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Is there sentinel demyelination before development of primary CNS lymphoma

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Sir,

We have with great interest read the paper by Ng and colleagues, recently published in the Journal of Clinical Neuroscience.[1] Authors have reported a case of a young female patient who initially experienced an episode of neurological symptoms caused by histologically proven demyelinating lesion, and who after four years of remission developed primary central nervous system lymphoma (PCNSL). The conclusion was made that demyelinating lesions of the central nervous system (CNS) may precede development of PCNLS for more than four years.

We agree with the authors' statement that PCNSL should be considered in patients presenting with space-occupying lesions even if the histology shows classical perivascular cuffing of small lymphocytes and extensive myelin destruction. However we think that this connection in this particular patient is not fully explored.

First, demyelinating lesions of the central nervous system can be caused by many diseases, other than multiple sclerosis.[2,3] The initial evaluation of these patients should include CSF examination looking for cell counts, atypical lymphoma cells, oligoclonal bands, serology for Borrelia, immunological tests like ANA, cardiolipin antibodies or SS-A and SS-B antibodies, and visual evoked potentials to look for demyelination of the optic nerve. As well history data of preceding viral illness or thick byte can be very useful. This is of special importance because all these diseases, like acute disseminated encephalomyelitis or neuroborreliosis can give similar findings on biopsy specimen pathology findings. We think that adding all this data to the first clinical presentation of reported patient can greatly help in evaluation of the first lesion. Another important fact is the lesion location. Although possible, basal ganglia demyelination is rare, and this is a typical location for the PCNSL.[4] As well, initial MRI is not

typical neither for tumefactive MS plack, neither for Balo's concentric sclerosis.[5] The nodular type of post Gadolinium enhancement is more suggestive of tumor etiology.

Second important fact is that corticosteroid treatment was given before the initial biopsy was performed. It is well known that corticosteroid treatment can mask clinical, CT or MRI appearance of PCNSL, and this is also true for the histopathological findings. Another question is was the specimen taken by stereotactic biopsy from the tissue surrounding the PCNSL or from the PCNSL itself. These are all factors that can make histopathological examination very difficult to interpret.

Third, although authors acknowledge the possibility that the initial lesion was the case of steroid-treated PCNSL, this is not fully explored. There are several, well documented literature reports of spontaneous remission of PCNSL. In some of these cases the remission was more than three years, it was not influenced with corticosteroid therapy, and the recurrent tumor was on the different location than the previous one.[6,7] The possible explanation for the this is that some kind of immune trigger leads to an increased ration of the natural killer cells to lymphoma cells and thus causes remission.[6] Another interesting phenomena is an observation that many remissions, especially in Burkitt's lymphoma are triggered by incision biopsy.[8] This is a possibility in the reported patient, as the initial lesion was diagnosed with stereotactic biopsy.

Finally, Epstein-Barr virus (EBV) infection is implicated in the pathogenesis of PCNSL[4], systemic lymphoma[9] and multiple sclerosis[10] (representing the most frequent demyelinating disease of the CNS). Our group has recently described a patient with Hodgkin's lymphoma, who subsequently developed MS.[11] This association is particularly interesting because EBV is implicated in the pathogenesis of lymphomas and it is considered one of the triggers for development of MS. It would be interesting to explore this association on the patient presented by the authors, especially EBV seropositivity in the initial stages of the disease.

To conclude, although sentinel demyelination has occasionally been reported in patients with PCNSL, there is no convincing evidence to suggest that this is a true association or just previously unrecognized cases of PCNSL.

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