Clinical Case Report

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Neurolymphomatosis in non-Hodgkin lymphoma with cranial multineuritis

A case report

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Abstract

Rationale: Neurolymphomatosis (NL) is a rare syndrome of lymphoma and leukemic infiltration of cranial or peripheral nerves.

Patient concerns: We report a case of non-Hodgkin Lymphoma (NHL) in a 24-year-old man presented with difficulty in swallowing, hypersalivation, hoarseness, ptosis, facial paralysis, and facial hypoesthesia associated with NL.

Diagnosis: NL was diagnosed based upon cranial magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) examination.

Interventions: The patient was treated with intrathecal methotreaxate (12.5 mg) and cytosine arabinoside (70 mg), systemic high-dose methotrexate therapy, and cranial radiotherapy.

Outcome: Due to the deterioration of general condition of the patient, he was admitted to intensive care unit, but died 22 days after the onset of symptoms in spite of aggressive treatment.

Lessons: In this case, we present a patient with T cell lymphoma and multineuritis of NL diagnosed by MRI and as far as we know, this is the first reported case in which so many cranial nerves (3, 5, 7, 8, 9, and 10 th) were involved. Briefly, in a patient with hematologic malignancy and neurological complaints, NL should be considered. Early and effective use of imaging modalities such as positron emission tomography (PET-CT), MRI, and aggressive therapies are important for prolonged survival.

Abbreviations: CHOP = cyclophosphamide, doxorubicin, vincristine, prednisolone, CNS = cranial nervous system, CSF = cerebrospinal fluid, EPOCH = etoposide, adriamycin, vincristine, cyclophosphamide, prednisolone, IDARAM = cytosine arabinoside, dexamethasone, idarubicin, methotrexate, cytosine arabinoside and methotrexate, intrathecally, MRI = magnetic resonance imaging, NHL = non-Hodgkin lymphoma, NL = neurolymphomatosis, PET-CT = positron emission tomography, PTCLs = peripheral T-cell lymphomas, US = ultrasonography.

Keywords: cranial nerve, magnetic resonance imaging, neurolymphomatosis, non-Hodgkin lymphoma

1. Introduction

Neurolymphomatosis (NL) is a rare syndrome of lymphoma and leukemic infiltration of cranial or peripheral nerves. It is generally a manifestation of an unknown or known B cell nonHodgkin's lymphoma (NHL), and rarely T-cell Lymphoma. It is a rare clinical entity and the incidence is 0.2% of all NHL patients. NL can occur as the initial manifestation of NHL, but is more often seen with relapse or the progression of a previously diagnosed lymphoma or leukemia.[1] Symptoms are various and patients with NL typically present with multiple neuropathies that may affect peripheral or cranial nerves as described in this case. Cranial neuropathy is an unusual manifestation of NL which is sometimes difficult to diagnose and patients present with different types of symptoms depending on the sites involved.[2] Several studies have reported primary or secondary NL with single or multiple cranial nerve involvement. In this case, we present a T-cell Lymphoma patient with multineuritis of NL diagnosed by magnetic resonance imaging (MRI) and as far as we know, this is the first reported case where so many cranial nerves (3, 5, 7, 8, 9, and 10th) were involved.

2. Case report

The study was approved by our institutional review board, and informed consent was obtained from the patient. A male 24-year-old Turkish student presented to the hematology clinic with swelling in the neck, shortness of breath, and weakness. He had cervical, axillary, and mediastinal lymph nodes in radiological imaging which raised the suspicion of a malignancy. Cervical lymph node biopsy was performed and pathology revealed peripheral T-cell lymphoma with CD3 ve CD5 positivity and 90% Ki-67 proliferation index. Positron emission tomography (PET-CT) was performed to stage the disease which showed thoracic vertebrae involvement. Patient was diagnosed with stage 4 NHL and etoposide, adriamycin, vincristine, cyclophosphamide, prednisolone (EPOCH) (Etoposide 50 mg/m^2 iv, Adriamycin 10 mg/m^2 iv, Vincristine 0.4 mg/m^2 iv, Cyclophosphamide 750 mg/m^2 iv, prednisolone 2 × 50 mg/m^2 p.o.) chemotherapy protocol was initiated. There was not any comorbid factor,

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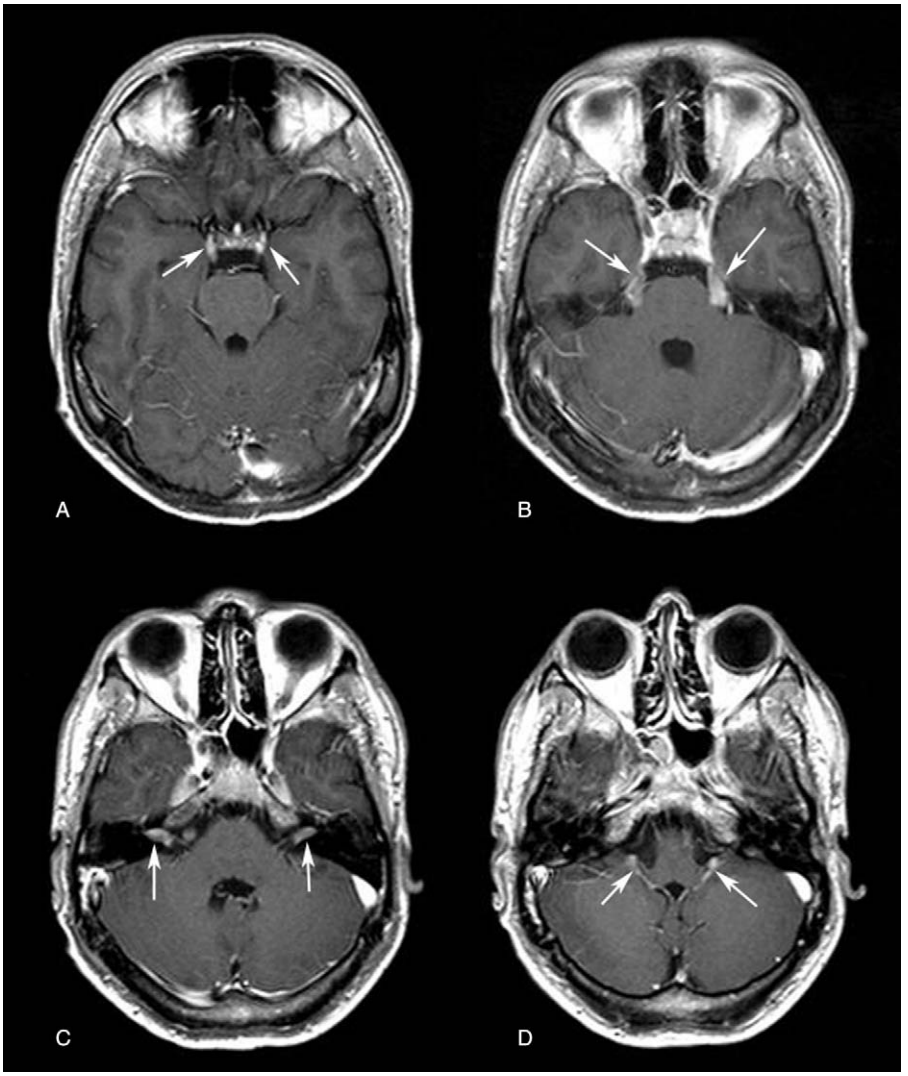

Figure 1. Contrast-enhanced T1-weighted images in the axial plane demonstrate thickening and marked enhancement of the 3th (A), 5th (B), 7 and 8th (C), and 9 and 10th (D) cranial nerves (arrows), consistent with neurolymphomatosis.

family history, or relevant past intervention that could lead to patient's illness. At the end of the second cycle, lymphadenopathy shrank, but patient presented with difficulty in swallowing, hypersalivation, hoarseness, ptosis, facial paralysis, and facial hypoesthesia. Hence, he was admitted to the clinic 10 days later. Serological tests were requested; Influenza virus type B, Coxsackie virus type A7, and Echo virus type 7 were positive. Neck and axillary ultrasonography (US) was performed to evaluate chemotherapy response which revealed a negative result and there was not any mass in thoracal MRI. Our primary diagnosis was viral encephalitis due to the positive chemotherapy response and we started 500 mg iv acyclovir treatment. We requested consultation from otolaryngology department due to hoarseness. Restriction of movement in both vocal cord abduction and hypersalivation around the esophagus were detected. We performed a cranial MRI to exclude cranial involvement with lymphoma which revealed bilateral 3, 5, 7, 8, 9, and 10th nerve thickening and enhancement (Fig. 1). A spinal tap was performed which showed a large number of histiocytes and infrequent small lymphocytes in cerebrospinal fluid (CSF) cytology. As symptoms were not relieved despite the antiviral treatment, findings were evaluated as cranial infiltration with lymphoma. However, cranial nerve biopsy was not performed because of the risks of the procedure. The new therapeutic approach, IDARAM protocol, was applicated. IDARAM protocol consists of; Cytosine arabinoside 1.0 gr/m^2 iv, 1-hour infusion, days 2 and 3; dexamethasone 100 mg, 12-hours infusion, days 2, 3, and 4; idarubicin 10 mg/m^2 iv,15-minute infusion, days 2 and 3; methotrexate 3 gr/m^2, 6-hour infusion, day 4; and cytosine arabinoside 70 mg plus methotrexate 12 mg, intrathecally, days 2 and 8 were initiated with cranial radiotherapy. The patient tolerated the chemotherapy well, but the patient was admitted to intensive care unit due to general condition impairment and died 22 days after the onset of symptoms.

3. Discussion

Peripheral T-cell lymphomas (PTCLs) are rare, heterogeneous diseases that comprise 10% to 15% of all adult NHL cases.[3] Disease progression during chemotherapy occurs in 30% to 40% of the patients and durable remissions after CHOP

(cyclophosphamide, doxorubicin, vincristine, prednisolone) treatment are uncommon. The clinical course is aggressive and can involve unusual sites.[4]

NL typically presents with any of the 4 clinical scenarios:[1] painful or painless peripheral mononeuropathy or mononeuritis multiplex,[2] painful peripheral polyneuropathy or polyradiculopathy,[3] painless polyneuropathy, and[4] painful or painless cranial neuropathy. NL is further classified as primary and secondary. Primary NL occurs as the first manifestation of a hematologic malignancy; if nerves are a site of relapse or progression of a previously diagnosed lymphoma or leukemia, it is called as secondary NL.[5]

Diagnosis is often difficult and delayed because of variability of presenting symptoms and wide differential diagnosis including viral, inflammatory or paraneoplastic neuropathy, cranial neuritis multiplex, leptomeningeal lymphomatosis, and nerve root compression.[6]

Cranial neuropathy is a rare presentation of NL which is sometimes hard to diagnose by using the conventional imaging modalities. The definitive diagnosis is made by histopathologic examination of the affected cranial nerve and demonstration of malignant lymphocyte infiltration. However, nerve biopsy may not always be possible owing to the possible complications and it is often nondiagnostic.[7] CSF examination may have a diagnostic value in only 20% to 40% of cases with meningeal involvement. This is why imaging methods play an important role in NL. Although MRI is the most commonly used imaging modality, it does not always provide enough information about lymphoma infiltration. PET-CT imaging is quite useful for early detection of NL involvement and spread; lesions show nodular or linear shaped F18 FDG uptake. The diagnostic values of imaging methods are 84% for MRI and 77% for PET-CT. However, infection and inflammation can lead to false positive results.[2,7,8]

Our patient was diagnosed with PTCLs which is a type of high grade NHL, and NL occurred after the second cycle chemotherapy. PTCLs is an aggressive lymphoma and cranial nervous system (CNS) involvement is a sign of poor prognosis.[9] When the cranial nerves are involved, as described in this case here, facial paralysis, ptosis, diplopia, facial hypoesthesia and disequilibrium may occur. In a similar case reported by Kim et al,[2] the patient with cranial nerve NL also had ptosis, bilateral facial hypoesthesia. In our patient, neurological involvement was seen at the end of the second cycle, therefore it was not possible to differentiate as primary or secondary NL.

It is hard to diagnose NL when it is the only manifestation because it is generally associated with B-cell lymphomas based upon biopsy or autopsy findings.[10] Due to the fact that the patient had T-cell lymphoma and a positive chemotherapy response, symptoms related to cranial nerve involvement were considered viral encephalitis which caused diagnostic delay.

Treatment of NL includes either chemotherapy alone or combined with radiotherapy. Only few cases have shown adequate response to chemotherapy.[11] Our patient was started on intratecal and systemic methotrexate chemotherapy combined with localized radiotherapy. On the 8th day of the treatment, the patient's clinic deteriorated and he died 22 days after the onset of symptoms.

Neurological symptoms of lymphoma may be associated with paraneoplastic syndromes, infections, or chemotherapy. This condition brings about delay in NL diagnosis and causes fatal and rapid progression in most cases.

In conclusion, in a patient with hematological malignancy and neurological complaints, NL should be considered. Early and effective use of imaging modalities such as MRI and PET-CT and aggressive therapies are important for prolonged survival.

Author contributions

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