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Case Report

# Isolated Retrobulbar Optic Neuropathy Revealing Relapsed Non-Hodgkin Lymphoma: A Rare Clinical Presentation

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## Abstract

**Introduction:** Non-Hodgkin lymphomas (NHL) represent a heterogeneous group of hematopoietic malignancies. Their ophthalmologic manifestations are rare. In approximately 50% of cases, orbital fat infiltration may occur, potentially leading to compressive optic neuropathy. Direct involvement of the optic nerves and their sheaths by lymphoma cells remains exceptional.

**Case Report:** We present the case of a 53-year-old woman followed and treated for NHL. While she was considered in clinical remission after five cycles of chemotherapy, she developed a sudden unilateral decrease in left visual acuity, reduced to 'counting fingers'. Clinical examination revealed a left relative afferent pupillary defect. Brain MRI demonstrated infiltration of the left optic nerve without additional intraorbital abnormalities. Cerebrospinal fluid (CSF) analysis revealed lymphomatous meningitis, establishing the diagnosis of retrobulbar optic neuropathy (RBN) due to lymphomatous infiltration. Despite an initial improvement under treatment, with visual acuity recovering to 8/10 and clearance of neoplastic cells from CSF, the patient died of bone marrow aplasia eight weeks later.

**Conclusion:** In the presence of painful and rapidly progressive visual loss, the diagnosis of lymphomatous RBN should be considered and confirmed by MRI and cytopathological analysis of CSF. RBN may occur at any stage of NHL and represents a poor prognostic indicator.

**Keywords:** Optic Neuropathy; Lymphoma; Non-Hodgkin Lymphoma; Isolated Optic Nerve Involvement

## Introduction

Non-Hodgkin lymphomas (NHL) are malignant proliferations of B or T lymphocytes, primarily affecting lymphoid tissues such as lymph nodes, liver, spleen, and bone marrow. Definitive diagnosis is based on histological examination of a lymph node or an infiltrated organ biopsy [1]. Ocular involvement is rare in NHL and typically manifests as intraorbital masses, conjunctival-lacrimal infiltration, or posterior uveitis [2]. Optic neuropathies are even rarer complications, usually resulting from either compressive mass effect or direct infiltration of optic nerve fibers by lymphoma cells. We report here a case of unilateral optic nerve infiltration in a patient with systemic NHL.

## Case Report

A 53-year-old woman was followed in hematology for stage IV B-cell NHL. The diagnosis was suggested by the rapid onset of generalized edema and severe deterioration of general health. Imaging revealed nodal, hepatic, splenic, osseous, and sinonasal lymphomatous involvement.

At diagnosis, the patient presented with qualitative cellular immunodeficiency and abnormal proliferation of CD20+ B lymphocytes at the expense of T lymphocytes. Regarding humoral immunity, serum gammaglobulins were elevated at 17.0 g/L (normal: 8–13.5 g/L). Serologies for HIV-1, HIV-2, HTLV-1, and HTLV-2 were negative.

Treatment consisted of chemotherapy according to the CHOP protocol (cyclophosphamide, vincristine, doxorubicin, prednisolone). After four monthly cycles, clinical, biological, and radiological responses were favorable: improved general condition, reduction of nodal disease, and disappearance of hepatic and splenic involvement.

Before the fourth cycle, the patient presented with progressive visual loss in the left eye, evolving over one week. She described retrobulbar pain exacerbated by eye movements. Visual acuity in the left eye was reduced to 'counting fingers' at 30 cm, while the right eye remained 10/10. Examination revealed a left afferent pupillary defect. The anterior segments were quiet bilaterally, vitreous was clear, and optic discs appeared normal. Visual field testing showed a central scotoma in the left eye and a normal right eye. Color vision (15-Hue desaturated test) was diffusely impaired in the left eye but normal in the right. Optical coherence tomography (RNFL) was normal bilaterally.

Unenhanced CT scan of the brain and orbits was unremarkable. However, contrast-enhanced brain MRI revealed left optic nerve infiltration and thickening, with T1 hypointensity, T2/FLAIR hyperintensity, moderate diffusion restriction, and linear gadolinium enhancement of the optic nerve sheath. Associated intra-conal fat infiltration and ipsilateral palpebral soft tissue thickening were also seen (Figure 1). These findings supported the diagnosis of left retrobulbar optic neuropathy.

CSF analysis confirmed lymphomatous meningitis, with hypoproteinorachia (0.19 g/L, normal: 0.35–0.45 g/L), hypoglycorrhachia (0.28 g/L), and 1240 cells/$mm^3$, of which 1190 were CD20+ lymphomatous cells (96%; normal < 5 leukocytes/$mm^3$).

The patient was treated with intravenous methylprednisolone (1 g/day for 3 days), systemic chemotherapy (cytarabine, rituximab, cisplatin), and intrathecal therapy (methotrexate, cytarabine, prednisolone). After ten days, visual acuity improved to 8/10 in the left eye and CSF was free of neoplastic cells. Unfortunately, the patient died eight weeks later due to bone marrow aplasia.

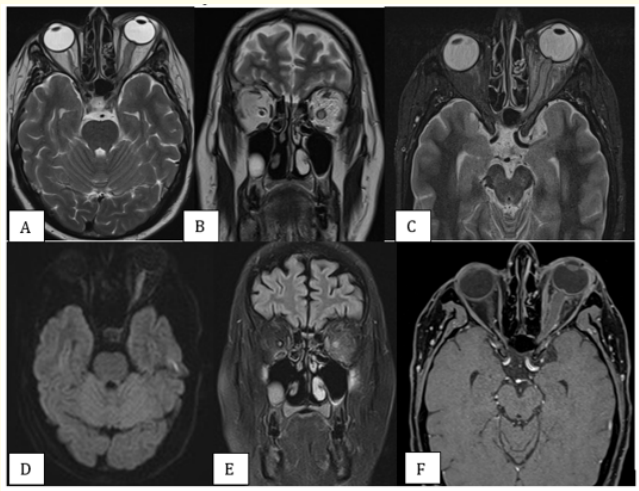


**Figure 1:** A, B: Axial and coronal slices from the T2 sequence. C: Axial slices from the T2 FS sequence. D: DWI sequence. E: Flair sequence. F: T1 FS with injection. These sequences revealed left optic nerve infiltration and thickening, with T2/FLAIR hyperintensity, moderate diffusion restriction, and linear gadolinium enhancement of the optic nerve sheath. Associated intra-conal fat infiltration and ipsilateral palpebral soft tissue thickening were also seen.

## Discussion

Optic nerve infiltration or compression is a rare cause of neuropathy. It may occur in isolated orbital tumors (glioma, meningioma, inflammatory pseudotumor), or as a complication of systemic diseases such as hyperthyroidism or hematologic malignancies. Acute leukemias may involve the optic nerve and disc through direct infiltration [3].

In systemic NHL, intraocular involvement (uvea: 6%) is less frequent than conjunctival (35%), eyelid (9%), or orbital (50%) localizations [2]. Orbital complications are usually compressive rather than infiltrative. Retrobulbar optic neuropathy due to infiltration is poorly documented and appears to be extremely rare. Only three cases have been reported in patients considered in remission [4–6], generally with predominant meningeal signs. Exceptionally, optic neuropathy may be the first manifestation of systemic lymphoma, as described by Henchoz., *et al*. [7].

Our case is unusual in that RBN developed unilaterally and in isolation, without initial meningeal signs. As in 30% of neoplastic meningitis cases associated with lymphoma or leukemia, meningeal involvement appeared during remission [8]. Neoplastic meningitis complicates about one-quarter of high-grade lymphomas, often associated with intracerebral disease (82% of cases), and carries a grim prognosis, with a median survival of four weeks [9].

Ocular involvement in malignant lymphomas is often linked to central nervous system (CNS) disease. Whitcup., *et al*. reported that 15–25% of patients with cerebral lymphoma develop ocular or optic nerve involvement within 6–18 months after diagnosis [10]. Similarly, Cassoux., *et al*. noted that 82% of patients with ocular or orbital lymphoma also had CNS involvement [9].

Optic nerve infiltration during lymphomatous meningitis may occur through direct contiguous spread from meninges or hematogenous dissemination from choroid or brain parenchyma [9]. Diagnosis relies on MRI and CSF cytology [11]. Other causes, such as drug-induced [12] or paraneoplastic neuropathies [13], should be considered in bilateral, slowly progressive cases with poor corticosteroid response.

Treatment of lymphomatous RBN typically combines systemic and intrathecal polychemotherapy with high-dose corticosteroids [14]. In cases complicated by myelitis, craniospinal radiotherapy followed by stem cell transplantation may be considered [8]. Despite treatment, the prognosis remains poor, especially when meningeal involvement is present.

## Conclusion

This case highlights the diagnostic and therapeutic challenges of retrobulbar optic neuropathy due to lymphomatous infiltration in the context of NHL. Although rare, this manifestation can occur at any disease stage, including during apparent remission, and is often associated with poor prognosis. Early recognition through prompt MRI and CSF analysis is crucial for timely intervention. Despite advances in chemotherapy and immunotherapy, survival remains limited, underscoring the need for more effective strategies to manage CNS and ocular involvement in NHL. Increased awareness of these rare complications among oncologists, hematologists, and ophthalmologists is essential to improve patient outcomes.

## Conflict of Interest

The authors declare no conflicts of interest related to this article.

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