A 50-year-old, previously healthy woman presented with memory impairment and handwriting changes. Brain magnetic resonance imaging (MRI) showed hyperintense lesions in T2 and fluid-attenuated inversion recovery (FLAIR) sequences in the left thalamus (Figure 1A and B). Diffuse large B-cell lymphoma was found in a specimen obtained by stereotactic brain biopsy. There were no signs of extraneural lymphoma dissemination. A diagnosis of primary central nervous system (CNS) large B-cell lymphoma (primary central nervous system lymphoma (PCNSL)) was made. The patient was treated with high-dose methotrexate and whole brain irradiation with completed resolution of clinical symptoms and radiological findings.

Two years later she developed headaches accompanied by dysgeusia, olfactory hallucinations and light-headedness. Brain MRI showed one hyperintense lesion of the right temporal lobe in T2 and FLAIR sequences with homogenous contrast enhancement surrounded with perifocal edema (Figure 1C and D) consistent with relapsed lymphoma. To confirm the relapse a brain biopsy was performed which showed findings consistent with acute disseminated encephalomyelitis (ADEM) (Figure 2). The patient was admitted to our department for further assessment. At that time her neurological examination was unremarkable and her symptoms ameliorated without receiving corticosteroid treatment. Also, the lesion in the right temporal lobe appeared significantly smaller and enhancement was not observed on repeated MRI. Cerebral spinal fluid (CSF) analysis showed 8 cells/mm³, predominately small lymphocytes; there were no oligoclonal IgG bands. Cytological and microbiological CSF analyses were unremarkable. Extensive work-up to exclude secondary demyelinating lesion was performed including immunological evaluation, HIV, hepatitis, Toxoplasma gondii, Treponema pallidum, Borrelia burgorferi, EBV and CMV serology, angiotensin-convertase and beta2-microglobulin levels. All findings were normal. She was diagnosed as having ADEM and not treated with corticosteroids. Follow-up MRIs, three and six months later, showed no lesions in the right temporal lobe. As well, cognitive evaluation on follow-up was normal. Twelve months later the patient is in remission without symptoms.

**DISCUSSION**

We describe a rare association of demyelinating lesion with histological characteristics of ADEM developing two years after PCNSL and suggest a term, reversed “sentinel”, for this association. Primary central nervous system lymphoma is a rare malignant tumor accounting for 4% of all intracranial neoplasms¹. Contrast-enhanced brain MRI is the standard neuroimaging method but, to distinguish PCNSL from other potential causes and make a definitive diagnosis, brain biopsy is required. The MRI features of newly diagnosed PCNSL have been described extensively, but there is only one paper describing MRI characteristics at relapse². Recurrence of PCNSL is suggested by newly developing enhancing parenchymal lesions detected by contrast-enhanced T1-weighted brain MRI.

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In summary, discrimination between a demyelinating lesion and PCNSL in patients treated for PCNSL with newly developed neurological impairment may be challenging with clinical and imaging methods. Accurate diagnosis is crucial to avoid delayed treatment of recurrent malignant disease and unnecessary administration of toxic therapies, so clinicians should rely on brain biopsy to confirm suspected relapses.

Despite the favorable scenario in this case, high level of clinical and neuroradiological vigilance is warranted and every new brain lesion in PCNSL patients should be considered tumor recurrence until reliably proven otherwise.

**Author Contributions**

**Study concept and design:** Barun and Habek. **Acquisition of data:** Barun, Kinda, Aurer, Žarković, Adamec and Habek. **Analysis and interpretation of data:** Barun and Habek. **Drafting of the manuscript:** Barun. **Critical revision of the manuscript for important intellectual content:** Barun, Kinda, Aurer, Žarković, Adamec and Habek. **Administrative, technical, and material support:** Barun, Kinda, Aurer, Žarković, Adamec and Habek.

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