Neurolymphomatosis in Primary Cutaneous CD4+ Pleomorphic Small/Medium-sized T-cell Lymphoma Mimicking Hansen’s Disease

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Abstract
Neurolymphomatosis (NL) refers to nerve infiltration by neurotropic neoplastic cells in the setting of a known or an unknown hematological malignancy. It typically presents as painful or painless peripheral mononeuropathy, mononeuritis multiplex, polyneuropathy, polyradiculopathy, or cranial neuropathy. A 32-year-old male presented with a hyperpigmented hypoesthetic plaque over the anterolateral aspect of the right leg with thickening of the right common peroneal nerve and foot drop clinically diagnosed as Hansen’s disease. Biopsy taken from skin showed infiltrates of pleomorphic small and medium sized lymphocytes in the dermis and subcutis. On immunohistochemistry, the cells were positive for CD3, CD4 and negative for CD8, CD20, and CD30. Ultrasonography-guided fine-needle aspiration of the thickened nerve showed infiltrates of atypical lymphoid cells. Based on these findings, a diagnosis of NL in primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma was made. The disease responded to systemic chemotherapy and localized radiotherapy with no evidence of relapse during 3 years follow-up. NL in primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma presenting with manifestations redolent of Hansen’s disease is not described in available literature. This case also demonstrates the utility of fine needle aspiration of nerve, a minimally invasive procedure in the diagnosis of NL.

Key Words: Fine needle aspiration, Hansen’s disease, neurolymphomatosis, primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma

Introduction
Cutaneous lymphomas encompasses a wide spectrum of diseases involving T, B, and natural killer lymphocytes, as well as their subsets, that infiltrate the skin and often progress to involve a variety of organ systems in the body. Neurolymphomatosis (NL) refers to nerve infiltration by neurotropic neoplastic cells, in the setting of a known or an unknown hematological malignancy. Here, we report a case of NL in a rare subtype of cutaneous T-cell lymphoma, primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma which closely mimicked Hansen’s disease.

Case Report
A 32-year-old male presented with a hyperpigmented lesion over the right leg noted since 3 years. Dermatological examination revealed a hyperpigmented ichthyotic plaque measuring 30 cm × 15 cm covering the anterolateral aspect of the right leg (Figure 1). Neurological examination revealed an impairment of temperature, touch and pain sensations over the lesion, and thickening of the common peroneal nerve on the right side. Right-sided foot drop was present. Based on these clinical features, a provisional diagnosis of Hansen’s disease was made and investigated further.

Routine biochemical parameters were within normal limits except for high serum lactate dehydrogenase. Slit skin smear for acid fast bacilli was negative. Skin biopsy showed a diffuse infiltrate of pleomorphic small...
and medium sized lymphocytes in the dermis extending up to the subcutis [Figure 2]. On immunohistochemistry, the cells were found to be positive for CD3 [Figure 3] and CD4 and negative for CD8, CD20, and CD30. The features were consistent with the diagnosis of primary cutaneous CD4 + pleomorphic small/medium-sized T-cell lymphoma.

We proceeded to investigate further to explore the prominent nerve thickening noted clinically in this patient. Nerve conduction study showed evidence of demyelination in the common peroneal nerve and electromyography showed normal motor potentials with no evidence of axonal degeneration. Magnetic resonance imaging of right lower leg revealed thickening of the common peroneal nerve. To avoid further nerve damage to the motor nerve, we opted for ultrasonography-guided fine needle aspiration cytology (FNAC) of the common peroneal nerve instead of biopsy, which revealed atypical lymphoid cells with irregular nuclei, coarse clumped chromatin and scanty cytoplasm [Figure 4]. Peripheral smear, cerebrospinal fluid analysis, bone marrow study and computed tomography scans of the abdomen, thorax and brain were normal. Serological tests to detect infection with human T-lymphotropic virus 1, human immunodeficiency virus and Borrelia burgdorferi were negative. Based on these results, a diagnosis of NL secondary to primary cutaneous CD4 + pleomorphic small/medium-sized T-cell lymphoma was made. The patient received six cycles of cyclophosphamide, doxorubicin, vincristine, prednisone regimen consisting of cyclophosphamide, hydroxydaunorubicin (adriamycin), oncovin (vincristine), and prednisolone and localized radiotherapy. On the follow-up, there was a significant decrease in the size of the cutaneous lesion, marked improvement in foot drop, markedly reduced infiltrate in skin biopsy. There was no evidence of relapse in 3 years follow-up period.

Discussion

Neurolymphomatosis has most commonly been reported in association with B-cell lymphomas and very rarely with T-cell lymphomas including mycosis fungoides and sezyzary syndrome.[2-4] It typically presents as any of the four clinical scenarios: (1) painful or painless peripheral mononeuropathy or mononeuritis multiplex, (2) painful peripheral polyniueopatby or polyradiculopathy, (3) painless polyneuropathy, and (4) painful or painless cranial neuropathy.[1] NL is further classified as primary and secondary. Primary NL is defined as NL that is the first manifestation of...
the hematologic malignancy, and secondary NL is when nerves are a site of relapse or progression of a previously diagnosed lymphoma or leukemia.[6]

Primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma as the name implies is a rare subtype of primary cutaneous T-cell lymphoma clinicopathologically different from classical mycosis fungoides.[6] It characteristically presents as solitary plaque as seen in our case generally affecting the face, neck, or upper trunk.[4] It rarely can present with multiple papules, nodules or tumors. Histopathology typically shows nodular or diffuse infiltrates of small/medium-sized pleomorphic neoplastic T cells within the dermis with a tendency to infiltrate subcutis. On immunophenotyping, these cells have shown to be CD3+, CD4+, CD8−, and CD30−. These lymphomas have a rather favorable prognosis with an estimated 5 years survival of 60%–80%. Cases with solitary or localized skin lesions show a marked response to radiotherapy and have an excellent prognosis.[7]

Our patient presented with a solitary localized plaque of 3 years duration associated with sensory impairment and peripheral nerve thickening. Localized plaque and hypoesthesia with thickened nerves in our patient clinically suggested Hansen’s disease. However, skin biopsy revealed diffuse infiltrate of pleomorphic small and medium sized lymphocytes in the dermis and subcutis diagnostic of cutaneous T-cell lymphoma. The absence of epidermotropism and lack of hematological disease ruled out the possibility of mycosis fungoides and Sézary syndrome, respectively. It is worth noting that the presence of pleomorphic CD3, CD4 positive and CD8, CD20, and CD30 negative cells in the dermis and subcutaneous fat suggest primary cutaneous CD4+ pleomorphic small/medium-sized T-cell lymphoma.

Diagnosis requires integration of clinical features with imaging studies and histopathology. Magnetic resonance imaging is the most sensitive and specific noninvasive diagnostic tool. Although the diagnostic gold standard of NL is nerve biopsy, the procedure is done only in less than half of patients.[2] In our case, we have opted for FNAC of common peroneal nerve to minimize damage, which revealed the presence of atypical lymphoid cells. However, clonality of skin and nerve T cells could not be studied.

NL is characterized by rapid and fatal progression in most cases. This is due to the limited information that is currently available, delay in establishing diagnosis and inability of chemotherapeutic agents to penetrate through blood-nerve barrier into peripheral nervous system.[6]

Treatment of NL includes either chemotherapy alone or combined with radiotherapy.[8] Only few cases have shown adequate response to chemotherapy. Our patient was started on systemic chemotherapy combined with localized radiotherapy to which the lesion responded well. There was markedly reduced infiltrate in repeat skin biopsy after treatment. The patient did not show any sign of relapse during the 3 years follow-up period.

Our case depicts the importance of considering NL as a differential in Hansen’s disease like presentation, the utility of FNAC, a minimally invasive procedure to establish early diagnosis and excellent treatment response to combination chemotherapy and radiotherapy in lymphoma affecting both skin and nerve.

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**Conflicts of interest**

There are no conflicts of interest.

**What is new?**

- Neurolymphomatosis can occur in cutaneous CD4+ pleomorphic small/medium sized T-cell lymphoma, a rare subtype of primary cutaneous T-cell lymphoma
- Clinical presentation of NL can mimic Hansen’s disease
- Fine needle aspiration of the involved nerve is a useful procedure to establish diagnosis early.

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