

Primary Brain Lymphoma in Immunocompetent People: About 3 Cases - Experience from the Onco-Radiotherapy Department of Chu Mohamed VI in Marrakech

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Abstract

Case Series

Introduction: Primary cerebral lymphoma is a rare condition that mainly affects elderly and immunocompromised individuals. Its occurrence in immunocompetent patients is unusual, representing 1% of non-Hodgkin lymphomas and 5% of all brain tumors. The goal of our study is to report 3 cases of primary lymphoma in immunocompetent patients and to discuss the epidemiological and clinico-anatomical features, as well as the treatment options and prognosis of this tumor through the literature. **Observations:** The first patient was a 52-year-old admitted for aphasia and headaches; the MRI showed a deep portal lesion invading the corpus callosum. The second patient, 75 years old, had hemiplegia without signs of increased intracranial pressure, with a brain CT showing a parietal lesion. As for the last patient, he consulted for headaches with a decline in general condition, and imaging revealed a large tumor process in the right fronto-temporo-parietal cranial vault. All three, after a biopsy-excision, whose histology described large B-cell non-Hodgkin malignant lymphomas, all received induction chemotherapy and intrathecal methotrexate injections followed by a whole-brain radiotherapy of 40Gy with a good response. **Conclusion:** LCP, once mainly seen in immunocompromised patients, is now increasingly common in older, immunocompetent individuals, often with deep-seated involvement. Its management is multidisciplinary, involving surgery mainly for diagnostic confirmation, chemotherapy, and radiotherapy. Despite this, the prognosis remains poor, with high recurrence rates and limited overall survival, especially in elderly or frail patients.

Keywords: Primary cerebral lymphoma; immunocompetent; chemotherapy; radiotherapy.

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INTRODUCTION

PCNSLs are defined as non-Hodgkin lymphomas that develop in the brain, possibly in the meninges and the eye, in the absence of any other systemic location [1]. They represent a rare type that holds a special place among malignant brain tumors. As extranodal non-Hodgkin lymphomas, they occur in both immunocompromised and immunocompetent individuals. Immunodeficiency, once considered a contributing factor, is now seeing an increase in incidence among immunocompetent people. This is a rare cancer, accounting for 1% of non-Hodgkin lymphomas and 5% of all brain tumors [1]. The aim of our study is to report our three cases and discuss the epidemiological and clinicopathological peculiarities, as well as the therapeutic options and prognosis of this tumor through the literature.

CASE 1

A 52-year-old patient with no significant medical history was admitted to the neurosurgery department for aphasia with headaches, without any eye symptoms or general condition deterioration. Clinical examination found right-sided hemiparesis with blunted deep tendon reflexes on the right side. Brain MRI revealed a deep-seated lesion invading the corpus callosum with a butterfly-like appearance measuring 54x32 mm. This lesion was hypointense on T1, hyperintense on T2, and enhanced heterogeneously with contrast. Another lesion was identified in the frontal region, measuring 30x18 mm with peri-lesional edema and mass effect on the frontal horn of the left lateral ventricle. Biopsy and IHC profile suggested a high-grade B-cell non-Hodgkin lymphoma. The patient was then referred to hematology-oncology, where, as part of the

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staging workup, a bone marrow biopsy was normal and a lumbar puncture showed no tumor proliferation. He then underwent induction chemotherapy using the CHOP protocol (cyclophosphamide 750 mg/m² on day 1 + doxorubicin 50 mg/m² on day 1 + vincristine 1.4 mg/m² on day 1 + prednisone 100 mg/m²/day from day 1 to 5) and 4 intrathecal methotrexate injections. Post-chemotherapy MRI showed cavitory lesions with hemorrhagic content replacing the frontal tumor masses, with reduced mass effect on adjacent structures and a normal neurological exam. Whole-brain radiotherapy was then performed at a dose of 40 Gy without complications, and post-radiation MRI noted residual lesions with gliosis foci. Finally, under surveillance, the patient showed no recurrence during 45 months of follow-up. He reportedly died 13 months after diagnosis due to other unexplained causes.

CASE 2

A 75-year-old man with a history of non-Hodgkin lymphoma (NHL) in the left arm, which was surgically treated and irradiated 2 years ago, was referred to the neurosurgery department for left-sided hemiparesis without signs of increased intracranial pressure. A brain CT scan showed a 35×34×22 mm right parasagittal parietal lesion, rounded and heterogeneous, with an isodense tissue component and a central hypodense necrotic zone, along with perilesional edema. He underwent a partial surgery, and the histopathology favored a high-grade B-cell non-Hodgkin lymphoma of the non-germinal center type. A CT scan for staging (CTAP) did not show any secondary lesions. He then received 5 courses of methotrexate and 8 courses of the CHOP protocol (cyclophosphamide 750 mg/m² on day 1, doxorubicin 50 mg/m² on day 1, vincristine 1.4 mg/m² on day 1, and prednisone 100 mg/m²/day from day 1 to 5). Follow-up MRI showed gliosis and scar edema without any signs of residual tumor, with persistent left-sided hemiparesis and no other symptoms. Subsequently, he received whole-brain radiotherapy of 40 Gy. Post-radiation effects included ongoing hemiparesis and the development of knee osteoarthritis. The patient reportedly passed away 5 years after his diagnosis due to complications of his disease.

CASE 3

A 75-year-old man presents with headaches that have been developing over 9 months in the context of a general health decline marked by weight loss. Brain MR angiography revealed a large tumor in the right fronto-temporo-parietal cranial vault with meningeal infiltration and involvement of the subarachnoid spaces, engulfing the superior sagittal sinus and the right frontal cerebral cortex. He underwent an excision biopsy, and the histopathological study was consistent with diffuse large B-cell lymphoma of germinal center type. CTAP scans found a few jugulocarotid and right spinal lymph nodes of lymphomatous origin. He then received 6 cycles of

intrathecal methotrexate with a good clinical response, but the patient was lost to follow-up.

DISCUSSION

From an epidemiological standpoint, PCNSLs are rare tumors, representing 4-6% of non-Hodgkin lymphomas and 5% of all malignant brain tumors, with an incidence rate of 0.4 to 0.5 per 100,000 (Mendez *et al.*, 2018[5]). The age at which this tumor occurs is typically in the sixth and seventh decades in immunocompetent individuals [2], with a median onset of around 65 years [3], and a male predominance [2]. This is the case in our study, where all patients were male with an average age of 67.33 years. It affects both immunocompetent and immunocompromised individuals [2]. The diagnosis of PCNSL is based on histological examination, most often from a brain biopsy [3].

Clinically, primary central nervous system lymphomas (PCNSL) differ from other malignant brain tumors due to a higher frequency of cognitive disorders and the rarity of epileptic seizures, because they tend to be located deep and diffusely [4]. In our study, none of the patients experienced an epileptic seizure.

The management of PCNSL is multidisciplinary and is based on methotrexate-based chemotherapy. A retrospective study in people under 60 showed that using whole-brain irradiation after chemotherapy improved progression-free survival without affecting overall survival [5]. For our three patients, there was a clear improvement in clinical signs after whole-brain irradiation, except for the third patient, who was unfortunately lost to follow-up before radiotherapy. Outside of clinical trials, an acceptable approach is to use irradiation only in cases of refractory disease (partial response, stabilization, progression) or relapse after complete response [8,10]; surgery has no role in PCNSL management except for obtaining histopathological confirmation.

The prognosis without treatment is poor; with treatment, the response is better, with clinical signs disappearing. In the literature, RAZAFINDRAFARA Herilalao Elisabeth reported survival of about 20-42 months, while Normand J. Laperriere found a median overall survival of 1.4 years (17 months) and a 5-year actuarial survival of 26% [5,10]. This survival aligns with our study, which recorded 5-year survival for the second patient.

CONCLUSION

Lymphoma of the central nervous system, once mostly seen in immunocompromised individuals, is now increasingly found in elderly patients with normal immune function, often in deep brain locations. Through this series of three cases, we highlight the need for early diagnosis based on imaging and biopsy, as well as the

importance of multidisciplinary management tailored to the patient's profile. High-dose methotrexate remains the cornerstone of treatment, while whole-brain radiotherapy still has a role, especially as a salvage option or for patients who aren't candidates for intensive chemotherapy, though it comes with significant neurocognitive side effects. Despite these interventions, the prognosis remains poor, with high relapse rates and limited overall survival, particularly in older or frail patients.

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