Letter

Oligodendrocyte Apoptosis Before Immune Attack In Multiple Sclerosis?

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Barnett and Prineas\(^1\) recently reported new morphological findings in the brain of a 14-year-old patient with relapsing-remitting multiple sclerosis (MS) who died within 24 hours of the onset of a new symptomatic and fatal brainstem lesion. Within this early lesion, they observed extensive oligodendrocyte cell death which they attributed to apoptosis. Strikingly, no T lymphocytes were detected in the region of oligodendrocyte death. In an accompanying editorial, Trapp\(^2\) suggests that this finding indicates that the immune response in MS is not the cause of the oligodendrocyte cell death but is secondary to oligodendrocyte death caused by an unknown primary disease mechanism. Before accepting this interpretation, two points need to be considered. First, the patient reported by Barnett and Prineas received an intravenous injection of 100mg hydrocortisone.\(^1\) Corticosteroid administration reduces the number of T lymphocytes in the central nervous system in rats with experimental autoimmune encephalomyelitis (EAE).\(^3\) This commences as early as 4 hours after subcutaneous corticosteroid administration.\(^3\) A dose of 0.25mg dexamethasone/kg (equivalent to 6.7mg hydrocortisone/kg) inhibits the development of EAE by an effect on lymphocyte migration rather than by inducing T-lymphocyte apoptosis.\(^4\) Assuming a body weight of 50kg for the patient reported by Barnett and Prineas, the dose of hydrocortisone administered was 2mg/kg, which might have been sufficient to clear T lymphocytes from the central nervous system after these cells had induced oligodendrocyte death. Second, even in the absence of T lymphocytes, antioligodendrocyte antibody can induce oligodendrocyte death and consequent demyelination in the absence of complement and macrophages.\(^5\) Such a mechanism also needs to be considered in MS.

References

3. McCombe PA, Nickson I, Tabi Z, Pender MP. Corticosteroid treatment of experimental autoimmune encephalomyelitis in the Lewis rat results in loss of V8.2\(^+\) and myelin basic protein-reactive cells from the spinal cord, with increased total T-cell apoptosis but reduced apoptosis of V8.2\(^+\) cells. J Neuroimmunol 1996; 70: 93-101.