

Diagnostic and Surgical Pitfalls of an Unusual Primary Central Nervous System Lymphoma

ABSTRACT

BACKGROUND: Here we describe a case of PCNSL which was located peripherally as a single lesion and showed no evidence of pathological findings of lymphoma at the first biopsy.

CASE DESCRIPTION: A 56-year-old man was admitted to the hospital with a talking disorder and attention deficit. The neurological examination was normal. There was a left temporoparietal, 24x20 mm. enhanced lesion on MRI. The patient underwent a craniotomy and the lesion was excised totally. The pathological examination revealed glial tissue which showed reactive astrocyte proliferations. A month later, an MRI was performed and a recurrent tumor was seen near the first lesion's location. The second operation was performed via the same craniotomy, the tumor was excised totally and the second pathological examination revealed diffuse large-cell, B-lymphoma. There were no pathological findings on abdominal, thoracic and bone marrow investigations.

CONCLUSION: PCNSL may show various biological behaviors. Using steroids before the biopsy may lead to diagnostic and therapeutic failure.

KEY WORDS: Primary CNS Lymphoma, Craniotomy, Pathology, Spontaneous remission, Tumor regression

ABBREVIATIONS

- AIDS: Acquired Immune Deficiency Syndrome
DNA: Deoxyribonucleic Acid
ELISA: Enzyme-linked Immunosorbent Assay
FLAIR: Fluid-attenuated inversion recovery (on MRI)
HIV: Human Immunodeficiency Virus
MRI: Magnetic Resonance Imaging
PCNSL: Primary Central Nervous System Lymphoma
T1-W: T1-Weighted sequence (on MRI)
T2-W: T2-Weighted sequence (on MRI)

Primary central nervous system lymphoma (PCNSL) is defined as non-Hodgkin lymphoma limited to the neuraxis without systemic disease (10,16). It accounts for 0,3-3% of intracranial tumors (3,5,6,8,17). Although corticosteroid-induced regression of PCNSL is well known, spontaneous disappearance is exceedingly rare (1,2,4,17). PCNSLs are often multiple and are commonly located around the midline structures and the leptomeninges (9,11,12,16,18). On the other hand, PCNSLs may be located peripherally and result in meningeal thickening or enhancement adjacent to peripherally located mass lesion on contrast-enhanced MRI; this so-called "dural tail sign" or "flare sign" is almost specific for meningiomas (7,14).

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We describe a case of PCNSL located peripherally where the first biopsy showed no evidence of lymphoma, and recurred on the site near the first lesion. The second biopsy revealed a large B-cell lymphoma.

CASE REPORT

A 56-year-old male patient was admitted to the hospital with difficulty in talking and loss of attention. Neurological examination was normal except intermittent halting of thought flow. A cranial MRI showed a solid mass lesion which is considered

in intraaxial compartment. It was in the left temporooccipital cortical gray matter/subcortical white matter junction, about 20 mm in radius, iso/hypointense on T1-W, iso/hyperintense on T2-W and FLAIR sequences, and enhanced homogenously and intensely after iv. contrast injection. A wide edema was seen around the mass lesion. The left lateral ventricle was compressed. A 5 mm midline shift was observed. Multiple ischemic gliosis was seen in left posterior peritrigonal zone and forceps major (Figure 1A,B,C,D). Screening for AIDS was HIV-negative by ELISA test. The patient was

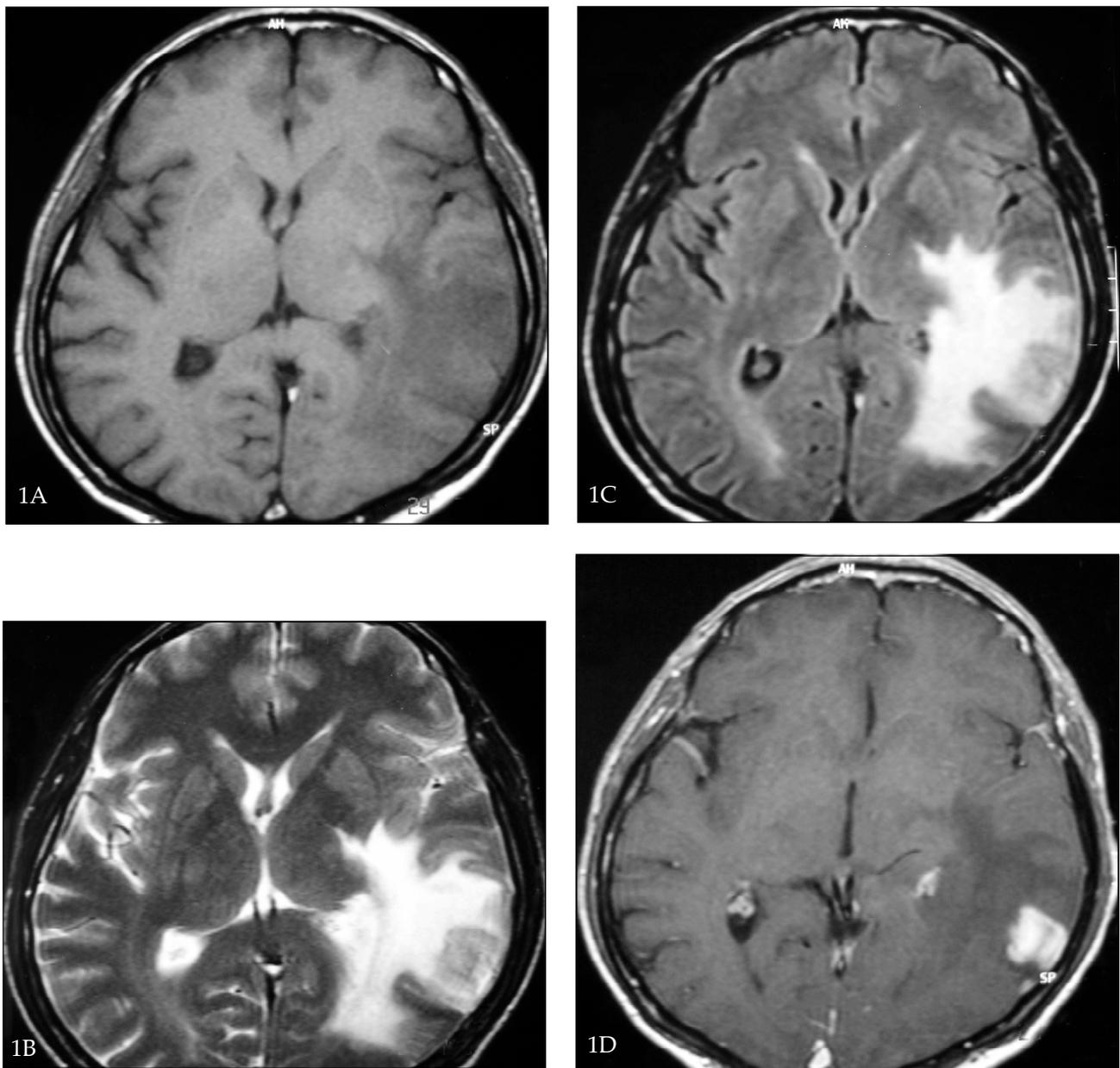


Figure 1: An intraaxial 2 cm diameter mass lesion is seen as iso/hypointense lesion on T1-W (A), iso/hyperintense on T2-W and FLAIR (B,C) sequences of preoperative axial MRI and intensely enhanced after iv contrast administration (D).

operated on with the prediagnosis of glioma or metastatic tumor under the lights of these radiological findings. At the same time, antiedema treatment with dexamethasone 16 mg/day and prophylactic anticonvulsant medication with phenytoin 300 mg/day were given. A left temporoparietooccipital craniotomy was performed. After opening the dura, it was seen that the brain had swollen. A corticectomy was performed at 2 cm beyond the left ear external meatus and 2 cm superior of the left temporal basis on the left temporal lobe. The lesion was located in the cortical/subcortical zone was soft, whitish purple in color, about 2x2 cm in size and mildly vascular with margins not clearly separated from peritumoral

neural tissue. The lesion was excised nearly totally under the operating microscope. Pathological examination revealed a glial tissue sample that showed reactive astrocyte proliferation (Figure 2A,B). After this diagnosis, an MRI was performed

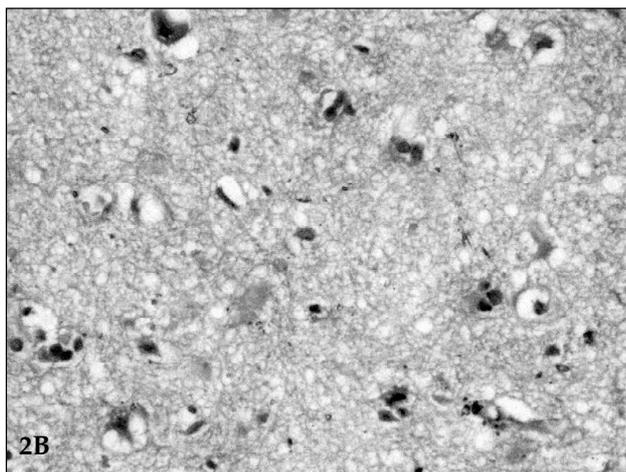
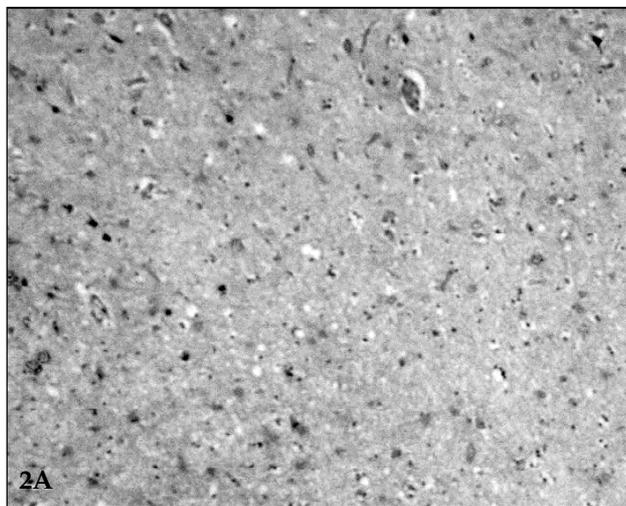


Figure 2: In microscopic examination of H-E sections, a non-tumoral glial tissue with evenly distributed reactive astrocytes in a fibrillary background was observed (A). Cellularity was minimally increased. Some reactive astrocytes had abundant eosinophilic cytoplasm was seen (B). Mitosis and cytological atypia was not observed.

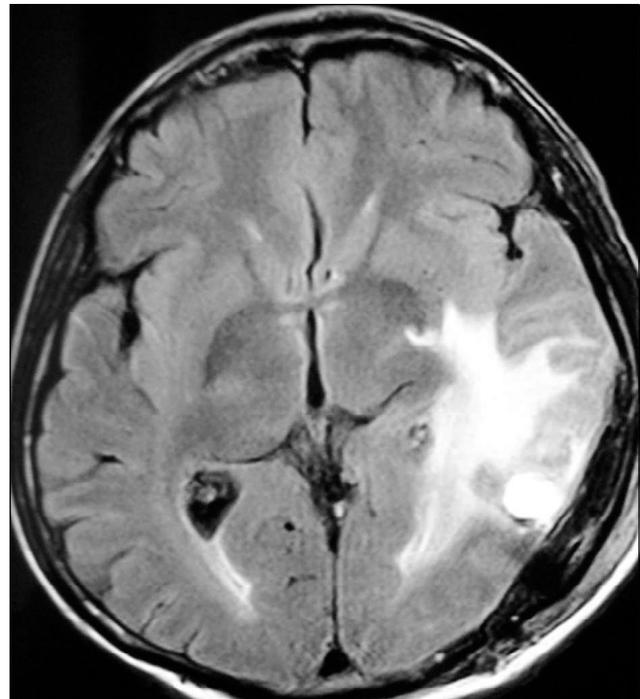


Figure 3: Hemorrhages in the lesion location are observed on the immediate postoperative MRI. Residual lesion is not seen.

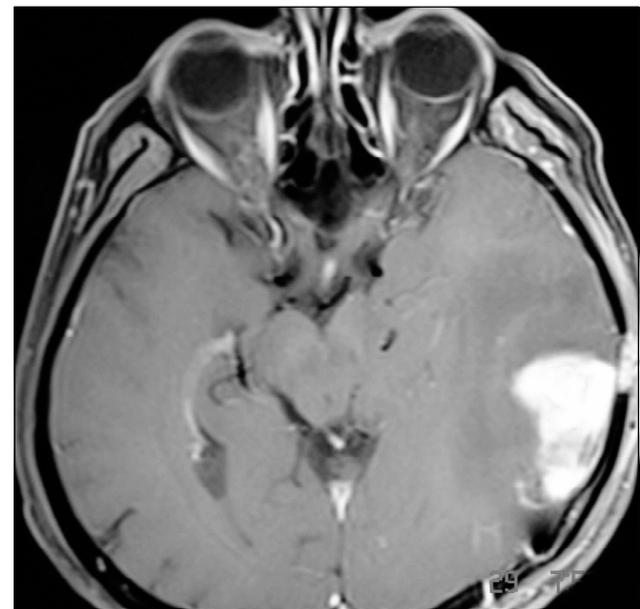


Figure 4: A new or a recurrent lesion is seen near the first lesion's location on MRI performed one month after operation.

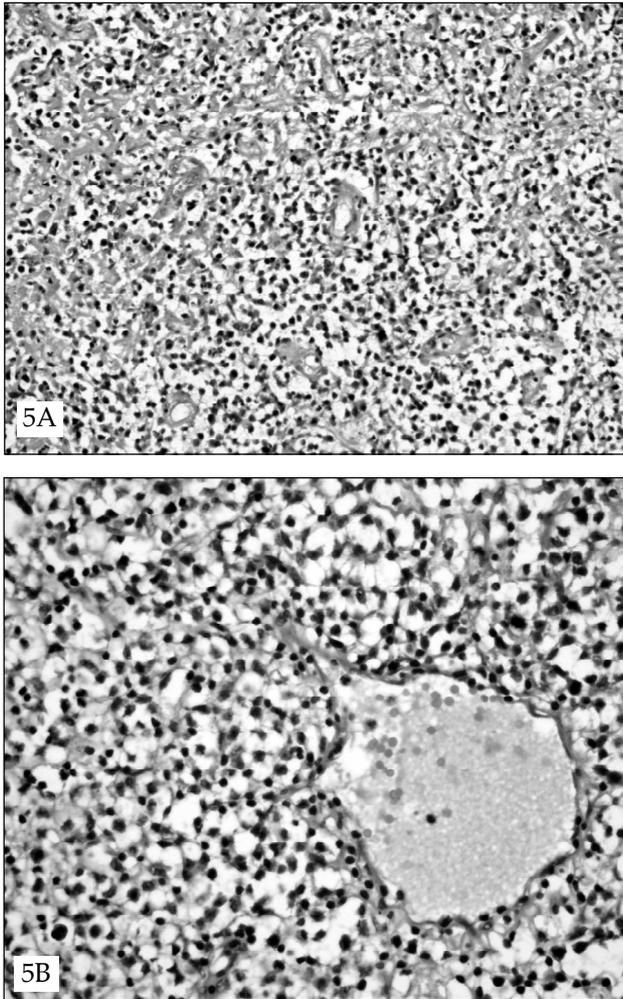


Figure 5: Lymphoid cells which diffusely infiltrating glial tissue are observed (HEX200) (A), Atypical lymphoid cells with hyperchromatic nucleus and narrow cytoplasm which are intensely located around the vessels are seen (HEX400) (B).

immediately and hemorrhage in late subacute- early chronic phase with blood destroying elements was seen at the location of the lesion. No residual lesion was observed (Figure 3). A month later a control cranial MRI was performed. An intraaxial 4x3x4 cm mass was found in the left middle temporal angular gyrus which intensely enhanced after gadolinium administration (Figure 4). The patient was reoperated on via the same craniotomy. The margins of the new tumor started at the anterior edge of the lodge of the first tumor and extended inferiorly and superiorly. The cleavage of the lesion was not clear. It was whitish purple, harder than the previous mass, mildly vascular and invading. The pathological examination revealed a diffuse, big B-

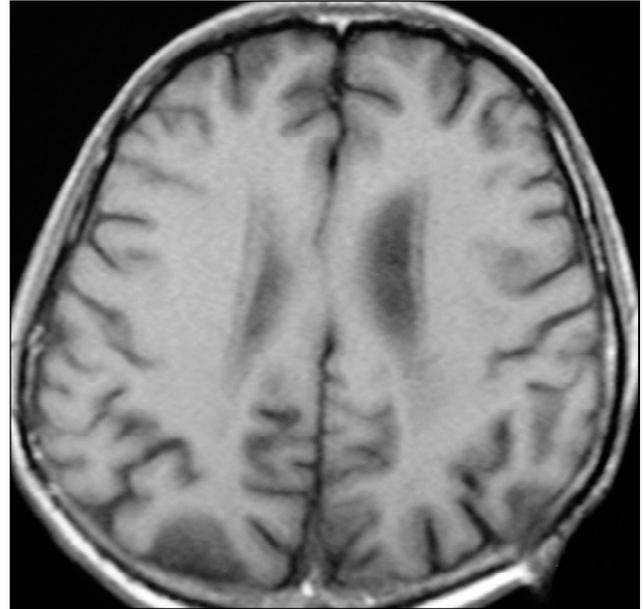


Figure 6: Any recurrent lesion is not observed on two and a half years control MRI.

cell hematolymphoid neoplasm with approximately 50% Ki-67 proliferation index (Figure. 5A,B). The patient was admitted to the oncology department for systemic lymphoma surveys and follow-up. He received radiotherapy and chemotherapy. Two and a half years after the surgery a follow-up MRI showed no recurrence (Figure. 6).

DISCUSSION

Spontaneous disappearance of the PCNSL or after steroid administration is a well-known phenomenon (1,2,3,10,12). Approximately half of the vanishing lesions in the literature are PCNSL (3). The biopsy of the lesion may therefore not be diagnostic (1). However, there is no case in the literature that was excised near-totally with a diagnosis of reactive glial tissue, and recurred near the site of the first lesion with diagnosis of large B-cell lymphoma. This can not be explained with previous theories on lympholytic effect of steroids (2). Not having seen the lymphoma cells in the first pathological examination makes the other theories regarding some immune mechanisms-induced increase of Natural killer cells/Lymphoma cells irrelevant (2).

One of the possible explanations may be that the first lesion was caught before lymphocytic infiltration. The development of reactive gliosis may be seen due to the developing adjacent tumor. Astrocytic reactions can be marked especially in the peripheral parts of the tumor and in the adjacent

brain, but may also be found in the more central zones (15). T-lymphocyte markers and rare B-lymphocytes can be found and may not be revealed during the early period of development of lymphoma. To find the second lesion near the lodge of the first tumor may support this hypothesis.

The recurrence period of sentinel PCNSL lesions is approximately 7-11 months. The recurrence time is presented between 1 to 54 months in other reports (3). As the lesion was removed near totally in this case, the expected pathogenetic process may be shortened and B-cell infiltration time may be accelerated. The recurrence period of this case may therefore have been short.

Another possibility can be a different sentinel mass of the first lesion. For instance, reactive gliosis can be seen in multiple sclerosis or renal cell carcinoma (1,3). The second lesion may be a pure lymphoma. It is speculated that they might occur simultaneously by emerging from different clones in an immunocompetent patient and the lymphoma may vanish later with steroid coverage. The first pathological examination may therefore have revealed only reactive gliosis associated with the other lesions.

Whether the primary and recurrent cases of lymphomas arise from the same clone or different clones may be considered. Some cooperative studies of immunoglobulin heavy chain gene rearrangement and DNA sequence analyses of the PCNSL and its recurrence revealed that both tumors used the same immunoglobulin gene segment. Clonal evolution rather than subclone selection appears to underlie the development of tumor recurrence of PCNSLs (13).

CONCLUSION

PCNSL may show various biological behaviors such as differentiating to B-cell (17). The immune status of the patient, steroid usage and surgery are closely related to this behavioral change.

Steroids should not be used before biopsy if PCNSL is one of possible diagnoses as they will lead to diagnostic confusion. The patient may be operated on unnecessarily instead of being treated medically. A biopsy should be performed immediately and appropriate treatment must be planned. Lymphoma must always be considered in the differential diagnosis.

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