Subacute Sclerosing Panencephalitis in an American-Born Adult

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We describe a case of an adult born in the United States who had subacute sclerosing panencephalitis (SSPE). We discuss the possibility that the patient contracted subclinical measles during the 1989–1991 measles epidemic in the United States.

Because of widespread measles immunization, subacute sclerosing panencephalitis (SSPE) is now an exceptionally rare disease in the United States. A measles outbreak that occurred in the United States in 1989–1991, however, placed a new generation at risk for SSPE. Two childhood cases of SSPE related to the 1989–1991 measles epidemic have been reported [1, 2]. The first case involved a boy born in New Jersey who had a history of measles at 8 months of age in 1991 and who developed subacute neurological deterioration typical of SSPE at 4 years of age [1]. The second case involved a girl born in California who had a history of measles at 1 year of age in 1990 and who had onset of symptoms develop at 9 years of age [2]. We now report a case of SSPE in an adult born in the United States that is possibly also related to the recent epidemic.

A previously healthy 22-year-old man presented in June 1995 with progressive confusion, crying spells, and social withdrawal. He was born in Philadelphia in January 1973, and he had received all routine childhood immunizations, including measles-mumps-rubella (MMR) vaccine given in July 1974 (when he was 18 months of age). No clinical history consistent with measles was reported at any time. Three months after the onset of symptoms, he developed intermittent dystonic posturing of the left arm and leg, occurrence of 3+ knee jerks bilaterally with flexor plantar responses, and gait ataxia. An electroencephalogram revealed periodic, high-voltage, generalized sharp waves occurring every 8 s, followed by periods of marked attenuation. A lumbar puncture revealed 0 cells, a glucose level of 65 mg/dL, and a protein level of 47 mg/dL. MRI revealed increased T2 signal intensity, without enhancement, in the bilateral parieto-occipital white matter. Results of an HIV test were negative. Serum ceruloplasmin and urinary copper levels were normal. Results of serum and urine toxicology screens were negative. Serum levels of arsenic, mercury, and lead were normal. Evaluations (including evaluations of serum amino acids, urine organic acids, serum lactate and pyruvate, CSF lactate and pyruvate, and lysosomal enzymes) for hereditary metabolic diseases were unrevealing. Serum measles IgG titer was markedly elevated at >160 EIA units (normal, <10). The CSF measles IgG titer was markedly elevated at >160 EIA units (normal, <10). The CSF measles IgG index was also elevated at 3.7 (normal, <1.0), indicating intrathecal synthesis of measles IgG.

SSPE was diagnosed and isoprinosine therapy was begun. During the fourth month of illness, the patient developed symmetric myoclonus every 5–10 s, progressive decreased responsiveness, spasticity, hyperreflexia, and extensor plantar responses. By the fifth month, the myoclonus ceased. He became unresponsive and mute, and he displayed intermittent hyperpyrexia and tachycardia that suggested autonomic dysfunction. He died 6 months after the onset of symptoms. An autopsy was refused.

Cases of both measles and SSPE have dramatically declined since measles immunization was begun in the United States in 1963. In the prevaccine era, >500,000 cases of measles were reported annually; most of these cases occurred in school-aged children. In 1993, by contrast, only 227 cases of measles were reported [3]. Similarly, 41.3 cases of SSPE per year were reported in 1967–1975, and only 4.2 cases per year were reported in 1982–1986 [4]. The decline of measles in the United States was disrupted when an epidemic (with approximately 55,000 cases reported) occurred in 1989–1991 [5]. Most of the cases occurred in California, Texas, New York, New Jersey, and Pennsylvania. The epidemic was attributed to a failure to vaccinate preschool children.

SSPE is believed to be caused by a persistent infection of the CNS caused by a mutated measles virus [6]. Clinical symptoms typically appear 6–15 years after natural measles infection in early childhood [6]. Adult-onset cases are rare. SSPE is thought

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to require preexistent measles infection, since no convincing case of vaccine-related SSPE has been reported [7]. SSPE that occurs after suspected subclinical measles infection has been reported [7] and this is probably the mechanism of infection in the patient described in the present report. When would such a subclinical measles infection have occurred in this patient? One possibility is that it occurred during infancy, since children <2 years of age who contract measles are at the highest risk for SSPE [4, 6]. This possibility is unlikely in this case, however, since measles was extremely rare in 1973–1974 (when the patient was an infant) and since the delay between natural measles infection and the onset of SSPE would have been unusually long (21 years). Another possibility (although impossible to prove) is that the Philadelphia-born patient contracted subclinical measles infection during the measles epidemic of 1989–1991, in which Philadelphia was a major site of outbreak [5]. The delay between measles infection and onset of symptoms of SSPE would then be within the usual 6–15-year window.

Primary vaccine failure is one possible explanation for the patient’s susceptibility to the measles/SSPE virus. The primary efficacy of the MMR vaccine used in the early 1970s has been estimated to be 93%–98%, whereas the primary efficacy of the current vaccine is estimated to be 98%–100% [3]. Waning immunity is another possibility, although only a slight decline in measles antibody usually occurs over time [3]. Unless primary or secondary vaccine failure occurred, serum measles IgG titers should be well within a laboratory’s normal range for a patient who received a single MMR vaccine 20 years ago. Some CSF measles-specific IgG may also be present in normal vaccinated individuals as a result of diffusion of blood-based IgG into the CSF, but evidence of independent CNS production of measles IgG is pathologic [6].

The initial differential diagnosis of a young adult with subacute encephalopathy, dystonia, and myoclonus is quite broad and includes progressive myoclonic epilepsy, Huntington’s disease, Jakob-Greutzfeldt disease, Wilson’s disease, mitochondrial diseases, adult-type neuronal ceroid lipofuscinosis, and SSPE. When there is a history of measles in infancy present, the diagnosis of SSPE should be suspected. The diagnosis is more challenging in patients with no clinical history of measles. Useful laboratory tests include EEG and measles-specific IgG analysis. EEG classically shows periodic, high-voltage, sharp and slow-wave bursts alternating with mild suppression. The bursts often occur every 5–10 s and correlate with clinical myoclonic jerks. Measles-specific IgG is elevated in both the serum and the CSF [6], and independent production of measles IgG by the CNS can be documented using a CSF:serum measles IgG index. In this patient, the typical EEG pattern, markedly elevated serum levels, and CSF measles-specific IgG confirmed the diagnosis of SSPE.

The clinical course of SSPE in the young adult described in this report was more fulminant than the 2 childhood cases of SSPE recently reported elsewhere [1, 2]. Although all 3 patients progressed through the typical clinical stages for SSPE—subacute encephalopathy, followed by symmetric myoclonus and, ultimately, global neurological deterioration, the 22-year-old patient in the present report progressed from onset of symptoms to death within 6 months. Such variation in the rapidity of progression through the stages of SSPE has been well described [6]. There remains no effective treatment for SSPE.

It is possible that additional cases of SSPE that stem from the 1989–1991 measles epidemic can be expected to occur in the next 5–10 years. The diagnosis should be considered in both children and adults with subacute neurological deterioration who may have been exposed to measles during the 1989–1991 epidemic.

References