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Serum Il-6 and Il-2r as supportive biomarkers in the diagnostic suspicion of primary central nervous system lymphoma: A case report

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Introduction

Primary Central Nervous System Lymphoma (PCNSL) is a rare, aggressive non-Hodgkin lymphoma confined to the brain, spinal cord, leptomeninges, or eyes. Its highly variable presentation often mimics other neurological disorders, delaying diagnosis and treatment. We report a diagnostically challenging case of PCNSL in an immunocompetent elderly patient with nonspecific neurological symptoms and extensive brain lesions, establishing a broad differential diagnosis. This case is particularly remarkable because of the striking involvement of the corpus callosum, the marked corticosteroid responsiveness—an expected feature of PCNSL-and the elevation of serum IL-6 and IL-2R. These cytokines, increasingly recognized as useful biomarkers in the context of suspected PCNSL, may provide additional supportive evidence when conventional diagnostic tools are inconclusive. The convergence of these elements made the diagnosis complex yet educational, underscoring the importance of maintaining high clinical suspicion, reinforcing the need for early biopsy, and highlighting the potential role of emerging biological markers such as IL-6 and IL-2R in guiding clinical suspicion of PCNSL.

Case presentation

A 78-year-old man with type 2 diabetes mellitus and benign prostatic hyperplasia presented with progressive gait instability, cognitive decline, and recurrent falls over three weeks. Neurological examination revealed bradypsychia, disorientation, mild left facial asymmetry, dysarthria, bilateral limb weakness (4-/5), dysmetria, truncal ataxia, and severe postural instability. He was afebrile and showed no systemic involvement.

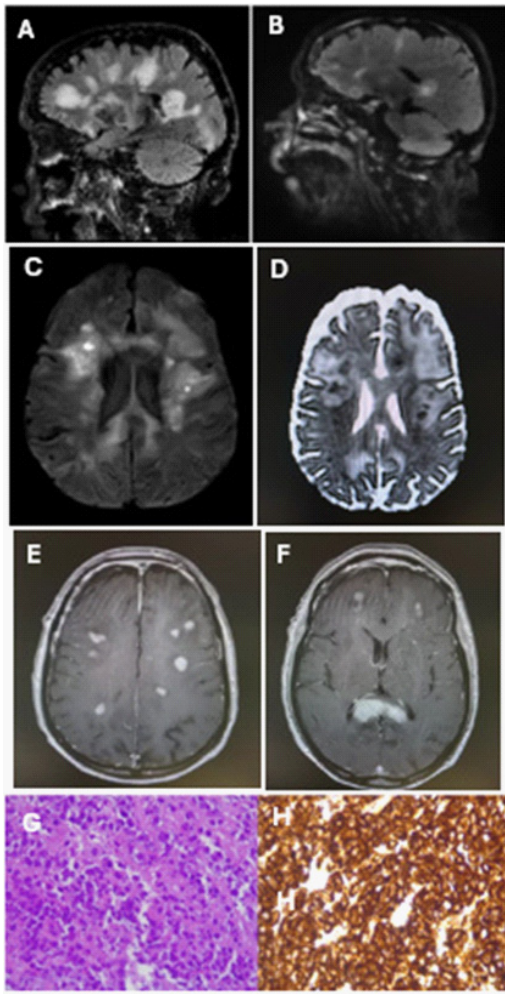

Figure 1: (a) Brain MRI T2 FLAIR sagittal section showing multiple supra- and infratentorial lesions, with striking involvement of the splenium of the corpus callosum, with perilesional edema and mass effect. **(b)** BRAIN MRI T2 FLAIR sagittal section showing decrease in number and size of brain lesions after an empirical 5-days cycle of intravenous methylprednisolone bolus (1 g/day). **(c** & **d)** Brain MRI DWI axial section and brain MRI ADC axial section, demonstrating hyperintense brain lesions on DWI with corresponding hypo intensity on the Apparent Diffusion Coefficient (ADC) map, consistent with diffusion-restricting lesions. **(e)** Brain MRI post-contrast T1 FLAIR axial section showing supratentorial lesions with homogeneous contrast enhancement. **(f)** Brain MRI post-contrast T1 FLAIR axial section showing splenial involvement with homogeneous contrast enhancement. **(g)** Sample obtained by brain biopsy. Hematoxylin-eosin staining, where neoplastic cell proliferation is observed with cells of increased size, round and pleomorphic nuclei. **(h)** Cellular positivity for CD20.

Initial brain Computed Tomography (CT) revealed multiple supra- and infratentorial lesions with vasogenic edema and diffuse contrast enhancement, suggestive of cerebral metastases. Brain Magnetic Resonance Imaging (MRI) showed hyperintense lesions on T2/FLAIR with mass effect (Figure 1A), strong diffusion restriction (Figure 1C/1D), homogeneous contrast enhancement (Figure 1E/1F) and striking involvement of the splenium of the corpus callosum (Figure 1F) findings pointing toward an inflammatory, infectious, or neoplastic process.

Cerebrospinal Fluid (CSF) analysis showed elevated protein (129 mg/dL), glucose of 66 mg/dL, and 31 mononuclear leukocytes/µL. Serologies and autoimmunity studies-including Antinuclear Antibodies (ANA), antimitochondrial antibodies, antismooth muscle antibodies, antiparietal cell antibodies, Antineutrophil Cytoplasmic Antibodies (ANCA), rheumatoid factor, complement, IgA, IgG, anti-phospholipid syndrome markers, Oligoclonal Bands (OCB) in serum and CSF, and antibodies against Myelin Oligodendrocyte Glycoprotein (antiMOG) and Aquaporin-4 (AQP4)-were negative. CSF flow cytometry was unremarkable.

An empirical five-day course of high-dose intravenous methylprednisolone (1 g/day) led to notable clinical and radiological improvement (Figure 1B). The patient was later admitted to the Intensive Care Unit (ICU) due to respiratory complications. After stabilization, his neurological condition worsened. Repeat MRI showed increased lesion size and number.

In the broad differential diagnosis, all those entities that could cause multifocal enhancing Central Nervous System (CNS) lesions in elderly patients were included. From a tumoral perspective, metastases were excluded due to the absence of systemic cancer and a negative body work-up, together with the presence of homogeneous rather than ring-like enhancement. Glioblastoma was considered but typically presents with a dominant necrotic mass, irregular borders and ring-enhancement, unlike the diffuse callosal involvement seen here. From an infectious standpoint, abscesses were unlikely, despite intense diffusion restriction on brain MRI, as the patient remained afebrile, inflammatory markers were normal, and CSF showed lymphocytic rather than neutrophilic pleocytosis. Toxoplasmosis was excluded on the basis of an immunocompetent status, negative serologies, absence of the eccentric target sign and dramatic steroid response. Within the inflammatory spectrum, demyelinating disorders such as MS, NMOSD, or MOGAD were considered, but negative oligoclonal bands, negative AQP4 and MOG antibodies, and the presence of mass effect with homogeneous enhancement argued against them. Neurosarcoidosis was unlikely given the absence of systemic involvement, normal Angiotensin-Converting Enzyme (ACE) levels, negative autoimmune panels and no leptomeningeal enhancement. Primary CNS vasculitis was also considered, but negative autoimmune serologies, bland CSF profile, and normal vascular imaging excluded this possibility.

Given the lesion pattern-including striking splenial involvement-and homogeneous enhancement with restricted diffusion, together with rapid steroid responsiveness, PCNSL was suspected. Serum interleukin-6 (IL-6) and soluble interleukin-2 receptor (IL-2R) levels were markedly elevated. A stereotactic brain biopsy confirmed Diffuse Large B-Cell Lymphoma (DLBCL), consistent with PCNSL (Figure 1G/1H). A systemic work-up, including body CT, revealed no extracranial disease.

Prognosis was assessed using the International Extranodal Lymphoma Study Group (IELSG) score [1], placing the patient in a high-risk category. Due to his age, comorbidities, and clinical deterioration, methotrexate-based chemotherapy was not initiated. Palliative care was provided, and the patient died five months after symptom onset.

Discussion and conclusion

PCNSL presents with diverse clinical and radiological features, making diagnosis challenging and requiring high suspicion from the beginning. Our patient showed cognitive dysfunction, truncal ataxia, and multifocal MRI lesions with mass effect, contrast enhancement, and diffusion restriction. The differential included metastases, glioblastoma, abscess, toxoplasmosis, vasculitis, neurosarcoidosis, multiple sclerosis, and neuromyelitis optica, which were ruled out. The marked response to corticosteroids, splenial involvement [2], and elevated IL-6 and IL-2R supported the diagnosis, confirmed by biopsy.

PCNSL accounts for ~2% of brain tumors, most being DLBCL [3]. Diagnosis is difficult due to overlap with other CNS pathologies. Methotrexate is the standard therapy [4], but relapses are frequent and prognosis remains poor [5].

In conclusion, PCNSL should be considered in elderly patients with multifocal enhancing brain lesions and atypical clinical presentations. Diagnostic delays are frequent given the nonspecific manifestations and overlap with a wide range of infectious, inflammatory, and neoplastic conditions. This case stands out due to the prominent involvement of the corpus callosum, the pronounced corticosteroid responsiveness-an anticipated characteristic of PCNSL-and the elevation of serum IL-6 and IL-2R. These cytokines, which are gaining recognition as valuable biomarkers in the setting of suspected PCNSL, can offer complementary supportive evidence when standard diagnostic approaches fail to yield conclusive results. Maintaining a broad differential diagnosis, sustaining a high level of clinical vigilance, and pursuing early histological confirmation are therefore essential to avoid misclassification and ensure timely patient management, with IL-6 and IL-2R serving as promising adjunctive markers to support the suspicion of CNS lymphoma.

Declarations

Ethics statement: Informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article. Ethical approval to report this case was obtained from the institutional review board (PI-25- 262-C).

Data availability: No datasets were generated or analysed during the current study.

Author contributions: EVM: Writing- original draft, Writing- review & editing, Data curation, Conceptualization, Methodology, Formal analysis. JFA, SPG, AFG and APR: Writing- review & editing. PMC: Writing- original draft, Writing- review & editing, Supervision, Project administration, Formal analysis, Conceptualization.

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References

1. Ferreri AJM, Blay JY, Reni M, Pasini F, Spina M, et al. Prognostic scoring system for primary CNS lymphomas: the International Extranodal Lymphoma Study Group experience. J Clin Oncol Off J Am Soc Clin Oncol. 2003; 21(2): 266-72.
2. Bataille B, Delwail V, Menet E, Vandermarcq P, Ingrand P, et al. Primary intracerebral malignant lymphoma: report of 248 cases. J Neurosurg. 2000; 92(2): 261-6.
3. Camilleri-Broët S, Martin A, Moreau A, Angonin R, Hénin D, et al. Primary central nervous system lymphomas in 72 immunocompetent patients: pathologic findings and clinical correlations. Groupe Ouest Est d'étude des Leucénies et Autres Maladies du Sang (GOELAMS). Am J Clin Pathol. 1998; 110(5): 607-12.
4. De Angelis LM, Yahalom J, Thaler HT, Kher U. Combined modality therapy for primary CNS lymphoma. J Clin Oncol Off J Am Soc Clin Oncol. 1992; 10(4): 635-43.
5. Pasqualucci L, Dalla-Favera R. The genetic landscape of diffuse large B-cell lymphoma. Semin Hematol. 2015; 52(2): 67-76.