Non-multiple sclerosis recurrent demyelinating disorders: an ongoing debate

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Sir, We have read Lassmann's commentary (Lassmann, 2010) which deals with a topical and fascinating question in the sphere of CNS demyelinating disorders, with great care and interest. The differential diagnosis between acute disseminated encephalomyelitis (ADEM) and multiple sclerosis is a challenge for the neurologist both at disease onset (Tavazzi et al., 2008) and during follow-up when, in both cases, the patient can present with relapses in which the same or different districts may be affected. Strangely, the author questions whether 'recurrent' forms of ADEM even exist, despite the wide availability of literature on this topic (Brinar, 2004; Leake et al., 2004; Marchioni et al., 2005; Wingerchuck, 2006), certainly an important debate given the difficulties in achieving differential diagnosis not only versus multiple sclerosis, but also versus several other forms of systemic connectivitis in which, rarely, encephalomyelitits can be the presenting feature (Sjögren’s syndrome, systemic lupus erythematosus and anti-cardiolipin antibody syndrome). In any case, both clinical practice and the literature demonstrate beyond doubt the existence of post- and para-infectious forms of encephalomyelitis that, having shown typical features at onset (delirium, vigilance impairment, focal signs, CSF pleocytosis, blood-brain barrier damage and multifocal lesions on MRI), may, in the wake of a variable degree of recovery, within the space of 12–18 months show an evolution towards recurrent forms. In our experience, 15 (25%) of the 60 studied patients showed a relapsing course, classifiable either as recurrent (13/15) or multiphasic (2/15); the first relapse was either spontaneous [nine (60%) patients] or associated with an infection [four patients (26.6%)]) or influenza vaccination [two patients (13.3%) relapsed after receiving the influenza vaccine]. The mean latency to the first relapse was 10.93 months (range 3–36 months); 75% of relapses occurred within the first 14 months and 100% of the cases relapsed within 36 months. We observed multiple relapses (from two to four) in 6 (40%) of 15 patients (Leake et al., 2004). Moreover, we ourselves have frequently observed—and this is a finding that is difficult to interpret—that relapses in recurrent forms of ADEM, even ones characterized by brain involvement at onset, can take the form, exclusively, of myelitis or myeloradiculitis. In some cases, after the first relapse, the clinical picture evolves, progressively, into a disabling form of myelopathy. Serial follow-up investigations fail to disclose systemic disorders underlying these forms, which from an aetiological point of view, remain idiopathic. Most patients in this ‘niche group’ are in their 6th or 7th decade and do not show oligoclonal banding in their CSF; furthermore, on serial MRI, their brain lesions are found to disappear in parallel with the worsening of the spinal cord abnormalities. Clearly, all of these characteristics are incompatible with the diagnosis of multiple sclerosis. They are, as the author says, poorly defined variants, but they are nevertheless ones that cannot be ignored in the nosographic classification of demyelinating disorders, given the clear need to identify the most appropriate therapeutic strategies for these conditions (Marchioni et al., 2008).

In our experience, the main obstacle to increased understanding of these forms is the tendency to want to include only the monophasic forms in the syndromic spectrum of post-infectious CNS, a rather artificial classificatory restriction that, if applied, would lead to the exclusion of this ‘niche group’ of patients from cohort studies and therapeutic trials.

References


