B lymphoblastic leukemia/lymphoma presenting as seventh cranial nerve palsy

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B lymphoblastic leukemia/lymphoma (B-LBL) typically presents with symptoms related to anemia, thrombocytopenia, and neutropenia. CNS involvement is not uncommon during the disease course; however, it is rare as the initial presentation, making B-LBL with cranial nerve (CN) palsy a diagnostic challenge. Our objective is to show that B-LBL can present initially as CN palsy, and to share our approach to this challenge.

Case report

A 27-year-old Hispanic woman with an unremarkable medical history was evaluated at the MD Anderson Cancer Center (MDACC) for a 7-week history of gradual onset and progression of right face tingling along with right lower lip/gingival numbness, right facial droop, and weak right eye closure. She was initially diagnosed with Bell palsy and treated with oral acyclovir and prednisone for 1 week. She underwent right wisdom tooth extraction without clinical improvement. Initial leukocyte count was 18 K/ μ L. Five weeks later, she was referred to the MDACC for further evaluation and found to have peripheral blood leukocytosis (33.5 K/ μ L) with 72% blasts on differential leukocytic count. Neurologic examination revealed right peripheral facial palsy with hyperacusis and complete loss of sensation in ipsilateral V3 distribution (figure, A).

Evaluation of a bone marrow (BM) biopsy and clot sections revealed extensive involvement by neoplastic cells (figure, B). The BM aspirate smears showed 90% blasts (figure, C). Flow cytometric immunophenotypic studies of a sample from the BM aspirate demonstrated a distinct lymphoid blast population expressing CD10, CD15 (partial), CD19, CD22, CD38, CD45 (dim), CD49d, CD52 (dim), CD79a (cytoplasmic), CD81, CD123 (partial), CD184, immunoglobulin M (cytoplasmic), HLA-DR, and TdT (dim). Blasts were negative for CD34, kappa, lambda, and all other lymphoid and myeloid markers examined. A diagnosis of B-LBL was established based on these findings.

CSF cytology (CC) was negative for neoplastic cells. The patient underwent an MRI of the brain/skull base with/without contrast; the findings suggested leptomeningeal disease (LMD) involving the right VII-VIII CN complex (figure, D), suspecting lymphoma in the right mandible angle, involving the right inferior alveolar nerve (figure, E). Also, there was a nodular, extra-axial

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Figure Clinical, histopathologic, and radiologic findings in a patient with B-LBL and multiple cranial neuropathies

(A) Clinical findings were evident for multiple cranial nerve involvement. Right facial nerve palsy and loss of sensation in the right inferior alveolar nerve distribution (shadowed area). (B) Histologic sections from the bone marrow biopsy show complete replacement of the normal architecture by extensive infiltrate of neoplastic cells consistent with blasts. The blasts demonstrate scant cytoplasm and contain rounded nuclei with fine chromatin ($\times 400$; hematoxylin & eosin stain). (C) The bone marrow aspirate smear shows markedly increased blasts that demonstrate intermediate size, round or folded nuclei, high N:C ratio, fine chromatin, and occasional prominent nucleoli ($\times 1,000$; Wright-Giemsa stain). (D) MRI of the skull base with and without contrast shows enhancement of the distal right VII-VIII nerve complex in the right internal auditory canal suggesting leptomeningeal disease. (E) Bone lesion at the right angle of the mandible, affecting the inferior alveolar nerve on the right. (F) Nodular extra-axial enhancement in the right middle cranial fossa suspicious for nodular leptomeningeal disease. B-LBL = B lymphoblastic leukemia/lymphoma.

focus of enhancement in the right middle cranial fossa that may represent nodular LMD vs dural-based disease, and not consistent with parenchymal leukemia/lymphoma (figure, F).

We began treatment with a 4-day course of IV dexamethasone (40 mg daily), systemic chemotherapy with PEG-asparaginase, rituximab, cyclophosphamide, doxorubicin, and vincristine. She also received intrathecal methotrexate twice weekly (4 courses) and a single course of intrathecal free cytarabine. The Radiation Oncology service recommended radiation therapy with a total dose of 20 Gy in 10 treatments to the skull base area.

Two weeks after discharge, repeated BM biopsy indicated complete remission but neurologic examination showed only slight improvement of right facial palsy and unchanged sensory symptoms.

DISCUSSION

B-LBL is more commonly seen in children and young adults. There are approximately 100 immunophenotyped cases reported in the literature, mostly as single case reports or small series.¹

Patients with B-LBL typically first present with symptoms related to anemia, thrombocytopenia, and neutropenia including fatigue, easy bruising/bleeding, and infections. B symptoms are often present. Hepatosplenomegaly and lymphadenopathy can be seen in up to half of adult patients. CNS involvement is not uncommon during the disease course, but is rare as initial presentation.

Patients with B-LBL usually present with massive involvement of BM (>25% blasts) and peripheral blood. Less commonly, it presents with involvement of lymph nodes (LN) or extranodal sites. The most frequent sites of B-LBL lesions are the skin, bone, soft tissue, and LN.² A study of 53 children with B-LBL enrolled in 3 prospective trials reported the following areas as the main location of disease at the time of diagnosis: bone (26%), skin (23%), mediastinum/pleura (11%), BM (13%), LN alone (13%), gonads (6%), head/neck (4%), or kidney/digestive system (2% each). Upon further evaluation, 43% had BM involvement and 6% had CNS involvement at diagnosis.²

We report a case of B-LBL presenting initially as V and VII CN palsy. This case illustrates an atypical B-LBL presentation and the potential risk for severe CN damage due to late diagnosis, as well as poor clinical response of neurologic deficits after indicated treatment including high-dose steroids and systemic/intrathecal chemotherapy, even after complete remission was achieved. In our case, CC was negative, and CSF flow cytometry (FCM) was not performed. Recent studies have demonstrated that FCM assessment could increase the proportion of positive cases detected with CNS dissemination compared with CC.³

The diagnosis of LMD was suspected by the presence of related signs/symptoms and confirmed by neuroimaging. In the setting of high clinical suspicion of cancer and supportive imaging, diagnosis of LMD could be made without requiring CSF cytologic confirmation.⁴ Recognition of B-LBL with LMD as initial presentation is critical to early institution of appropriate therapy and prevention of severe residual CN deficit.

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