Recent data suggest that the antigen presenting cell (APC) function of B cells may explain their role in MS pathogenesis. Remarkably, fragments of self-peptides derived from HLA-DR2 proteins themselves were found to bind intact DR2 molecules on B cells and serve as antigens for presentation to T cells. Memory CD4+ T cells derived from CSF responded to these self-peptides bound to DR2 molecules and, in some cases, these self-peptides were cross-reactive with myelin antigens, RAS guanyl-releasing protein 2 (RASGRP2) previously found to be a possible T-cell autoantigen in MS, EBV, and Akkermansia muciniphila, a commensal gut bacterium associated with dysbiosis in MS patients. Thus, the MS-associated HLA proteins contain fragments that might trigger autoimmunity through molecular mimicry with viral, bacterial, or cell-surface autoantigens.

DIAGNOSIS

There is no single diagnostic test for MS. Diagnostic criteria for clinically definite MS require documentation of two or more episodes of symptoms and two or more signs that reflect pathology in anatomically noncontiguous white matter tracts of the CNS **(Table 444-3)**. Symptoms must last for >24 h and occur as distinct episodes that are separated by a month or more. In patients who have only one of the two required signs on neurologic examination, the second may be documented by abnormal tests such as MRI or evoked potentials (EPs). Similarly, in the most recent diagnostic scheme, the second clinical event (in time) may be supported solely by MRI findings, consisting of either the development of new focal white matter lesions on MRI or the simultaneous presence of both an enhancing lesion and a nonenhancing lesion in an asymptomatic location. In patients whose course is progressive from onset for ≥6 months without superimposed relapses, documentation of intrathecal IgG synthesis may be used to support a diagnosis of PPMS.

TABLE 444-3 Diagnostic Criteria for Multiple Sclerosis (MS)