Recurrent ADEM or MS?

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Acute disseminated encephalomyelitis (ADEM) is a well-established clinicopathologic entity. Clinically, it shows acute encephalitic, myelitic or encephalomyelitic features often in postinfectious, parainfectious, postexanthem or postvaccinal clinical situations, with preferred occurrence in childhood and adolescence (1). Pathologically, it is characterized by numerous foci of demyelination scattered throughout the brain and spinal cord, varying from 0.1 to several millimeters in diameter and invariably surrounding small and medium-sized veins (1). Although ADEM usually takes a monophasic clinical course, it may be followed by one or more attacks involving the central nervous system (CNS). It can be either recurrences (relapses) of ADEM or a transformation into multiple sclerosis (MS), though the distinction between these two has been a matter of controversy. With regard to recurrences (relapses) of ADEM, Poser proposed a classification of two types [unpublished paper; citation from Khan et al (2)]; one type is recurrent disseminated encephalomyelitis (RDEM), where an initial episode of ADEM is followed by the recurrences that are characteristically stereotyped, that is, the symptoms are always the same, although the complete original syndrome is not necessarily present. The other type is multiphasic disseminated encephalomyelitis (MDEM), where there are two or more separate acute episodes that differ in clinical presentation. We must be aware that “recurrent (or relapsing) ADEM” (3, 4) is the term which means only the recurrences of ADEM, irrespective of RDEM or MDEM.

RDEM and MDEM are sometimes difficult to differentiate from MS on purely clinical grounds. Khan et al (2) stated, however, that it is possible based on comprehensive examinations of clinical symptoms and the CSF and MRI findings. The clinical symptoms may be identical in both disseminated encephalomyelitis (DEM) and MS, showing sudden onset of multifocal neurologic disturbances such as optic neuritis, visual field defect, motor and sensory deficits, and ataxia, while fatigue, fever, impaired consciousness, focal or generalized seizures, psychosis and meningoencephalopathy with meningeal irritations prefer DEM rather than MS (2). In patients with DEM, CSF commonly shows a moderate pleocytosis and an increase in total protein, though both may be high (2). Oligoclonal IgG bands are often positive in MS, but usually negative in DEM, which is especially important to discriminate MS from DEM (5). The MRI in DEM is characteristic, revealing that unlike the images in MS, the lesions are extensive, often following the outline of the cortical ribbon, or may consist of very large, globular areas of increased signal intensity that do not produce a mass effect (2). The cerebellum and cerebral cortex are often involved in DEM, as are occasionally the thalamus and the basal ganglia (2), in contrast to the fact that the involvement of thalamus is exceedingly rare in MS (6). In DEM the corpus callosum is usually not affected and the periventricular distribution of the lesions is not as constant as in MS (5). All of these features are also true of ADEM and MS even at the initial presentation (7).

It remains unclear that the phenotypic differences above described between DEM and MS mean the essential distinction in pathogenesis of these diseases. It is known that some proportions of the patients with ADEM develop definite MS later. In the series of Schwarz et al (8), 35% of the 40 patients with an initial diagnosis of ADEM developed clinically definite (Poser criteria) MS over a mean observation period of 38 months. In the multicenter study of Anlar et al (9), 13 of 39 (33%) children with ADEM had relapses. The four patients had more than one relapse presented with a new symptom at each attack. In this respect, the classical question “ADEM is a distinct disease or part of the MS spectrum?” still remains (10). Therefore, a scrutiny into the recurrent types of ADEM is important. According to the retrospective study of Cohen et al (4), 8 of 21 (38%) patients with ADEM developed recurrent disease episodes; 2 patients were definite MS (Poser criteria), 1 had brain involvement of systemic autoimmune disease, and the remaining 5 (24%) had recurrent ADEM confirmed by brain biopsy. In the latter 5 patients, recurrence involved the same brain territory in 6 of 9 recurrences, and in the other 3 recurrences the new symptoms and signs were attributed to a different brain territory. This means both RDEM and MDEM can occur in the same ADEM patient. Conclusively, ADEM seems to be a considerably homogenous disease because it has pathogenetic similarity to acute experimental autoimmune encephalitis, which is mediated by autoreactive CNS-specific T cells (11). On the contrary, MS has a likelihood to encompass heterogenous pathology, which can include ADEM as part of the spectrum (10).

Recently, a case of RDEM with an extremely long symptom-free interval was reported from Japan (12). The patient had three episodes of headache, fever and unconsciousness;
the first was at age 6, the second at 7, and the third at 19.

See also p 764.

The last episode exhibited the similar symptoms even 12 years after the second. Head MRI showed the lesions in the left basal ganglia and bilateral medial temporal lobes throughout the three episodes. This is the typical case of RDEM. The exceedingly long interval between the second and third episodes may show the predisposition to ADEM persists very long, if once established. Although this patient had psychiatric symptoms as sequelae after steroid-pulse therapy, corticosteroids usually show beneficial effects even at the recurrences (4, 9). Therefore, the possibility of recurrence of ADEM should be taken into consideration when neuropsychiatric symptoms appear in patients with a history of old ADEM.

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References