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Secondary CNS Involvement in Blastoid Mantle Cell Lymphoma: A Case Report

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ABSTRACT

Mantle cell lymphoma (MCL) is an uncommon B-cell non-Hodgkin lymphoma in which central nervous system (CNS) involvement is rare and associated with a poor prognosis. We report the case of a 71-year-old man with recently diagnosed stage IV blastoid mantle cell lymphoma who developed progressive drowsiness, confusion, and personality changes one month after diagnosis. Cerebrospinal fluid analysis was negative for malignant cells and infection. Brain magnetic resonance imaging demonstrated bilateral leptomeningeal abnormalities, including left temporal leptomeningeal thickening with post-contrast enhancement and right parasagittal parietal gyriform leptomeningeal thickening, without an associated intraparenchymal mass. In the context of known aggressive systemic lymphoma, these findings were highly suggestive of secondary leptomeningeal CNS involvement. The patient's clinical condition rapidly deteriorated despite reduced-intensity chemotherapy, and he died approximately one week after the diagnosis of CNS involvement. This case highlights the aggressive behavior of the blastoid variant of MCL and emphasizes the crucial role of contrast-enhanced MRI in detecting secondary leptomeningeal involvement, particularly when cerebrospinal fluid cytology is initially negative.

KEYWORDS

Mantle cell lymphoma, blastoid variant, central nervous system lymphoma, leptomeningeal involvement, leptomeningeal enhancement, magnetic resonance imaging, secondary CNS lymphoma

MAIN ARTICLE

INTRODUCTION

Mantle cell lymphoma (MCL) is an uncommon B-cell non-Hodgkin lymphoma, accounting for about 3–10% of cases. It often presents with advanced-stage disease involving multiple extranodal sites such as bone marrow, spleen, liver, or gastrointestinal tract (3). Central nervous system (CNS) involvement by MCL is relatively rare occurring in <5% of case (1). When MCL does involve the CNS, it most often presents as leptomeningeal disease rather than a focal parenchymal mass (2). Such secondary CNS lymphoma carries a very poor prognosis, with median survival of only 3–4 months despite therapy (3). Early recognition is therefore crucial. We report a case of an elderly patient with blastoid mantle cell lymphoma who developed secondary CNS involvement manifesting as diffuse leptomeningeal enhancement. This case underlines the imaging features of leptomeningeal lymphoma and highlights the diagnostic and therapeutic challenges of CNS involvement in MCL.

CASE PRESENTATION

A 71-year-old man was admitted to our hospital with a recent diagnosis of blastoid variant mantle cell lymphoma, made on liver biopsy after hepatosplenomegaly was detected on CT imaging (Ann Arbor stage IV). One month after the initial diagnosis, and prior to initiation of multi-agent chemotherapy, the patient developed new neurological symptoms. He became progressively drowsy with episodes of confusion, and his family noted personality changes. No seizures or focal limb deficits were observed. In addition, laboratory evaluation revealed evidence of central hypothyroidism suggesting pituitary axis dysfunction. There was no history of head trauma or corticosteroid use to explain the pituitary abnormality.

On examination, the patient was somnolent with no signs of meningeal irritation. Given the altered mental status in a patient with known lymphoma, an infectious or leptomeningeal process was suspected. Laboratory tests showed pancytopenia: hemoglobin 8.0 g/dL, white blood cell count 3,900/µL (with neutrophils 2,900/µL), and platelets 32,000/µL. Serum electrolytes and glucose were within normal range. Liver function tests were mildly elevated consistent with his hepatic lymphoma involvement. C-reactive protein was not elevated, and urinalysis and urine culture showed no infection. Lumbar puncture showed acellular fluid, normal protein and glucose levels, and no malignant cells or organisms identified.

Brain MRI demonstrated abnormal leptomeningeal signal changes. On the left side, the temporal region showed leptomeningeal hyperintensity on T2-weighted and FLAIR sequences associated with contrast enhancement after gadolinium administration (Figure 1).

On the right side, a gyriform parasagittal parietal leptomeningeal thickening was observed, appearing hyperintense on T2-weighted and FLAIR images (Figure 2), without clear focal nodular enhancement. No intra-parenchymal mass lesion was identified. These imaging findings were suggestive of secondary leptomeningeal involvement in the context of known mantle cell lymphoma.

In addition, there was evidence of an empty sella in the pituitary region. The pituitary gland was flattened against the sellar floor and largely replaced by cerebrospinal fluid signal, consistent with an arachnoidocele. No pituitary tumor was visible. The infundibulum (pituitary stalk) was thinned but appeared midline. These findings suggest that the pituitary dysfunction (central hypothyroidism) in this patient was likely secondary to compression by the arachnoidocele. No hydrocephalus was present on the MRI. The ventricular size was normal, indicating that CSF pathways were not obstructed. Overall, the imaging supported the diagnosis of secondary CNS lymphoma with leptomeningeal involvement.

After the diagnosis of secondary CNS lymphoma was presumed based on the MRI, the patient was started on chemotherapy. Given his deteriorating condition, the planned intensive regimen was not initiated, instead, he received a single cycle of a reduced-intensity regimen that included vincristine. Unfortunately, the patient's neurologic status rapidly worsened over the next few days and he developed septic shock while in the intensive care unit, despite broad-spectrum antibiotics and supportive care, his condition declined. The patient passed away approximately one week after the MRI confirmed CNS involvement, reflecting the aggressive nature of blastoid MCL and the grave prognosis once the CNS is involved.

DISCUSSION

Mantle cell lymphoma is typically a systemic lymphoma with frequent extranodal involvement, but CNS involvement is an uncommon and ominous manifestation. Our patient's clinical course illustrates how secondary CNS lymphoma can present with nonspecific neurologic decline. In general, secondary CNS involvement by systemic lymphoma occurs in about 10–15% of non-Hodgkin lymphoma patients, and is most often seen in more aggressive subtypes such as diffuse large B-cell, Burkitt, lymphoblastic lymphoma, and mantle cell lymphoma (4). Within MCL, the incidence of CNS involvement has been reported in the range of ~5% of cases overall (1). The CNS involvement in MCL usually occurs at relapse or later in the disease course (over 80% of cases are in relapsed disease (3). Uniquely, in this case the CNS infiltration became apparent only about one month after the initial diagnosis, suggesting an extremely aggressive course.

Leptomeningeal disease is the predominant pattern of CNS involvement in MCL, as opposed to large parenchymal brain masses. Approximately two-thirds of secondary CNS lymphomas present with diffuse or multifocal leptomeningeal spread (4). Clinical signs can be quite variable and often include cranial neuropathies, headaches, altered mental status, or spinal nerve root symptoms, reflecting the diffuse involvement of the neuraxis (5). In our patient, the main manifestations were altered consciousness.

Diagnosis of leptomeningeal lymphoma can be challenging. The gold standard for diagnosis is the detection of malignant lymphocytes in the CSF through cytology or flow cytometry. However, a study about cytological detection of the cerebrospinal fluid in primary CNS lymphoma showed that the CSF analysis can have false-negative rates, due to the spread range, CSF volume, and other factors (6). In our patient, the initial lumbar puncture was negative despite clear MRI evidence of meningeal disease. This is not an uncommon scenario – multiple CSF samples or even meningeal biopsy may be required to confirm the diagnosis, but often the clinical and radiologic picture guides treatment decisions. Neuroimaging is thus critical for the early identification of leptomeningeal metastases and MRI with gadolinium is the preferred modality, as it can reveal the characteristic meningeal enhancement, cranial nerve enhancement, or other features of CNS lymphoma. It is recommended to image the entire neuraxis (brain and spinal cord) if leptomeningeal spread is suspected, since lymphoma can seed any part of the CNS pathways (4). In our case, brain MRI was sufficient to demonstrate widespread involvement; spinal imaging was not performed due to the patient's rapid decline, but spinal leptomeningeal metastases might have been present as well.

The prognosis for MCL once it involves the CNS remains extremely poor. Historically, reported median survival is only around 3–4 months after CNS involvement is diagnosed (3). In secondary CNS lymphoma (including MCL), the mainstay of treatment is high-dose antimetabolite chemotherapy such as high-dose methotrexate (HD-MTX) which can penetrate the CNS, sometimes combined with intrathecal chemotherapy and/or cranial irradiation (3,5). Unfortunately, our patient was not a candidate for HD-MTX given his poor performance status and organ function; he only received vincristine (which by itself has minimal CNS penetration), and his disease rapidly progressed. Novel therapies are being explored to improve outcomes in MCL with CNS involvement.

From a radiologic perspective, this case highlights the importance of recognizing subtle MRI findings that could indicate CNS spread of lymphoma in a patient with known systemic disease. The bilateral leptomeningeal enhancement pattern in our patient, though lacking a

molecular confirmation, was virtually diagnostic of leptomeningeal lymphomatosis when taken in context.

CONCLUSION

Secondary CNS involvement by mantle cell lymphoma is an uncommon but devastating complication, particularly associated with the blastoid variant of MCL. This case demonstrates how leptomeningeal lymphoma can present with diffuse meningeal enhancement on MRI. The diagnosis often relies on clinical suspicion and imaging findings, as CSF analyses can be negative early on. Unfortunately, the development of CNS involvement in MCL portends a very poor outcome, as illustrated by our patient's rapid decline. Aggressive CNS-directed chemotherapy (e.g. high-dose methotrexate-based regimens) is the cornerstone of treatment but many patients are unable to tolerate or do not respond adequately to these therapies. In summary, for any MCL patient presenting with neurological symptoms, clinicians and radiologists should consider secondary CNS lymphoma in the differential diagnosis. Early MRI evaluation of the brain and spinal cord is warranted, as early detection of CNS involvement could guide timely intervention. Collaboration between oncologists, neurologists, and radiologists is essential to manage this complication, although effective treatment remains a major challenge.

FIGURES

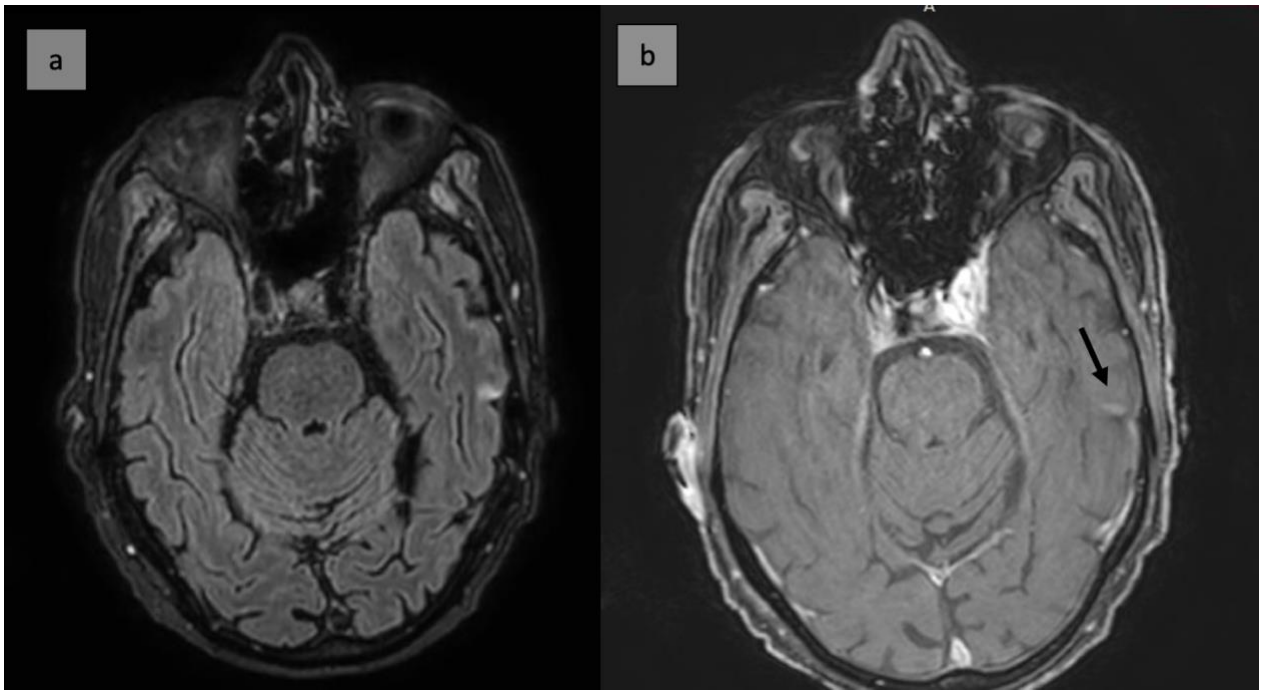

Figure 1. *Axial FLAIR image (a) demonstrating left temporal leptomeningeal thickening, with corresponding enhancement on the axial post-gadolinium T1-weighted image (b) (black arrow)*

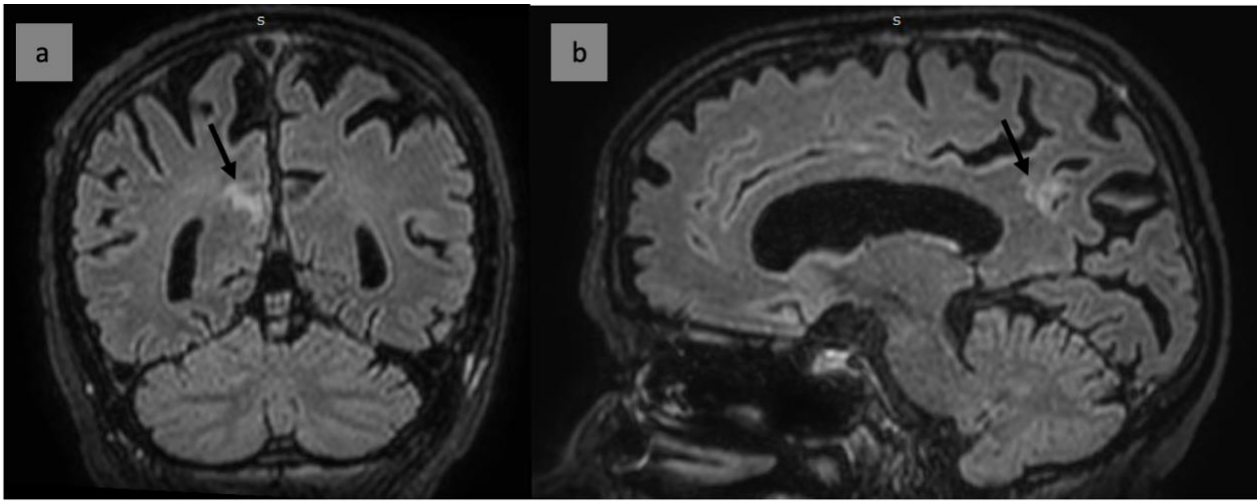

Figure 2. *Coronal (a) and sagittal (b) FLAIR images demonstrating gyriform leptomeningeal thickening in the right parasagittal parietal region, appearing hyperintense on FLAIR. (Black arrow)*

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