Patients with acute, fulminant form of SSPE

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Subacute sclerosing panencephalitis (SSPE) usually begins insidiously and follows a subacute course with relentless but slow progression to death. In recent years, however, patients with acute or fulminant course were reported. In this article, we report on three patients (2 girls, 1 boy) with SSPE who developed an acute and fulminant course.

Subacute sclerosing panencephalitis may be seen with more atypical symptoms and more acute and fulminant courses due to various undetermined reasons. Early diagnosis is very important for the effectiveness of treatment. Children presenting with acute or subacute neurologic symptoms should be examined for SSPE, especially if they have no risk factors for hereditary neurodegenerative/ neurometabolic diseases, and it is more important if those children were not vaccinated or were infected with measles.

Key words: SSPE, acute-fulminant course, atypical findings.

Subacute sclerosing panencephalitis (SSPE) is a progressive inflammatory disease of the central nervous system caused by a persistent measles virus[1]. It usually begins insidiously and follows a subacute course with relentless but slow progression to death. In the typical course of the disease, further clinical stages include stereotypic attacks (myoclonia/atonia), worsening dementia, long tract involvement, autonomic failure, mutism, and decerebrated, decorticated rigidity[2]. Clinically, SSPE has a four-stage course over many months to two or more years. However, in about 10% of patients, clinical manifestations of SSPE were not typical, and patients with acute or fulminant course were reported[3-6]. Acute, fulminant course is diagnosed as the patient develops at least 66% neurologic disability (as measured by the neurologic disability index) in the first three months or death within six months[7].

Here, we report on three patients with SSPE who developed an acute, fulminant course.

Case Reports

Case 1

A 14-year-old-girl was admitted with acute dysarthria for the last four days. Her past medical history was unremarkable. No record of measles immunization or infection was found. She had been attending a school for normal children and had received good results from an examination a week previously. Family history was negative for neurologic disorders.

Her mental and motor development and physical examination were normal. During neurologic examination, she was conscious. It was found that she had dysarthria, auditory agnosia, and also increased tonus on her left side. The rest of the neurologic examination was found normal. Blood biochemistry, metabolic screening, blood lactic/pyruvic acid levels, and cerebral magnetic resonance imaging (MRI) were normal. An electroencephalogram (EEG) showed spike and wave, and sharp wave paroxysms especially on right frontal and central zones. Ten days after admission, she presented head drop attacks. Analysis of cerebrospinal fluid (CSF) was performed. The biochemistry of CSF was normal, but increased titers of anti-measles antibodies in CSF were measured by enzyme-linked fluorescent assay (ELFA) as 1:320. She was treated with intravenous immunoglobulin, carbamazepine, isoprinosine (100 mg/kg/d) plus subcutaneous beta-interferon 1a. Her neurological disability index (NDI) deteriorated from 13 to 62 in two months. She died at home four months after her first symptoms.

Case 2

A three-year-old girl presented with poor coordination, inability to walk, and head nodding for the last 15 days. Mental and motor status was normal. In her medical records, there was no data about immunization or infection with measles. Family history was unremarkable, except for parental consanguinity. Her physical examination was also normal. During the neurological examination, she was confused, slowed in her responses. She had dysarthria and cerebellar signs on her left side.

In laboratory examination, blood chemistry, metabolic screening and cerebral MRI were found normal. EEG showed suppression-burst pattern. CSF biochemistry was normal; however, anti-measles antibody titers in CSF were elevated (1:320). She was put on carbamazepine, isoprinosine and beta-interferon 1a therapy. In spite of treatment, her NDI score was deteriorated in one month (from 20 to 65), and she died after two months.

Case 3

A 5.5-year-old boy presented with inability to walk in the last four days. Six days before admission, he had upper respiratory tract infection, but no medical therapy was given. His past medical history revealed measles virus infection at the age of 10 months. His physical and mental development were normal. During neurologic examination, he was conscious, but had slurred speech, mild truncal ataxia, and mild pyramidal signs. His NDI score was 16. Cranial nerve examination and funduscopic examination were normal. During the course of hospitalization, he exhibited head drop attacks. Cerebral MRI was normal. EEG showed periodic, paroxysmal sharp and slow wave discharges on a diffusely slow background. SSPE was diagnosed on the basis of abnormally elevated anti-measles antibodies both in serum and CSF (1/640). He was treated with carbamazepine, beta-interferon 1a and isoprinosine. In spite of the therapy, his neurologic status worsened progressively. The clinical stage of disease progressed to vegetative form in two months. The NDI score was 64 two months after his first admission.

Discussion

In the classical form of SSPE, slow progression of neurologic symptoms goes through four characteristic stages: (I) slowly evolving behavioral and intellectual deterioration; (II) various types of involuntary movements; (III) severe pyramidal and extrapyramidal hypertonus and disappearance of hyperkinesias; and (IV) chronic vegetative state and death. Stage I may last from several weeks to several years, stage II typically lasts from three months to one year. Stages III and IV often last from six months to one year[8,9]. The rate of progression is variable. In the majority, death occurs within 1-3 years after onset of symptoms. In the series of Risk and Haddad[10], approximately 10% of patients had a fulminant course. PeBenito et al.[7] reported 25 cases with acute, fulminant form of SSPE between 1953 and 1997. Marjanovic et al.[3] reported two patients with acute presentation of SSPE. One of them presented with episodes of night terror. He died 2.5 months after the onset of the night terror attacks. The second patient was admitted to hospital with sudden onset of partial seizures, and he died four months after the onset of the first partial seizure. In another report, a girl aged 15 years 9 months presented with drop attacks and died less than three months after the initial presentation[4]. Chung et al.[11] reported a 14-year-old boy who manifested the acute fulminant form of the disease and presented a month before with transient visual agnosia. Takayama et al.[12] also reported a 12-year-old child with fulminant SSPE who died within four months. They reviewed the cases of fulminant SSPE in the literature and reported that half of the cases involved visual agnosia as an initial symptom. We did not find this symptom in our patients. Our patients presented acute neurological findings during the first examination but did not have the symptoms or evidence of behavioral and intellectual deterioration at the beginning of the disease. In spite of the therapy, the neurologic status of all patients worsened progressively. In rapidly progressive SSPE, various stages of disease cannot be recognized. The exact mechanism producing an acute fulminant course is not known. Several factors such as exposure to measles at an early age, viral virulence, impaired host defense mechanisms, and concurrent infections with other viruses have been suggested as responsible for producing a rapid course of the disease[13]. Probable derangement of T-cell subsets and alterations of T-lymphocyte functions in patients with SSPE is thought to be one of the causative factors[14].

Most patients with SSPE have a history of primary measles infection at an early age (<2 years), and present after a latent period of 6-8 years. Measles infection under one year of age carries a risk of SSPE 16 times greater than that in children over five years of age. Widespread immunization has produced greater than 90% reduction in the incidence of disease in the developing countries. When the disease occurs in vaccinated children, it is thought to result from a subclinical measles infection. In the history of the first two patients, no data was found regarding measles infection or immunization. This would indicate that they had subclinical infection. For the diagnosis of SSPE, subclinical infection cannot be ruled out even in patients with no history of measles.

Diagnosis of SSPE is based on a positive history of measles infection, clinical picture, typical electroencephalographic finding (suppression-burst pattern), and elevated serum and CSF anti-measles antibody titer[1,2]. Reverse transcriptase polymerase chain reaction technique and brain biopsy may be useful in confirming the diagnosis in SSPE with negative CSF findings[11]. MRI is more sensitive in detecting white-matter abnormalities. In the early stages of the disease, cerebral MRI shows lesions usually involving parieto-occipital cortico-subcortical regions asymmetrically. In time, symmetric periventricular white matter changes become more prominent. However, MRI findings can be normal, especially in the early stages of the disease, as seen in our patients. Öztürk et al.[15] concluded that there seems to be no correlation between the clinical stages and either the duration from the onset of SSPE or the MRI findings. Rarely, atypical MRI findings such as brain stem involvement and cerebellar atrophy have also been reported[15-17].

The clinical profiles of SSPE have revealed varied presentations. Some signs and symptoms of SSPE at an early stage such as hemiparesis, papilledema, headaches, generalized tonic-clonic seizures, nausea, and vomiting can lead to an erroneous diagnosis such as acute encephalitis, acute disseminated encephalomyelitis or some intoxications[5,6,18-21], but typical drop attacks, and EEG, CSF and MRI findings can lead to the SSPE diagnosis. At times, SSPE may need to be distinguished from various neurodegenerative conditions characterized by myoclonus, ocular findings, and progressive dementia and from some other progressive neurological disorders, such as Unverricht-Lundborg disease, Lafora disease, juvenile ceroid lipofuscinosis, myoclonic epilepsy with ragged red fibers and neuraminidase deficiency. The action myoclonus, ataxia, predominant generalized tonic-clonic seizures, marked clinical and EEG photosensitivity, slight mental retardation, and trend toward stabilization of the condition are typical for Unverricht-Lundborg disease; ataxia, severe action and resting myoclonus, predominant occipital abnormalities, and constant photosensitivity in the EEG are characteristic of Lafora disease; retinitis pigmentosa, slow evaluation of neurologic deficits, and delayed seizure manifestation are typical for juvenile ceroid lipofuscinosis; deafness, myopathic or neuropathic signs, ataxia, and polymorphic neuroimaging abnormalities are consistent with myoclonic epilepsy with ragged red fibers; and burning hands and feet and prominent facial myoclonus are typical of neuraminidase deficiency[5]. The SSPE diagnosis may also be confirmed by the typical CSF findings. Occasionally, patients with SSPE can present with lateralizing neurological signs, partial seizures, or papilledema; these findings can lead to an erroneous diagnosis of an intracranial space occupying lesion. The diagnosis is based upon typical CSF changes and a characteristic electroencephalography pattern. The diagnosis of SSPE can be reliably established if the patient fulfils three of the five criteria given by Dyken[1].

Treatment for SSPE is still undetermined. Antiviral agents, such as amantadine and ribavirin or immunomodulators, such as isoprinosine, interferon, immunoglobulin and corticosteroids, have been used[22-24]. Although Cases 2 and 3 were younger than six years, we administered beta-interferon therapy because of progressive disease; however, we found no effect on the progression. It is known that the sooner the disease is diagnosed, the better the results of treatment[25-27]. However, the results of the treatment of SSPE are not yet totally satisfactory. Since the treatment of SSPE is only partially effective in some patients, immunization against measles remains the only preventive intervention against this fatal disease.

In conclusion, SSPE has recently been seen with more atypical symptoms and more acute and fulminant courses due to various undetermined

reasons. SSPE must be considered also in patients with acute neurologic presentation such as ataxia, dysarthria, and inability to walk. Early diagnosis is very important for the effectiveness of treatment[15,18]. Children presenting with acute and/or subacute neurologic symptoms should be examined for SSPE, especially if they have no risk factors for hereditary neurodegenerative/neurometabolic diseases, and it is more important if those children were not vaccinated and/or were infected with measles.

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