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An Expanding Shadow in the Brain: A Case Series with a Review of Literature on Primary CNS Lymphoma

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Abstract

Primary central nervous system lymphoma (PCNSL) is a rare, aggressive subtype of non-Hodgkin lymphoma that arises within the central nervous system, often affecting immunocompromised individuals, particularly those with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). Diagnostic and therapeutic challenges stem from its diverse clinical presentations, deep parenchymal involvement, and the protective effect of the blood–brain barrier, which limits chemotherapeutic penetration. While most cases are diffuse large B cell lymphomas, rare T cell variants highlight the critical role of tissue biopsy and immunohistochemistry in confirming diagnosis.

We present five patients diagnosed with PCNSL who exhibited varied neurological symptoms, including headache, vomiting, behavioral changes, and focal deficits. Diagnostic workup included magnetic resonance imaging, positron emission tomography/computed tomography, cerebrospinal fluid (CSF) analysis, and stereotactic or open brain biopsy. Treatment was tailored based on immune status: immunocompetent patients received rituximab, methotrexate, procarbazine, and vincristine, while immunocompromised patients were treated with methotrexate, temozolomide, and rituximab. Radiotherapy was used selectively. One case involved surgical excision for a suspected meningioma, later confirmed as a rare T cell variant.

Outcomes ranged from long-term remission to early mortality, particularly in HIV-positive patients with profound immunosuppression. This series emphasizes the importance of early treatment initiation, tailored therapy, and the consideration of rare pathological variants. Novel biomarkers, such as myeloid differentiation primary response 88 mutations and CSF cytokines such as interleukin-10 and chemokine CXCL13, show potential for improving diagnosis and prognosis but require further validation.

Keywords

- case series
- primary CNS lymphoma
- biomarkers
- T cell
- imaging

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Introduction

Epidemiology

Primary central nervous system lymphoma (PCNSL) has an incidence of ~0.4 per 100,000, increasing with age and seen more in males, immunocompromised individuals, and Western populations.[1]

Molecular Pathogenesis and Classification

PCNSL, also known as reticulum cell sarcoma, diffuse histiocytic lymphoma, and microglioma, accounts for ~90% of cases of diffuse large B cell lymphoma (DLBCL), with the remaining cases consisting of T cell lymphomas, poorly characterized low-grade lymphomas, or Burkitt lymphoma.[1,2]

The DLBCL subtype of PCNSL is marked by immunoblasts or centroblasts arranged around blood vessels, showing an angiocentric growth pattern.[2] Though of lymphoid origin, PCNSL is classified as a brain tumor due to its central nervous system (CNS) localization.[2] Treatment is complicated by the blood–brain barrier and risks of cerebral toxicity.[2] Immunoglobulins contribute by binding to CNS-expressed self-proteins. Genetic alterations often involve B cell receptor signaling, toll-like receptors, and nuclear factor κ-light-chain-enhancer of activated B cells pathways. Clinical presentation depends on the specific CNS regions affected.[2]

Early genetic alterations in DLBCL PCNSL include mutations in the B cell receptor pathway and alterations in myeloid differentiation primary response 88 (MYD88), CD79B, and the loss of CDKN2A. These genetic changes suggest that these pathways may significantly contribute to the initial tumorigenesis of PCNSL.[2]

In the context of the human immunodeficiency virus (HIV) associated with PCNSL, Epstein–Barr virus (EBV) plays a crucial role in the malignant transformation of cells. EBV induces the expression of oncogenic genes, including latent membrane proteins (LMP-1 and LMP-2), EBV nuclear antigen, and EBV-encoded RNAs). Although EBV is not replicated within the CNS, infected cells are believed to originate outside the CNS and infiltrate as the patient's immune system deteriorates.[3]

Presentation

PCNSL) often presents with rapidly progressing neurological symptoms that may mimic conditions such as multiple sclerosis or manifest as vitritis. Common features include personality changes, cognitive decline, and limb weakness due to white matter involvement, especially in the corpus callosum and internal capsule. Hemorrhagic lesions can cause language deficits and paresis. Signs of cerebral edema—headache, vomiting, and hiccups—are frequent. In patients with acquired immunodeficiency syndrome (AIDS), seizures are a more common presentation. Though primarily a CNS disease, systemic involvement may occasionally coexist.

Diagnosis

Diagnosis is typically established through computed tomography (CT) or magnetic resonance imaging (MRI). Whole body CT or positron emission tomography (PET) is done to rule out the occurrence of any systemic malignancy, ophthalmic examination, cerebrospinal fluid (CSF) analysis, and stereotactic needle biopsy.[1]

Treatment

Following diagnostic confirmation, the mainstay of therapy involves high-dose methotrexate (HD-MTX) with or without cytarabine, whole-brain radiotherapy (WBRT), and rituximab. First-line treatment typically involves induction and consolidation stages. Induction therapy is based on MTX with or without rituximab or cytarabine. Consolidation therapy may include low-dose WBRT, Ara-C (cytarabine), etoposide, and autologous stem cell transplantation (ASCT) with thiotepa-based conditioning.[2]

The few available treatment regimens for PCNSL are rituximab, methotrexate, procarbazine, and vincristine (R-MPV); methotrexate, temozolomide, and rituximab (MTR); HD-MTX, *A*ra-C (cytarabine), *T*hiotepa, *R*ituximab (MATRix); HD-MTX, De Angelis; WBRT alone; and ASCT. The pros and cons are summed up in ►**Table 1**.

- De Angelis typically includes the following agents:

- HD-MTX
- Procarbazine
- Vincristine
- Dexamethasone
- Intrathecal methotrexate (in some versions)
- Followed by WBRT and high-dose cytarabine (Ara-C)

Drugs used in immunotherapy are: monoclonal antibodies, such as rituximab, checkpoint inhibitors, such as nivolumab and pembrolizumab, bispecific T cell engagers, including blinatumomab (CD19 × CD3), chimeric antigen receptor T cell anti-CD-19 (currently under trials); others, lenalidomide, pomalidomide, and mechanistic target of rapamycin inhibitors.

An optimal diagnostic workup for PCNSL includes neurological and ophthalmological evaluation, contrast-enhanced MRI or CT of the brain, and spinal MRI if indicated. Diagnosis requires a stereotactic brain biopsy, ideally before corticosteroid use. CSF analysis should include cytology, flow cytometry, and EBV polymerase chain reaction. For ocular involvement, slit-lamp examination and vitreous biopsy are advised. Systemic disease must be ruled out with PET-CT, bone marrow biopsy, and testicular ultrasound (in males). Baseline laboratory tests should include complete blood count, liver and renal function tests, lactate dehydrogenase, HIV, hepatitis B and C serologies, and cardiac evaluation.

This report presents five cases of primary CNS lymphoma to discuss the clinical presentation, diagnostic approach, and treatment strategies.

Case Series

Case 1

A 59-year-old man with a known history of Type II diabetes mellitus presented with complaints of headache and vomiting persisting for 15 days. Additionally, the patient exhibited acute-onset neuropsychiatric symptoms of the

Table 1 Summing up the pros and cons of different regimes available

Regimen	Pros	Cons
R-MPV	Effective and shows a high response	Adverse effects are neurotoxicity; however, its intensive nature can be a pro and a con
MTR	Good for the elderly and people showing immunocompromised status or organ dysfunction	Slightly lower complete response rate
MATRix	Highly effective	Very toxic
	This is usually repeated for two to four cycles, often followed by consolidation with autologous stem cell transplant or whole-brain radiotherapy in eligible patients	
HD-MTX	Simple	Low response
De Angelis	One of the first to show high complete remission rates	However, concerns about neurotoxicity, particularly in older patients, have led to the development of alternative regimens with better tolerability
WBRT alone	Quick relief	Not durable
ASCT	Excellent long-term outcomes in fit patients	

Abbreviations: ASCT, autologous stem cell transplantation; HD-MTX, high-dose methotrexate; MTR, methotrexate, temozolomide, and rituximab; MATRix, HD-MTX, Ara-C (cytarabine), *T*hiotepa, *R*ituximab; R-MPV, rituximab, methotrexate, procarbazine, and vincristine; WBRT, whole-brain radiotherapy.

same duration, which were rapidly progressive. These included decreased sleep, aimless searching behavior, paranoid ideation, fearfulness, irrelevant speech, self-talking, confusion, irritability, and diminished oral intake. The clinical picture progressed to persistent nocturnal wakefulness and a disoriented state suggestive of delirium, possibly due to PCNSL. Routine serum electrolyte analysis was within normal limits.

A contrast-enhanced computed tomography (CECT) scan of the brain demonstrated a well-defined hypodense lesion with peripheral ring enhancement located in the body of the corpus callosum. Further neck, chest, abdomen, and pelvis imaging showed no abnormalities. Subsequently, an open brain biopsy was advised, and the patient was referred to a tertiary care center specializing in psychiatric, neurological, and neurosurgical conditions.

Histopathological analysis revealed sheets of small- to medium-sized lymphoid cells with crushed artifacts, a finding characteristic of lymphoma. The diagnosis of Grade II PCNSL was confirmed through histopathology and supported by immunohistochemistry (IHC) (►**Fig. 1**).

The patient was initiated on the R-MPV chemotherapy protocol, which includes rituximab, methotrexate, procarbazine, and vincristine. The treatment regimen comprised the following dosing schedule: methotrexate 3.5 g/m^2 intravenous (IV) on days 2 and 16; procarbazine 100 mg/m^2 orally on days 7 through 13; vincristine 1.4 mg/m^2 (maximum dose 2.0 mg) IV on days 2 and 16; and rituximab 500 mg/m^2 IV on days 1 and 15. A total of six chemotherapy cycles was planned.

Follow-up MRI showed tumor regression with marked clinical improvement, and the patient has remained well on regular follow-up for 5 years.

Learning Points

Primary CNS lymphoma can present with rapidly progressive neuropsychiatric symptoms, especially when midline structures are involved. Diagnosis requires biopsy and IHC due to nonspecific imaging findings. The R-MPV regimen is the standard first-line treatment, with high-dose methotrexate as its cornerstone. Early diagnosis and prompt therapy are essential for optimal outcomes. This case demonstrates durable remission with a 5-year disease-free follow-up.

Case 2

A 64-year-old man presented with complaints of abdominal pain persisting for 1 month, accompanied by two to three episodes of vomiting daily. To evaluate the underlying cause, a whole-body PET/CT scan was performed. Imaging revealed metabolically active, ill-defined enhancing lesions in the subependymal region of both the lateral third and fourth ventricles. No other metabolically active lesions were identified in the rest of the body. Laboratory reports were sought, and serum creatinine was 1.4 mg/dL.

Based on these findings, the patient was initiated on the MTR chemotherapy regimen comprising methotrexate, temozolomide, and rituximab. He was admitted and received methotrexate 8 g/m^2 intravenously on days 1 and 15; temozolomide 150 mg/m^2 orally on days 7 through 11; and rituximab 375 mg/m^2 intravenously on days 3 and 17. A total of six chemotherapy cycles was planned.

The patient tolerated the immunochemotherapeutic regimen well and demonstrated symptomatic improvement. Upon completion of the planned treatment, a follow-up whole-body and brain PET/CT scan was advised 1 month later. The post-treatment scan, dated January 16, 2025, compared with the baseline scan from August 20, 2024, demonstrated resolution

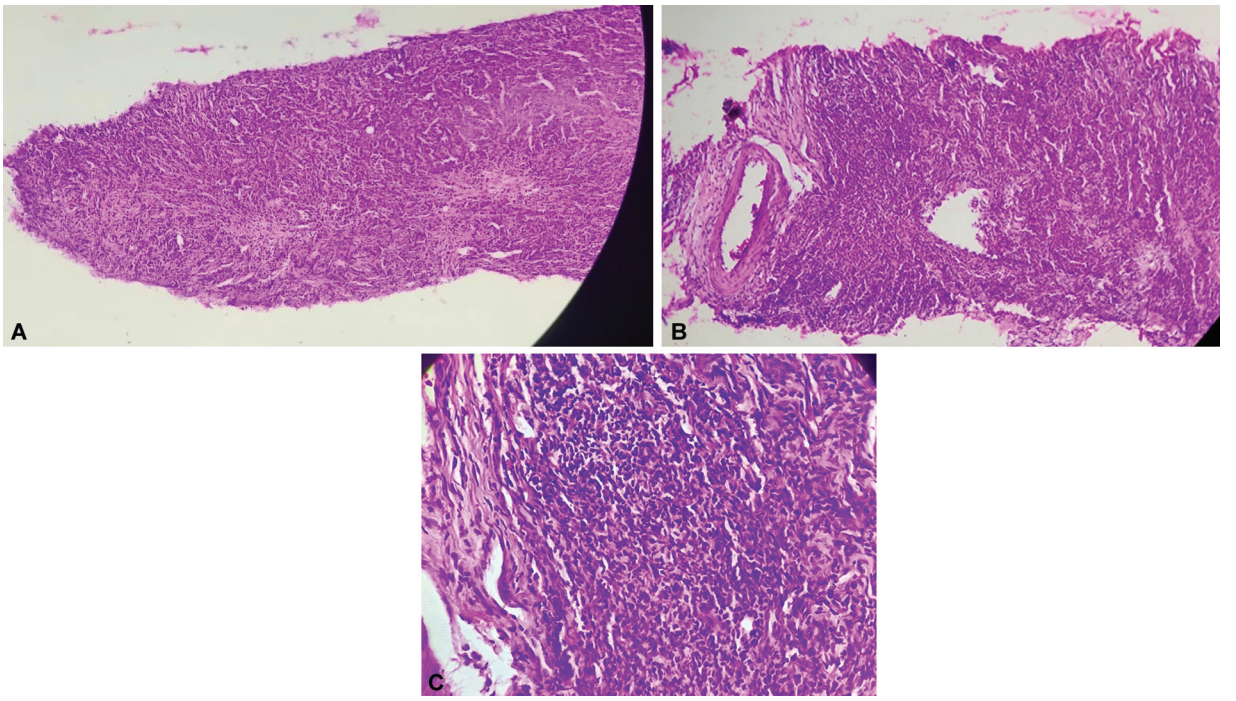

Fig. 1 (A) ×10, (B) ×40, and (C) ×100. Histopathology showing small- to medium-sized lymphoid cells in sheets with a crush artifact.

of the previously identified metabolically active lesions in the subependymal regions of both lateral ventricles and the third and fourth ventricles. No new metabolically active lesions were identified in the whole-body survey. These findings indicated a favorable response to therapy (►**Fig. 2**).

Learning Points

Primary CNS lymphoma can present as isolated subependymal and intraventricular lesions without systemic involvement. The MTR regimen is effective for such presentations. PET/CT is essential for both diagnosis and treatment monitoring. Early therapy can achieve complete metabolic remission, as seen in this case.

Case 3

A 61-year-old man presented with complaints of imbalance and headache for 2 days, accompanied by progressive weakness in both lower limbs. The onset of symptoms was gradual, with steady deterioration. The patient had a known history of chronic liver disease.

A noncontrast CT scan of the brain revealed ill-defined heterogeneous density lesions in the bilateral cerebellar hemispheres, extending into the bilateral middle cerebellar peduncles and the pons. Additionally, a lesion was noted involving the pons and bilateral dentate nuclei, with diffuse hypodensity across the pons (►**Fig. 3**). A whole-body PET/CT scan was performed, which showed no other metabolically active lesions elsewhere in the body.

The patient was admitted with a presumptive diagnosis of PCNSL and planned for MTR chemotherapy. However, treatment was initially delayed due to the development of pneumonia caused by *Klebsiella pneumoniae*. Following stabilization with appropriate antibiotic therapy, the patient was initiated on the MTR chemotherapy regimen, similar to the second case. This included MTR, with six planned cycles. The patient completed four cycles before being lost to follow-up. Despite this, clinical improvement was observed, with signs of neurological recovery and symptomatic relief noted during treatment.

Learning Points

Primary CNS lymphoma can involve the cerebellum and brain stem, presenting with imbalance and limb weakness. PET/CT is vital to confirm isolated CNS disease. The MTR regimen is effective but may be delayed by infections in immunocompromised patients. Even partial treatment can lead to neurological improvement, as seen in this case.

Case 4

A 74-year-old woman with a known history of Type II diabetes mellitus presented with acute-onset memory loss lasting 1 day. There was no associated history of headache, trauma, fever, visual disturbances, loss of consciousness, giddiness, seizures, or vomiting.

MRI of the brain revealed a lesion in the left frontal region with both intra- and extracranial extension, resulting in displacement of the frontal lobe. Based on clinical and radiological evaluation, an initial diagnosis of invasive meningioma was considered. The patient underwent a bicoronal incision with frontal craniotomy and complete excision of the lesion, followed by mesh placement under general anesthesia. The intra- and extracranial components and the involved bone were submitted for histopathological examination.

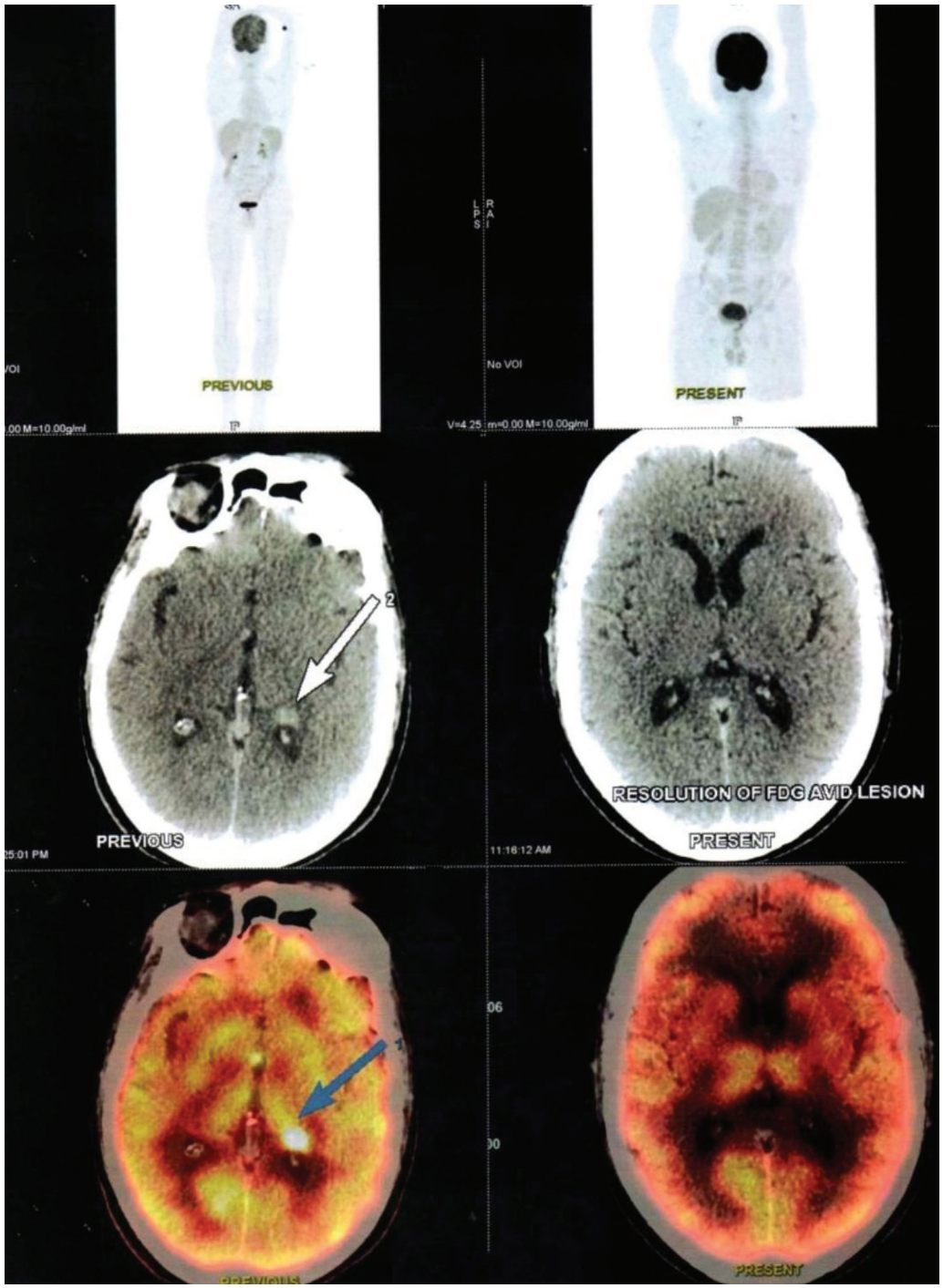

Fig. 2 Pre- and postchemotherapy scans suggest good tolerance to treatment, with favorable comparative findings.

Microscopic evaluation revealed sheets of a cellular neoplasm composed of large atypical cells with regular nuclear membranes, hyperchromatic nuclei, prominent nucleoli, and moderate cytoplasm. The tumor cells were interspersed with thin-walled blood vessels (►**Fig. 4**). IHC showed that the neoplastic cells were positive for CD45 and CD3, indicating a T cell lineage (►**Fig. 5**). The final diagnosis was PCNSL, T cell type, involving the frontal lobe.

The patient was initiated on the R-MPV chemotherapy regimen following the protocol described in Case 1. Six cycles of chemotherapy were planned. Three weeks after completing chemotherapy, the patient was started on radiotherapy, receiving a total dose of 54 Gy in 30 fractions over 6 weeks.

Upon completion of both chemotherapy and radiotherapy, the patient was advised to follow-up with a CECT) scan of the brain after 1 month. The imaging showed regression of the previously noted lesion.

However, 2 months later, the patient presented with new-onset behavioral disturbances and disorientation. A repeat MRI of the brain demonstrated postoperative changes in the

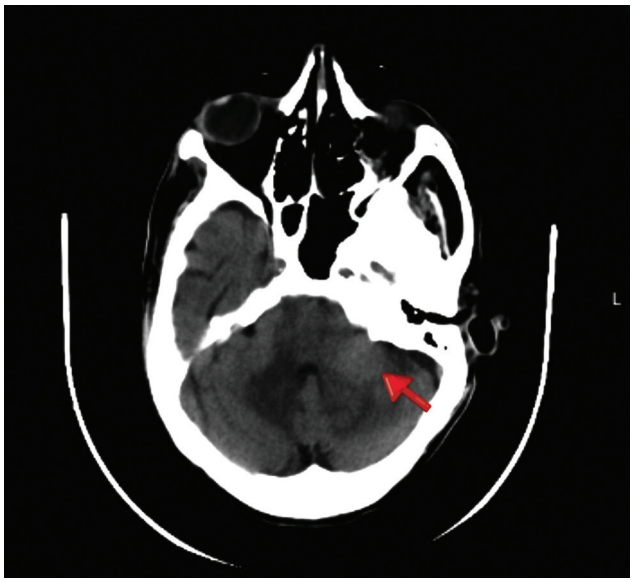

Fig. 3 Space-occupying lesion in the cerebellum extending to the pons (lesion marked with red arrow).

left frontal lobe with gliosis and a subacute hematoma. Real-time ultrasonography of the abdomen revealed additional findings, leading to a final diagnosis of recurrent PCNSL postchemotherapy and radiotherapy, with newly diagnosed metastatic carcinoma of the pancreas, metabolic encephalopathy, and obstructive jaundice.

Given her declining condition and poor prognosis, the patient's relatives declined further radiotherapy. Repeat cycles of R-MPV chemotherapy were initiated; however, her clinical condition continued to deteriorate. The patient was transitioned to symptomatic and supportive care and ultimately succumbed to complications of PCNSL.

Learning Points

Primary CNS lymphoma can mimic invasive meningioma, especially with intra- and extracranial extension. This case highlights the rare, aggressive T cell variant of PCNSL, confirmed by CD45 and CD3 positivity. Despite initial response to R-MPV chemotherapy and radiotherapy, recurrence and systemic complications led to poor prognosis, emphasizing the need for vigilant follow-up.

Case 5

A 39-year-old woman, known to be HIV positive and on antiretroviral therapy consisting of tenofovir 300 mg, lamivudine 300 mg, and dolutegravir 50 mg, presented with a history of persistent headaches over the past 6 months. Clinical evaluation revealed altered sensorium and disorientation, symptoms that had gradually worsened over the previous 3 months. The neurological decline followed intermittent episodes of fever accompanied by chills and headache.

Initial investigations conducted at an external facility included CSF analysis, CT of the head, and both plain and contrast MRI of the brain. Additionally, PET/CT of the whole body was performed to rule out systemic malignancy. Based

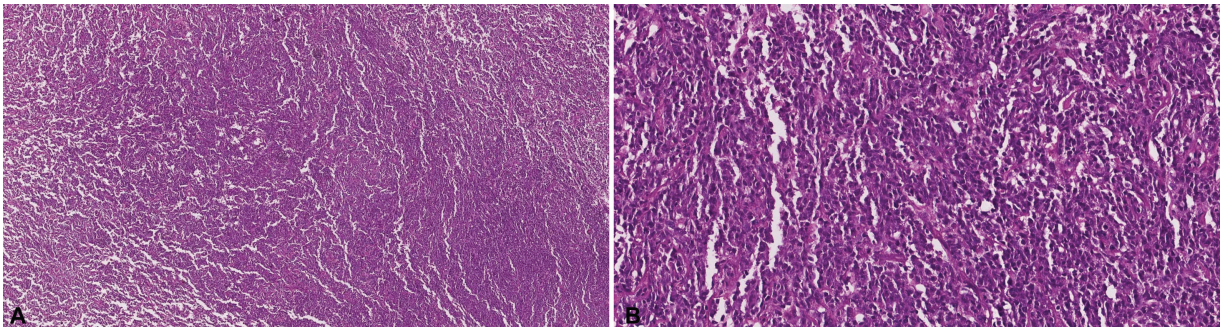

Fig. 4 (A) Histopathology showing sheets of lymphoid cells (hematoxylin and eosin [H & E], ×40). (B) Histopathology showing sheets of small- to medium-sized lymphoid cells having hyperchromatic nuclei (H & E, ×100).

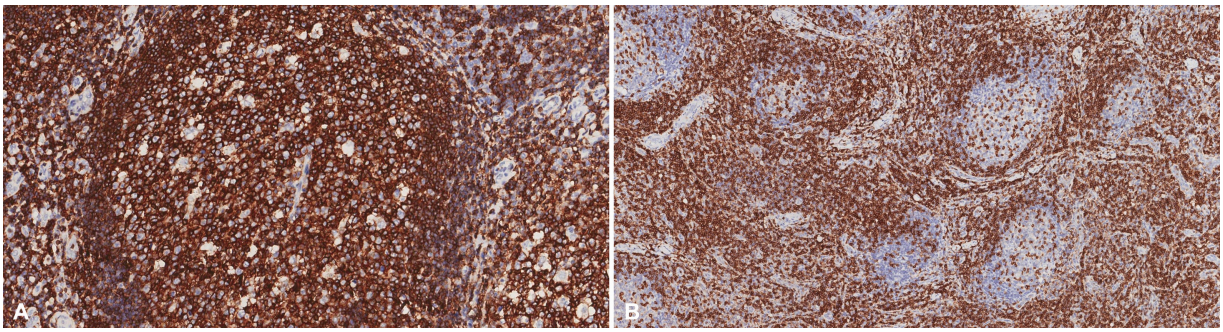

Fig. 5 (A) Immunohistochemistry showing CD45 positivity (×200). (B) Immunohistochemistry showing CD3 positivity (×200).

on the clinical and radiological findings, a diagnosis of PCNSL was established.

The patient was noted to be emotionally distressed, particularly apprehensive about the future care of her children. Progressive memory impairment was observed, and a secondary diagnosis of depressive disorder due to an organic condition was made. Laboratory findings revealed elevated total leukocyte and platelet counts. MRI of the brain demonstrated significant contrast enhancement of altered signal intensity foci in the splenium of the corpus callosum and the right gangliocapsular region.

The patient was scheduled to receive the MTR chemotherapy regimen, consisting of methotrexate, temozolomide, and rituximab, following the same protocol described in Case 2. A total of six chemotherapy cycles was planned. Three weeks after initiation of chemotherapy, the patient underwent focal radiotherapy to the lesion, receiving a dose of 14.4 Gy in eight fractions.

During the administration of the sixth cycle of immunochemotherapy, the patient developed pneumonia and experienced difficulty maintaining adequate oxygen saturation on room air. She was managed with a non-rebreather mask and intravenous antibiotics after being transferred to the intensive care unit. Despite supportive treatment, her condition deteriorated due to underlying immunosuppression, and she ultimately succumbed to opportunistic infections, likely exacerbated by low CD4+ T cell counts.

Learning Points

Primary CNS lymphoma is common in immunocompromised patients, especially those with HIV/AIDS. This case highlights PCNSL involving the corpus callosum and basal ganglia in an HIV-positive patient, treated with MTR chemotherapy and focal radiotherapy. Opportunistic infections, such as pneumonia, are a major cause of mortality during treatment due to immunosuppression and low CD4+ counts. The case underscores the need for infection vigilance and supportive care in HIV-associated PCNSL.

A summary of the case series is noted in ►**Tables 2** and **3**.

Discussion

PCNSL remains a rare and aggressive malignancy, frequently presenting with nonspecific neurological symptoms such as headache, memory loss, and behavioral changes. Our cohort reflected this, with headache being the most common symptom and the corpus callosum emerging as a frequently involved site[4] (►**Table 3**).

PCNSL is known to occur in both immunocompetent and immunocompromised patients. Among the latter, especially HIV-positive individuals, the disease tends to have an aggressive course with a median CD4+ count of 16 cells/μL at diagnosis.[3] Diagnostic imaging plays a crucial role; MRI and PET/CT help localize lesions and differentiate PCNSL from

Table 2 Summary of case series

Case number	Presentation	Diagnosis	Treatment	Survival and follow-up
1	59-year-old man with Type II diabetes, headache, vomiting, abnormal behavior, delirium	PCNSL Grade II confirmed by biopsy and IHC	R-MPV	Regression of tumor size with symptomatic improvement. Regular follow-up planned
2	64-year-old man with abdominal pain and vomiting, metabolically active	PCNSL diagnosed through imaging (PET/CT). Lesions on PET/CT in subependymal regions	MTR	Good response to therapy. No new lesions observed in follow-up PET/CT
3	61-year-old man with imbalance, headache, and weakness	PCNSL suspected based on CT findings. Confirmed by biopsy and imaging. CT showed lesions in cerebellar hemispheres and pons	MTR	Improvement during initial treatment but failed to complete all planned cycles due to non-compliance.
4	74-year-old woman with memory loss	PCNSL diagnosed as T cell type by biopsy and IHC. Lesion in left frontal region on MRI. Suspected invasive meningioma	R-MPV chemotherapy and radiotherapy (54 Gy/30 fractions)	Recurrent symptoms posttreatment developed pancreatic metastasis. Eventually succumbed to the disease
5	39-year-old woman with HIV, progressive memory disturbances	PCNSL diagnosed based on imaging (MRI), confirmed by biopsy. Contrast enhancement in corpus callosum and gangliocapsular region	MTR chemotherapy and radiotherapy (54 Gy/30 fractions)	Developed pneumonia during treatment, succumbed to opportunistic infections due to low CD4+ counts

Abbreviations: IHC, immunohistochemistry; HIV, human immunodeficiency virus; MRI, magnetic resonance imaging; MTR, methotrexate, temozolomide, and rituximab; PCNSL, primary central nervous system lymphoma; PET/CT, positron emission tomography/computed tomography; R-MPV, rituximab, methotrexate, procarbazine, and vincristine.

Table 3 Summary of demographic and clinical variables in five PCNSL cases

Variable	Value/distribution
Number of cases	5
Mean age (y)	59.4 (39–74)
Sex distribution	3 males, 2 females
Comorbidities	Diabetes: 2 HIV: 1 Chronic liver disease: 1
Initial presentation	Headache: 4 Cognitive changes: 3 Vomiting: 3
Lesion locations	Corpus callosum: 2 Frontal: 1 Cerebellum/pons: 1 Subependymal: 1
Chemotherapy regimens used	R-MPV: 2 MTR: 3
Survival status	Alive and under follow-up: 2 Lost to follow-up: 1 Deceased: 2
Follow-up duration	4 mo to 5 y

Abbreviations: HIV, human immunodeficiency virus; MTR, methotrexate, temozolomide, and rituximab; PCNSL, primary central nervous system lymphoma; R-MPV, rituximab, methotrexate, procarbazine, and vincristine.

mimics such as gliomas or infections. The classic imaging features—iso- or hypointense on T1, slightly hyperintense on T2, and hyperintense on fluid-attenuated inversion recovery, with strong gadolinium enhancement—are consistent with PCNSL.[4–7] Involvement of the corpus callosum can produce a characteristic "butterfly lesion," and lesions may mimic gliomas or tumefactive demyelination, necessitating accurate differentiation[8] (►**Table 4**).

Histopathology and IHC remain the gold standards for confirming diagnosis. Our cases demonstrated classic PCNSL features—sheets of atypical lymphoid cells with high nuclear-to-cytoplasmic ratios and crush artifacts, confirmed by CD markers. While most PCNSL are B cell derived, Case 4 was a rare CD3+ T cell lymphoma.

Treatment centered on high-dose methotrexate-based chemotherapy.[5–8] In immunocompetent patients with stable disease profiles (Cases 1 and 4), the R-MPV regimen was used, followed by radiotherapy in Case 4.[9–11] In elderly or immunocompromised patients (Cases 2, 3, and 5), the MTR regimen was preferred due to its safer toxicity profile. Radiotherapy was used postchemotherapy in Cases 4 and 5.

Surgical intervention, though limited in PCNSL due to its infiltrative nature, was done in Case 4, where the lesion was initially suspected to be a meningioma, later confirmed as a rare T cell variant. This underlines the importance of tissue biopsy before steroid initiation to avoid diagnostic confusion.

Outcomes varied: Cases 1 and 2 improved and are under follow-up; Case 3 showed an initial response but was lost to follow-up; Case 4 relapsed and later succumbed; and Case 5, an HIV-positive individual, died of opportunistic infections despite therapy. These patterns align with the literature, which reports a 33% 5-year survival rate.[12,13] Quality of life improved notably in Cases 1 to 3 during therapy (►**Tables 2** and **3**).

Emerging biomarkers such as MYD88 L265P and CD79B mutations, along with elevated CSF cytokines such as CXCL13 and interleukin 10, are under investigation for diagnostic and prognostic roles.[14,15] Liquid biopsy using CSF-derived circulating tumor DNA (ctDNA) may soon complement tissue-based diagnostics, though validation is needed. The International Extranodal Lymphoma Study Group prognostic score remains a helpful tool, especially in immunocompetent individuals with deep brain involvement.[16]

Overall, PCNSL management requires early diagnosis, multimodal therapy, and personalized care tailored to immune status, lesion site, and comorbidities. Our series highlights real-world diagnostic and therapeutic variability, including uncommon variants such as T cell PCNSL. While emerging biomarkers show promise, their integration into routine clinical practice remains limited. This article reinforces the need for validated prognostic tools, standardized

Table 4 Radiological differences between PCNSL and gliomas

Feature	PCNSL	Glioma
Typical location	Deep periventricular regions (e.g., corpus callosum, basal ganglia)	Anywhere in the brain; often lobar (frontal, temporal)
Enhancement pattern	Homogeneous, strong enhancement	Heterogeneous; often ring enhancing in high-grade gliomas
Edema	Mild to moderate vasogenic edema	Often marked vasogenic edema
Necrosis	Usually absent	Common in high-grade gliomas
Margins	Well defined	Often irregular and infiltrative
DWI	Restricted diffusion due to high cellularity	Variable; typically less restricted than PCNSL
MR spectroscopy	Elevated lipid/lactate peaks, decreased NAA	Elevated choline, decreased NAA, and creatine
Response to steroids	Marked reduction in size/enhancement	Minimal or no response
Contrast uptake	Intense, solid enhancement	Patchy or ring-like, especially in glioblastomas

Abbreviations: DWI, diffusion-weighted imaging; MR, magnetic resonance; NAA, N-acetylaspartate; PCNSL, primary central nervous system lymphoma.

treatment protocols, and long-term studies to optimize PCNSL outcomes.

Conclusion

PCNSL is a rare, aggressive malignancy, often affecting HIV/AIDS patients and presenting with neurological symptoms. Diagnosis is primarily imaging-based (MRI, PET/CT), allowing for early treatment initiation; however, histology remains essential for identifying rare, aggressive subtypes, such as T cell PCNSL. Standard therapy includes high-dose methotrexate-based regimens (e.g., R-MPV, MTR), sometimes followed by radiotherapy, although neurotoxicity remains a concern. Despite a poor prognosis (~33% 5-year survival), outcomes can improve. Promising prognostic markers exist but need formal clinical integration.

Authors' Contributions

V.S., K.P.H.L., and M.R. conceptualized the study. D.P. and A.K. designed the study. D.P., V.S, and K.P.H.L. defined the intellectual content. D.P. performed the literature search. D.P., A.K., and V.S. conducted the clinical studies. A.K. and K.P.H.L. performed the data analysis. D.P. and K.P.H.L. prepared the manuscript. D.P., A.K., and M.R. edited the manuscript. D.P., A.K., V.S., and K.P.H.L. reviewed the manuscript. A.K. is the guarantor.

Ethical Approval

Institutional ethical committee approval was obtained.

Patient's Consent

Written consent from the patient/patient party has been obtained.

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None.

Conflict of Interest

None declared.

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