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ORIGINAL ARTICLE

Inflammatory Cortical Demyelination in Early Multiple Sclerosis

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N Engl J Med 2011; 365:2188-2197 | [December 8, 2011](#)

BACKGROUND

Cortical disease has emerged as a critical aspect of the pathogenesis of multiple sclerosis, being associated with disease progression and cognitive impairment. Most studies of cortical lesions have focused on autopsy findings in patients with long-standing, chronic, progressive multiple sclerosis, and the noninflammatory nature of these lesions has been emphasized. Magnetic resonance imaging studies indicate that cortical damage occurs early in the disease.

METHODS

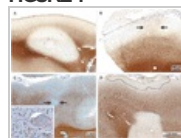
We evaluated the prevalence and character of demyelinating cortical lesions in patients with multiple sclerosis. Cortical tissues were obtained in passing during biopsy sampling of white-matter lesions. In most cases, biopsy was done with the use of stereotactic procedures to diagnose suspected tumors. Patients with sufficient cortex (138 of 563 patients screened) were evaluated for cortical demyelination. Using immunohistochemistry, we characterized cortical lesions with respect to demyelinating activity, inflammatory infiltrates, the presence of meningeal inflammation, and a topographic association between cortical demyelination and meningeal inflammation. Diagnoses were ascertained in a subgroup of 77 patients (56%) at the last follow-up visit (at a median of 3.5 years).

RESULTS

Cortical demyelination was present in 53 patients (38%) (104 lesions and 222 tissue blocks) and was absent in 85 patients (121 tissue blocks). Twenty-five patients with cortical demyelination had definite multiple sclerosis (81% of 31 patients who underwent long-term follow-up), as did 33 patients without cortical demyelination (72% of 46 patients who underwent long-term follow-up). In representative tissues, 58 of 71 lesions (82%) showed CD3+ T-cell infiltrates, and 32 of 78 lesions (41%) showed macrophage-associated demyelination. Meningeal inflammation was topographically associated with cortical demyelination in patients who had sufficient meningeal tissue for

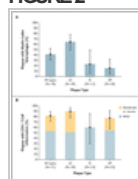
MEDIA IN THIS ARTICLE

FIGURE 1



Representative Types of Cortical Demyelinated Plaques in Early Multiple Sclerosis on Immunohistochemical Staining for Proteolipid Protein.

FIGURE 2



Inflammatory Features of Cortical Plaques.

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study.

CONCLUSIONS

In this cohort of patients with early-stage multiple sclerosis, cortical demyelinating lesions were frequent, inflammatory, and strongly associated with meningeal inflammation. (Funded by the National Multiple Sclerosis Society and the National Institutes of Health.)

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[Disclosure forms](#) provided by the authors are available with the full text of this article at NEJM.org.

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SOURCE INFORMATION

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