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# Bing-Neel syndrome as a rare neurological complication of Waldenström macroglobulinemia: A case report

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## ABSTRACT

Waldenström macroglobulinemia (WM) is a lymphoproliferative disorder characterized by lymphoplasmacytic infiltration and Immunoglobulin M (IgM) monoclonal gammopathy. Bing-Neel syndrome (BNS), a rare complication of WM, arises from direct infiltration of malignant lymphoplasmacytic cells into the central nervous system (CNS). This report presents a 66-year-old female patient who developed BNS 15 years after the initial diagnosis of WM. The patient presented with neurological symptoms including dizziness, imbalance, memory impairment, and speech disturbances. Brain magnetic resonance imaging (MRI) revealed leptomeningeal and dural enhancement accompanied by vasogenic edema. Laboratory findings showed IgM lambda monoclonal gammopathy and lymphoplasmacytic infiltration. Although histopathological confirmation could not be obtained, the clinical and radiological findings supported the diagnosis of BNS. Following treatment with a combination chemotherapy regimen of rituximab and bendamustine (R-BENDA), along with high-dose methotrexate, clinical and radiological regression was observed. This case highlights that BNS may develop years after the initial diagnosis of WM and should be considered in the differential diagnosis.

**Keywords:** Bing-Neel syndrome, Waldenström macroglobulinemia, Central nervous system, Magnetic resonance imaging, Case report

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## INTRODUCTION

Waldenström macroglobulinemia (WM) is considered a lymphoplasmacytic lymphoma characterized by bone marrow involvement and Immunoglobulin M (IgM) monoclonal gammopathy [1]. WM most frequently presents with clinical features such as anemia and lymphoplasmacytic infiltration, primarily affecting the bone marrow, lymph nodes, and spleen, with occasional involvement of other organs.

In WM, neurological involvement typically manifests in two primary ways. Peripheral nerve infiltration (10–15%) usually presents as a distal, symmetrical, and slowly progressive sensorimotor neuropathy, whereas symptoms such as visual and hearing loss, vertigo, and ataxia may occur due to hyperviscosity syndrome (10–30%) [2]. However, infiltration of the central nervous system (CNS) by malignant cells is a rare condition and poses diagnostic challenges [3]. The condition was initially identified in 1936 by Jens Bing and Axel Valdemar Neel, who characterized it as a distinct neurological manifestation now known as "Bing-Neel syndrome (BNS)" [4].

Neuroradiological evaluations play a crucial role in the diagnosis of Bing-Neel syndrome. Magnetic resonance imaging (MRI) is a valuable diagnostic tool, particularly for detecting leptomeningeal involvement and parenchymal infiltrative lesions. In this report, we compare the clinical and radiological features of BNS in a patient previously diagnosed with WM to cases reported in the literature.

## CASE REPORT

A 66-year-old female patient presented with complaints of dizziness, imbalance, memory loss, and word-finding difficulties persisting for approximately three months. Additionally, she reported a single episode of a suspected seizure lasting about 15 minutes. Over the past month, she also experienced fatigue, loss of appetite, and recurrent fever episodes reaching up to 38.5°C. Her medical history revealed a diagnosis of WM, for which she had been under follow-up for 15 years.

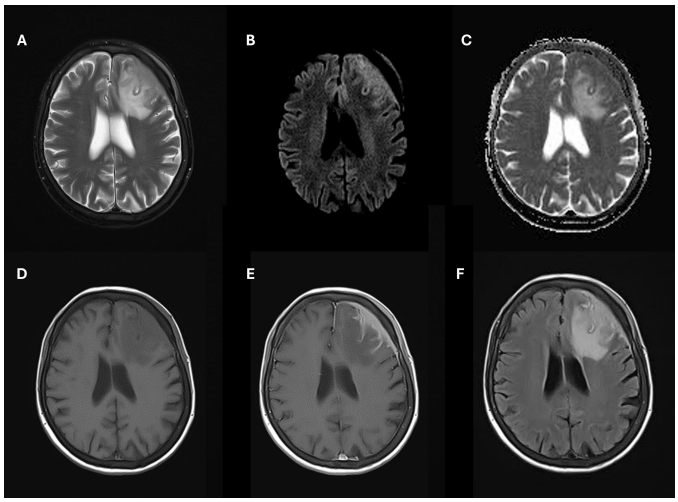


**Figure 1.** Magnetic resonance imaging findings at the time of diagnosis. On T2-weighted (A) and FLAIR (F) images, vasogenic edema adjacent to the lesion in the left frontal lobe is observed as a hyperintense signal. Diffusion-weighted imaging (B) and apparent diffusion coefficient map (C) demonstrate restricted diffusion within the lesion. The lesion appears hypointense on non-contrast T1-weighted image (D), while prominent contrast enhancement is seen on contrast-enhanced T1-weighted image (E).

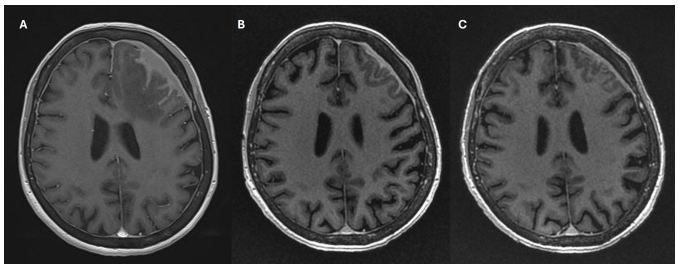


**Figure 2.** Contrast-enhanced thin-slice axial T1-weighted image at the time of BNS diagnosis is shown on the left (A). Follow-up images at 4 months (B) and 6 months (C) demonstrate marked regression of dural and leptomeningeal infiltration, with complete resolution of vasogenic edema.

The patient was in good general condition, cooperative, and oriented. Complete blood count: Mild anemia (Hb: 10.9 g/dL), lymphocytosis (LYM%: 51.8%), leukopenia (WBC: 3.4 K/μL), neutropenia (NEU: 1.08 K/μL). Elevated lactate dehydrogenase (LDH: 286 U/L) and hypergammaglobulinemia Serum immunofixation electrophoresis: IgM lambda monoclonal gammopathy. Bone marrow biopsy: Consistent with lymphoplasmacytic infiltration, confirming the diagnosis of WM.

Brain MRI revealed leptomeningeal enhancement with finger-like extensions into the left frontal parenchyma and prominent dural infiltration with contrast enhancement. On T2-weighted (T2W) images, signal hyperintensity consistent with vasogenic edema was observed in the adjacent left frontal lobe parenchyma, along with compression of the frontal horn of the left lateral ventricle. Diffusion-weighted imaging and apparent diffusion coefficient (ADC) maps demonstrated diffusion restriction in the areas of dural infiltration (Figure 1). Given the patient's known diagnosis of WM, the findings were considered consistent with Bing-Neel syndrome

The patient received alternating cycles of a combination chemotherapy regimen consisting of rituximab and bendamustine (R-BENDA), along with high-dose methotrexate (HD-MTX). In addition, dexamethasone therapy was initiated. We observed a marked improvement in the patient's neurological symptoms, alongside a noticeable recovery in cognitive function. Follow-up MRI at 4 and 6 months demonstrated partial regression of dural infiltration and complete resolution of the edema (Figure 2).

A signed informed consent form was obtained from the patient on June 18, 2024.

## DISCUSSION

While neurological complications can occur in patients with Waldenström macroglobulinemia (WM), central nervous system (CNS) infiltration by malignant cells, known as Bing-Neel syndrome (BNS), is exceptionally rare [2,3,5,6]. Due to its scarcity, the radiological features of BNS aren't yet fully defined.

Imaging findings in BNS are generally categorized into two subtypes: the diffuse infiltrative form and the tumoral form. The infiltrative type most commonly appears in the brainstem, periventricular white matter, and leptomeninges. In contrast, the tumoral form presents as single or multifocal mass lesions, typically in deep hemispheric regions [7].

Another study noted that leptomeningeal involvement was the most frequent imaging finding in BNS. Dural involvement was seen in over one-third of cases, and parenchymal infiltration was more often in the brain than the spinal cord. Approximately 40% of cases showed increased signal intensity on T2-weighted images, with diffusion restriction detected in about a quarter [3].

In our patient, we observed dural and leptomeningeal infiltration with contrast enhancement. The differential diagnosis included meningioma, dural and leptomeningeal metastatic tumors, primary dural lymphoma, and non-neoplastic dural lesions like tuberculosis. However, given the patient's known WM diagnosis and supportive laboratory findings, BNS was considered the most probable diagnosis. While histopathological confirmation wasn't obtained, the observed regression in clinical and radiological findings after treatment strongly supports this diagnosis, emphasizing the importance of imaging-based diagnosis in selected cases.

Recent literature highlights the diagnostic value of MRI in BNS, especially using contrast-enhanced T1-weighted and FLAIR sequences to detect leptomeningeal and parenchymal involvement. Schep et al. recommend systematic brain and spine imaging, particularly when a biopsy isn't feasible [8]. Our imaging findings align with these recommendations, underscoring MRI's critical role in the early recognition of BNS.


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A 2015 study by Simon et al., which evaluated 44 reported cases, found that approximately one-third of patients presented with BNS as their initial clinical manifestation before a WM diagnosis. The study also revealed that BNS can develop at highly variable intervals, up to 25 years after the initial WM diagnosis [9]. Another study reported the mean interval from WM diagnosis to BNS onset was around 7 years [10]. In our case, BNS developed approximately 15 years after the WM diagnosis, consistent with existing literature.

## CONCLUSION

Bing-Neel syndrome is a rare but clinically significant complication of Waldenström macroglobulinemia. Careful evaluation of radiological findings, interpreted within the clinical context, is paramount for early diagnosis and effective treatment.

**Informed Consent:** Written informed consent was obtained from the patient for publication and accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared by the authors.

**Financial Disclosure:** None declared by the authors.

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