Subacute sclerosing panencephalitis (SSPE) is rare in Taiwan. On admission to hospital, a 15-year-old boy was diagnosed with SSPE based on the clinical picture, electroencephalogram, cerebrospinal fluid studies, and brain biopsy. The initial clinical picture was a decline in school performance and a change in personality, followed by progressive tic-like involuntary movements and mental impairment for 8 months, then a rapidly progressive course. After the patient was treated with oral inosiplex and intraventricular interferon-α (IFN-α), his condition stabilized and the neurologic disability index score improved slightly. There were no major side effects during treatment except for a transient initial elevation of body temperature that lasted for several days. Oral inosiplex and intraventricular IFN-α appear to be safe and effective. Early identification and aggressive treatment of SSPE is important.
mumps-rubella (MMR) vaccination (age at vaccination unknown).

On admission, neurologic examination revealed severe general dystonia with intermittent asynchronized myoclonic jerks and a stuporous state. Deep tendon reflexes were symmetrically decreased bilaterally, although bilateral extensor plantar responses were present. An electroencephalogram (EEG) revealed a diffuse periodic complex with giant slow waves mixed with episodic sharp waves lasting from 0.5 to 1 second. The interval between each complex was about 1 to 3 seconds (Figure 1A). Video-EEG monitoring revealed a constant relationship between the periodic sharp wave complex and myoclonic jerk, a finding unique to the EEG pattern of stage II SSPE, the myoclonic stage [1]. This EEG pattern varied its period as time elapsed (Figure 1B).

Laboratory results were all within normal limits except for cerebrospinal fluid (CSF) studies, which revealed elevated immunoglobulin (Ig) G (> 20% of total protein; 14.1/57 mg/dL), slight pleocytosis (12 monocytes/mm$^3$), mild increase in protein concentration (57 mg/dL), and normal glucose CSF/serum ratio (74/102 mg/dL). The measles IgG antibody titer was 1:8 in CSF and 1:128 in serum. Rubella-specific IgG antibody study was also positive in both serum and CSF. Brain magnetic resonance imaging demonstrated high signal intensity in the left parietal-occipital lobe and right occipital lobe on T2-weighted image and fluid-attenuated inversion-recovery study. Both cortex and subcortical white matter were involved (Figure 2). Single-photon emission computerized tomography showed significant cold defects in the same areas.

Based on the specific EEG findings, clinical manifestations, and measles-specific IgG antibody in the CSF, the diagnosis of SSPE was confirmed. Combined treatment using oral inosiplex and intraventricular injection of IFN-α was started after informed consent was obtained from the patient’s family. The patient underwent brain biopsy with Ommaya reservoir implantation. Histopathologic examination of brain tissue revealed mild neuronal degeneration with the presence of intranuclear viral inclusion bodies in pyramidal cells and perivascular cuffing. Typical rod-shaped glial cells and eosinophilic Cowdry A inclusion bodies were also found (Figure 3).

Oral administration of inosiplex (100 mg/kg/day in two divided doses) and intraventricular IFN-α injection (10$^4$ U/m$^2$ with daily increments up to 10$^6$ U/m$^2$) were started on June 8, 2001, and continued for 6 weeks in one course according to the therapeutic regimen of Yalaz et al [10]. The neurologic disability index (NDI), designed for SSPE by Dyken et al [7], and the SSPE staging system, described by Risk and Haddad [11], were used in clinical evaluation. In this case, the clinical course rapidly progressed from stage IIa to IIIb in the month before inosiplex and intraventricular IFN-α were administered. One month after the administration of these two drugs, the patient’s condition had stabilized. The NDI decreased from a pretreatment score of 50% to a post-treatment score of
SSPE case in Taiwan over the last 10 years [12]. Ours is the first SSPE case to be reported in southern Taiwan. When we compared our case with previously reported cases, we found two interesting differences. First, our patient tested positive for rubella-specific IgG antibody in both serum and CSF studies, which led us to consider the possibility of concomitant rubella virus until the results of the brain biopsy were available. Since these two viral diseases have similar clinical courses, it is difficult to make a differential diagnosis between SSPE and progressive rubella panencephalitis (PRP) without histopathologic confirmation [13]. In this case, brain biopsy showed mild neuronal degeneration with staining of Cowdry A intranuclear inclusion bodies and intracytoplasmic inclusion bodies, which is characteristic of SSPE (Figure 3) [13]. PRP is rarely associated with stained inclusion bodies [14]. Second, the measles-specific IgG antibody titer was elevated after combination treatment with oral inosiplex and intraventricular IFN-α. This elevation may have been caused by INF-α activation of the immune system, which reacts against the defective measles virus by increasing measles-specific IgG antibodies, or by the subacute infection course of SSPE [15].

SSPE usually has a fatal course, and the pathophysiology of remissions or improvements brought about by different therapies remains unclear. IFN may have antiviral effects and may modify the immune response. Low levels of endogenous IFN in the central nervous system [16] and resistance of the virus to IFN [17] have been reported. Therefore, it seems reasonable that exogenous IFN could be used to treat SSPE. According to a follow-up study of SSPE patients by Anlar et al [5], combination treatment with oral inosiplex and intraventricular IFN-α injection increases survival and gives rise to remission or stabilization, especially in slowly progressive cases. Fortunately, our case improved and stabilized in response to combination treatment.

The initial presentations of SSPE are usually subtle cognitive dysfunction and disorganized behavior, problems that are usually the first to make patients visit neurologic or psychiatric clinics. Early identification of this illness might be helpful in the treatment and prevention of the associated rapid deterioration. It is necessary for physicians to understand the early manifestations in order to begin active treatment as quickly as possible.

**DISCUSSION**

SSPE is relatively rare in developed countries, but its incidence remains high in developing countries such as India and countries in the Middle East [6,10,11]. To our knowledge, there has only been one reported SSPE case in Taiwan over the last 10 years [12]. Ours is the first SSPE case to be reported in southern Taiwan. When we compared our case with previously reported cases, we found two interesting differences. First, our patient tested positive for rubella-specific IgG antibody in both serum and CSF studies, which led us to consider the possibility of concomitant rubella virus until the results of the brain biopsy were available. Since these two viral diseases have similar clinical courses, it is difficult to make a differential diagnosis between SSPE and progressive rubella panencephalitis (PRP) without histopathologic confirmation [13]. In this case, brain biopsy showed mild neuronal degeneration with staining of Cowdry A intranuclear inclusion bodies and intracytoplasmic inclusion bodies, which is characteristic of SSPE (Figure 3) [13]. PRP is rarely associated with stained inclusion bodies [14]. Second, the measles-specific IgG antibody titer was elevated after combination treatment with oral inosiplex and intraventricular IFN-α. This elevation may have been caused by INF-α activation of the immune system, which reacts against the defective measles virus by increasing measles-specific IgG antibodies, or by the subacute infection course of SSPE [15].

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**Figure 2.** Brain magnetic resonance image: fluid-attenuated inversion-recovery study revealed a high signal intensity lesion in the left parietal-occipital and right occipital lobe; both cortex and subcortical white matter were involved.

**Figure 3.** Brain biopsy of the right frontal cortex during Ommaya implantation showed: Cowdry A inclusion bodies (yellow arrows); perivascular cuffing with lymphocyte infiltration (green arrow); and rod-shaped glial cells (red arrows). (Hematoxylin & eosin, 10 × 40)
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