Primary CNS Lymphoma of the Choroid Plexus

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CASE SUMMARY

A 79-year-old presented with a one-month history of headaches worsened by lying flat. The patient had blurred vision, cognitive decline, disequilibrium, and hearing difficulty. On exam, the patient was neurologically intact. Initially, a head CT scan showed right temporal hypodensity concerning for infarction. An MRI scan showed multiple enhancing lesions of the choroid plexus (Figure 1). Cerebrospinal fluid analysis showed low glucose and significantly elevated protein. Flow cytometry and cytology were negative. An infectious workup was also negative.

The patient underwent right endoscopic cranial excisional biopsy of tumor with external ventricular drain placement, and biopsy results revealed aggressive B-cell lymphoma (Figure 2).

The patient was treated with high-dose methotrexate and rituximab. An MRI scan 2 weeks later showed improvement of the avidly-enhancing intraventricular and cerebellopontine angle lesions.

IMAGING FINDINGS

T1W of the brain demonstrated enhancing choroid plexus lesions from the lateral ventricles to temporal horns (Figure 1). These lesions exhibited periventricular "fluffiness," characteristic of many CNS lymphoma cases. Nodular enhancing lesions were also present in the third ventricle, foramen of Monro, and in the fourth ventricle extending out from the foramina of Luschka bilaterally (Figure 1). The lesions had surrounding edema on FLAIR sequence (Figure 1) and showed restriction on DWI (not available due to artifact).

DIAGNOSIS

Primary CNS lymphoma, confirmed with stereotactic-guided biopsy of choroidal lesion

DISCUSSION

Primary CNS lymphoma (PCNSL) is, by definition, a malignant lymphoma arising in the central nervous system without systemic dissemination at diagnosis.[1] PCNSL is an enigmatic tumor, as no cell of origin has been identified within neural tissue, and its diagnosis may be similarly elusive due to its varied diagnostic presentations. PCNSL represents 1-3% of all Non-Hodgkin Lymphoma[1,2,3,4] and 1-5% of all primary brain tumors.[1,3,4,5,6] Across specialties, from surgery to radiology to pathology, the wide array of lymphoma manifestations presents significant challenges to diagnosis and treatment.

PCNSL differs from other brain tumors in several ways. It is chemosensitive and radiosensitive, yet it carries a worse prognosis than lymphomas outside of the CNS.[7] Up to 95% of CNS lymphomas are large B-cell lymphoma, typically Diffuse Large B-Cell Lymphoma (DLBCL), and 99% are primary manifestations[8] while other less common cases exist, such as T-cell, Burkitt's, and lymphoblastic lymphoma.[1,6]

One major difficulty in obtaining an accurate diagnosis of PCNSL is the diversity of clinical presentation. Presenting symptoms may include focal neurologic deficits (50-80%), mental status and behavioral changes (32-43%), symptoms of increased intracranial pressure (headaches, vomiting, papilledema, 32-33%), and seizures (11-14%).[3,7] About 20% of patients have ocular involvement, and conversely, intraocular lymphoma spreads within the brain in >80% of cases.[2]

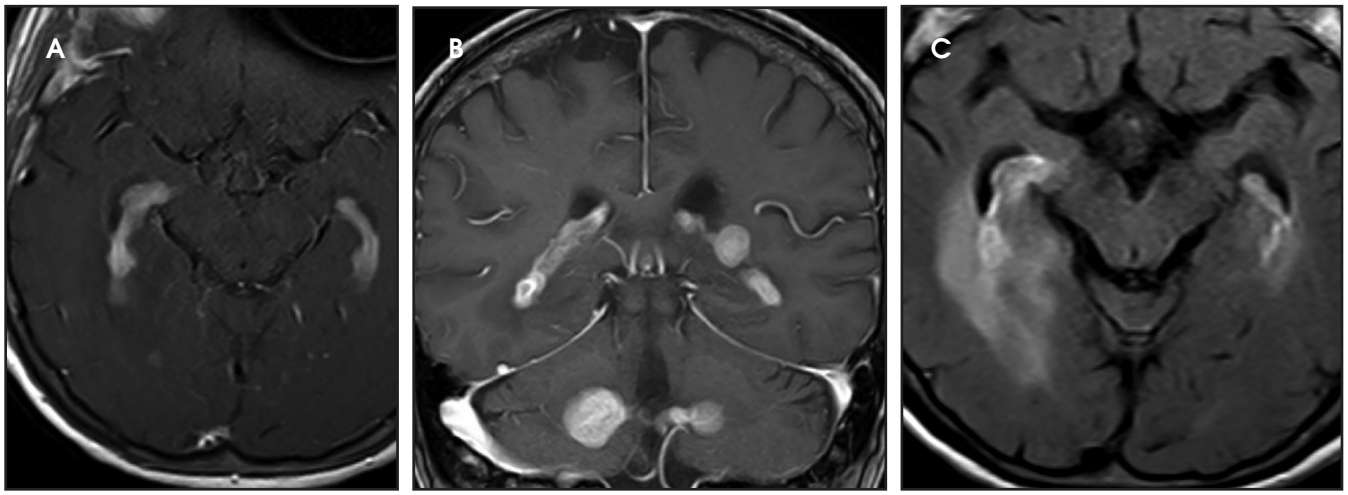

FIGURE 1. *Axial (A) and coronal (B) T1 MRI images with contrast demonstrate enhancing choroid plexus lesions from lateral ventricles to temporal horns. Nodular enhancing lesions in the third ventricle, foramen of Monro, and in the fourth ventricle extending to the foramen of Luschka are also present. (C) T2 FLAIR sequence demonstrates significant vasogenic edema surrounding the lesion.*

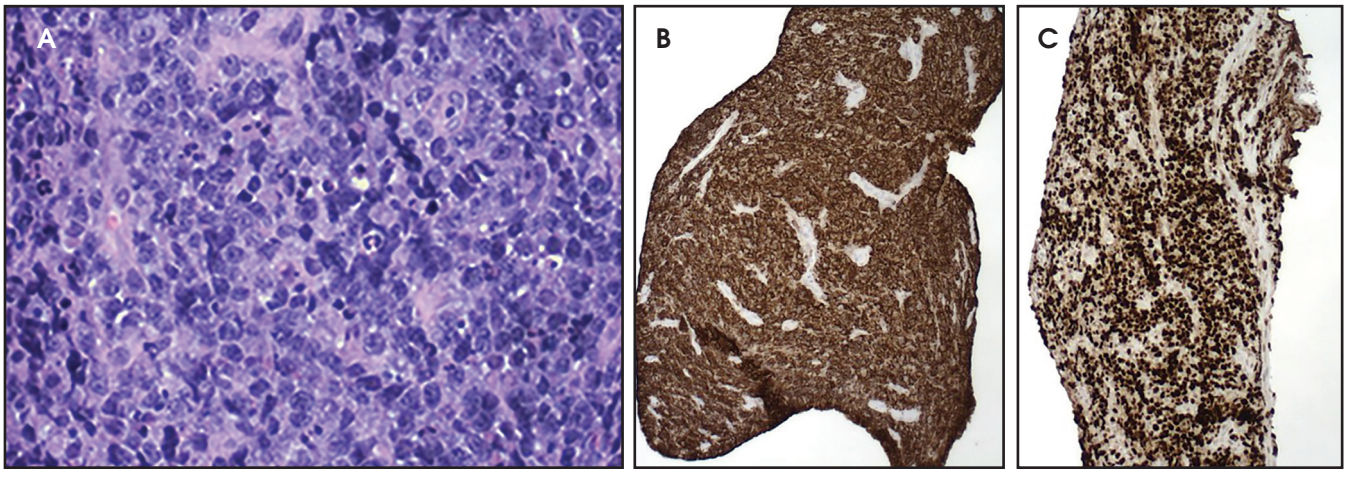

FIGURE 2. *Tissue sections show an aggressive B-cell lymphoma. H&E stained sections (A) show atypical lymphocytes with pleomorphic large nuclei, prominent nucleoli, increased mitoses and apoptosis. CD20 (B) and Ki-67 (C) are consistent with the diagnosis. Original magnification ×400 (A); ×100 (B): ×100 (C).*

Accurate diagnosis of PCNSL hinges upon brain MRI with contrast. All MRI findings for this disease are nonspecific; none can definitively confirm a diagnosis.[1] However, most PCNSL lesions in immune competent patients present on imaging as a single, homogeneously enhancing lesion, typically demonstrating vasogenic edema and mass effect.[9] In AIDS patients, irregular enhancement patterns are the norm, with about 75% showing ring-shaped enhancement.[4]

As in the body, lymphoma knows no boundaries in the CNS. It may involve the cerebral hemispheres (38%), basal ganglia (16%), corpus callosum (14%), periventricular regions (12%), and cerebellum (9%).[2] Lesions are most commonly supratentorial (87%) and often involve the frontoparietal lobes (39%). Less frequently, PCNSL lesions are found in the eyes (15% to 25%) or CSF (7% to 42%).[4] Notably, 95% contact a CSF surface (pia or ventricle).[2,10]

Neuroimaging often underestimates the extent of the disease for a multitude of reasons. Steroids, for example, can significantly affect both MRI and biopsy results, delaying accurate diagnosis, for years in some cases.[2] Characteristic imaging findings with newer advanced imaging techniques may potentially aid in the differentiation of CNS lymphoma from other brain lesions. Despite a number of advances in neuroimaging techniques, stereotactic brain biopsy remains the current standard diagnostic approach.[1,2]

Imaging features suggestive of PCNSL are attributable to hypercellularity, high nuclear/cytoplasmic ratio, disruption of the blood-brain barrier, and its predilection for the periventric-

ular and superficial regions.[4] In general, this hypercellularity translates into high density on CT and restricted diffusion on diffusion-weighted imaging (DWI).[1,10] Hypercellularity is relatively hyperintense to white matter on T2 sequences, but hypointense to surrounding edema.[3,4,8] Further imaging studies are often required to differentiate PCNSL from gliomas, metastasis, multiple sclerosis (MS), and infection. Such studies include diffusion MRI, perfusion MRI, PET, SPECT, and SWI.[4]

The success of stereotactic biopsy is limited by sample size and steroid use, and postoperatively there is temporary worsening in 5% of patients, permanent worsening in 1%, and 30-day mortality due to hemorrhage in fewer than 1% of patients.[3] Lymphoid tissue in CSF all but eliminates the need for biopsy; however, it is only 33% sensitive for PCNSL. Studies on highly specific microRNA expression in CSF, including miR-21, miR19b, and miR92a, claim sensitivities of up to 97%. Prospective clinical trials are necessary to elucidate the complete role of neurosurgical intervention on PCNSL.[9]

CONCLUSION

This case demonstrates not only PCNSL's proclivity for periventricular locations, but also the need for biopsy to obtain a confident, accurate diagnosis. Our case emphasizes the importance of coordinated neurosurgical, neuroradiological, pathological, and oncological expertise to arrive at an accurate diagnosis and appropriate treatment plan. Future success in recognizing this disease requires diligence in observing the ways PCNSL can present in person and on imaging, and finding significant similarities between the presentations.

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