter lesions involving the supratentorial white matter, the cerebellum and the pons. Senol et al.[4] reported involvement of the pons with extension to both cerebellar peduncles and substantia nigra in their two cases, emphasizing the peculiar pattern of the disease.

In a recent report[7], MRI of the brain was reported to reveal a focal lesion in the pons associated with other cerebral lesions (white matter and cortical areas of the occipital lobes, corpus callosum) in one case and hyperintense lesion on T2-weighted images in the pons associated with the peduncle of the cerebellum in the other case. The authors suggested that patients with SSPE should be monitored with MRI for progression of the disease.

Case 2 in this report was referred to our clinic with severe clinical signs, and his MRI showed involvement in the pons and middle cerebellar peduncles. Case 1 was presented with a mild clinical picture and normal MRI findings on admission, but his disease progressed rapidly, and his MRI showed brainstem, cortical and subcortical white matter involvement after six months.

In the series of Risk and Haddad[11], approximately 10% of patients had an acute fatal course. The exact mechanism of the relationship between acute fatal course and brainstem involvement is not clear. In a preliminary study, Tuncay et al.[12] stated that parenchymal lesions were significantly correlated with the duration of the disease, and they observed a significant relationship between MRI findings and clinical stage in the first year of the disease.

In an earlier published report by Ohya et al.[13], clinical, neurophysiologic and neuropathologic findings of SSPE were correlated in five cases. According to these researches, in the early stages, the disease chiefly affects the occipital areas, then spreads to the anterior portion of the cerebral hemispheres. Subcortical structures, brainstem, and spinal cord are involved later. Involvement of the brainstem by intranuclear inclusion bodies appears to be an almost constant finding[13].

In conclusion, although brainstem involvement, which may indicate a poor prognosis, is very rare in the children with SSPE, it should be remembered during radiologic investigations.

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