Measles Encephalitis: Direct Viral Invasion or Autoimmune-Mediated Inflammation?

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Encephalitis is an inflammation of the brain. The diagnosis of encephalitis can be established only by microscopic examination of brain tissue, and similarly the etiology is established only by the recovery from or the demonstration in brain tissue of an infectious agent. In clinical practice, however, the diagnosis of encephalitis frequently is based on neurologic manifestations, and the etiologic diagnosis is based on the recovery of infectious agents from other sites in the body, the serologic evidence of a specific infection, and relevant epidemiologic findings.

Encephalitis is classified as primary or as postinfectious. Primary encephalitis is an illness in which encephalitis is the major manifestation. Symptoms are caused by direct invasion and replication of an infectious agent in the central nervous system (CNS), resulting in objective clinical evidence of cerebral or cerebellar dysfunction. Postinfectious encephalitis occurs after other illness that is not CNS illness. Inflammation in CNS may be mediated immunologically. When neurologic clinical findings suggest encephalitis, but inflammation of the brain has not occurred, the condition is identified as encephalopathy.

Measles virus is known to be the cause of both the subacute form of encephalitis and the acute form of encephalitis. Subacute encephalitis is consisted from slow virus infection, i.e., subacute sclerosing panencephalitis (SSPE) and subacute measles encephalitis (SME). Altered measles virus (SSPE virus) was recovered from the brain tissue of patients with SSPE, and SSPE is considered to be a rare degenerative CNS disease caused by direct SSPE virus invasion. SME occurs by the CNS infection of wild type-measles virus in the immunocompromised host. The risk of SSPE developing in children who previously had natural measles is between 0.6 and 2.2 per 100,000 measles infections. The risk is greater in patients who acquire measles at an early age.

Clinically evident acute measles encephalitis occurs in approximately 0.5 to 1 of every 1,000 measles cases. Although both the mortality and the incidence of sequelae have varied in the available literature, the mortality rate is between 10 and 20 percent and the morbidity rate is between 20 and 40 percent of patients who recovered from measles encephalitis (1). Measles encephalitis occurs from direct viral-induced cellular damage or from an autoimmune-mediated tissue damage. Considerable controversy surrounds the mechanisms in measles encephalitis. Some investigators have recovered measles virus from the CSF and brain of affected patients (2, 3), which indicates that the virus is involved directly in the process. Other investigators have failed to isolate measles virus or to demonstrate measles virus RNA in the brain of affected patients (4). These findings have led to the belief that the illness is autoimmune.

Symptoms of acute encephalitis usually develop during the period of measles exanthema and within 8 days of the onset of illness. Occasionally, the onset of central nervous system signs and syndromes occurs during the prodromal period (5). Onset at an early phase may suggest primary viral invasion, and later onset may suggest autoimmune mechanisms. Examination of cerebrospinal fluid (CSF) in measles encephalitis usually reveals mild pleocytosis with a predominance of mononuclear cells, mildly elevated protein values, and a normal glucose level. In one study (6), 15 percent of the cases did not have pleocytosis in CSF, which may suggest the existence of encephalopathy in cases with neurologic manifestation. Myelin basic protein in CSF suggests autoimmune-mediated encephalitis. Detection of specific viral genome in CSF suggests primary viral encephalitis.

Jin et al (7) reported a case of fluminant adult-onset measles encephalitis. Acute measles encephalitis usually occurs in non-immunocompromised patients, most of whom are children and adolescents. In their reported case, neurologic manifestation was observed six days after measles onset. Pleocytosis with a predominance of mononuclear cells was observed and both oligoclonal IgG banding and myelin ba-
sic protein were detected in CSF at neurologic onset. Such findings suggest autoimmune-mediated encephalitis rather than direct viral invasion. Brain MRI findings showed marked and diffuse cerebralatrophy during chronic phase. T2-weighted, FLAIR, and DW images demonstrated widespread hyperintense lesions around the lateral ventricles, which are consistent with marginal subpial demyelinations described as characteristic pathological findings of postinfectious encephalomyelitis. MRI findings might be useful for the differential diagnosis of autoimmune-mediated encephalitis from primary viral encephalitis.

References