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CASE REPORT

Progressive neurolymphomatosis with cutaneous disease: Response in a patient with mycosis fungoides

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Abstract Peripheral neurolymphomatosis is a rare manifestation of advanced lymphoproliferative disorders. It is often associated with B cell lymphomas and rarely with cutaneous T cell lymphomas, such as mycosis fungoides and Sézary syndrome. In this case report, we present a 78-year-old male with a long-standing history of mycosis fungoides. The patient initially presented with chronic peripheral neuropathy in an ulnar nerve distribution. After an unsuccessful ulnar nerve transposition, the ulnar nerve was re-explored and a mass consistent with diffuse lymphomatous infiltration was diagnosed. Magnetic resonance (MR) imaging of the left brachial plexus and later of the sacral plexus demonstrated diffuse thickening and peripheral nodularity in keeping with neurolymphomatosis. The patient's clinical course rapidly deteriorated thereafter and the patient succumbed to his disease. Although uncommon, neurolymphomatosis may be considered in patients with chronic peripheral neuropathy and an underlying history of a lymphoproliferative disorder. US and MR may serve as helpful non-invasive adjuncts in making the diagnosis and identifying sites for biopsy.

Keywords Neurolymphomatosis · Cutaneous lymphoma · Sézary syndrome · Mycosis fungoides · T cell lymphoma

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Introduction

Neurolymphomatosis is characterized by lymphomatous infiltration of the cranial and/or peripheral nerves. This entity has been described commonly in B cell non-Hodgkin's lymphoma, however there has been only a few case reports describing this phenomena in cutaneous T cell lymphoma [1–3].

Mycosis fungoides is the most common form of cutaneous T cell lymphoma. Extracutaneous spread typically occurs in the later stages of the disease. The most frequently involved sites include regional lymph nodes, lungs, spleen, liver, and rarely the nervous system [4].

In this case report, we present a patient with a long-standing history of mycosis fungoides and symptoms of ulnar neuropathy. We present both the US and MR imaging features of this unusual entity.

Case report

The patient is a 76-year-old male with a 20-year history of mycosis fungoides. He was treated with multiple therapeutic modalities including PUVA, systemic methotrexate, topical nitrogen mustard, total body electron beam therapy, and Soriatane (acitretin) cream.

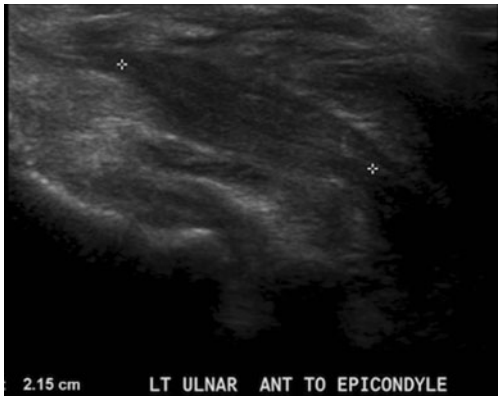

Fig. 1 Long-axis grey-scale ultrasound image of the left antecubital fossa demonstrating fusiform thickening of the transposed ulnar nerve

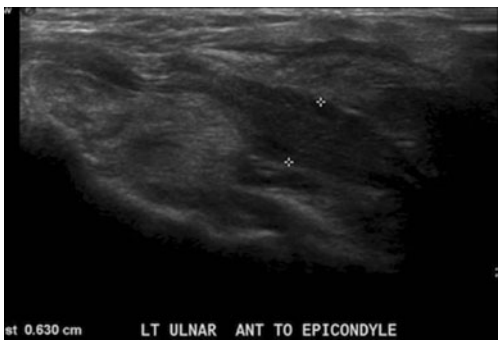

Fig. 2 Long-axis image of the ulnar nerve demonstrating thickening of the nerve (measuring AP dimension)

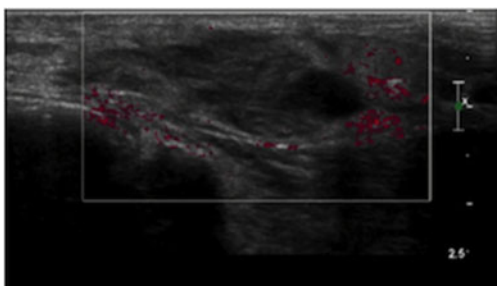

Fig. 3 Long-axis power Doppler ultrasound image of the left antecubital fossa demonstrating the thickened ulnar nerve without significant increased vascularity

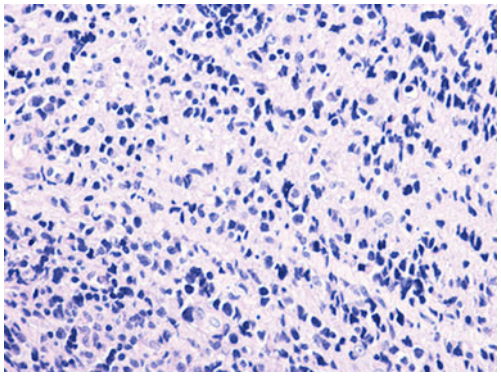

Fig. 4 H&E stain of the biopsied mass in the transposed ulnar nerve (40×) demonstrating diffuse increased cellularity

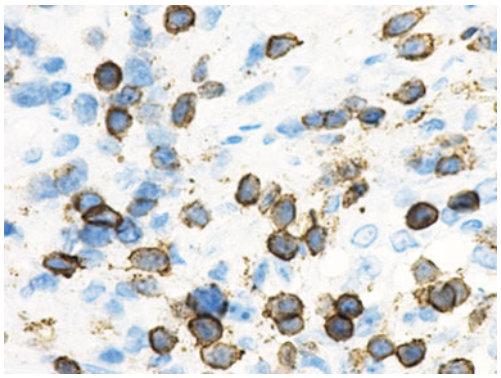

Fig. 5 CD3+ stain of the cells obtained from the biopsied mass (100×) in keeping with T cells

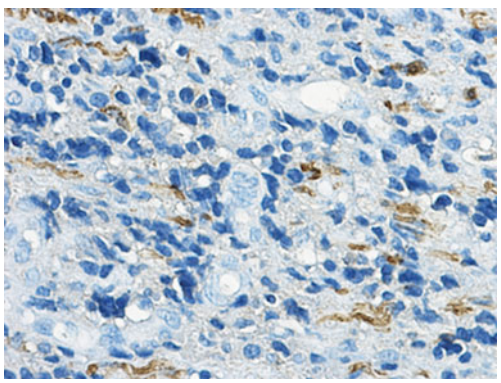

Fig. 6 S100 stain of the cells (60×) demonstrating the neural cells

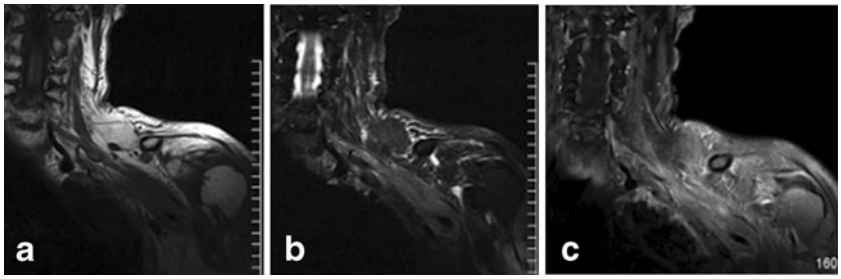

Fig. 7 **a** Coronal TSE T1W sequence (TR 684, TE 13), **b** STIR sequence (TR 3900, TE 64), and **c** TSE T1 FS W sequence post-contrast (TR 591, TE 13) of the left brachial plexus demonstrating diffuse nodular thickening, abnormal high T2 signal intensity, and enhancement of the left brachial plexus

At the time of presentation, the patient had multiple ulcerated plaques that progressed beyond 10 % of his total body surface area. The most prominent lesion was a 3×2 cm ulcerated plaque on the left buttock. There was no palpable adenopathy and a CT of the chest, abdomen, and pelvis was negative for metastatic disease.

Two years later, the patient started to complain of weakness and paraesthesias of his feet and hands. An EMG confirmed a left-sided ulnar neuropathy at the level of the cubital tunnel and bilateral mild carpal tunnel syndrome, implying neuropathy of the median nerves.

The patient also developed multiple new skin lesions over the upper extremities and the flexor surfaces of the lower extremities. Selective biopsies again demonstrated mycosis fungoides without Sézary cells, and subsequent imaging revealed splenomegaly.

The patient underwent a left ulnar nerve transposition and bilateral carpal tunnel releases. The patient had relief of his median neuropathy; however the ulnar neuropathy progressed with burning and tingling.

An ultrasound of the antecubital fossa demonstrated soft tissue thickening over the nerve, which was felt to be in keeping with an adventitial bursa secondary to nerve transposition. In addition, fusiform thickening of the transposed ulnar nerve (Figs. 1, 2 and 3) was documented. The ultrasound also revealed features of muscle atrophy and increased echogenicity, implying chronic denervation of several muscles around the elbow and within the forearm.

With no clinical relief for 12 months after the ultrasound examination, the surgeon decided to re-explore the ulnar nerve. A mass within the nerve was detected and biopsied. Pathologic assessment demonstrated soft white tissue fragments infiltrated with small lymphocytes that were CD3 positive and S100 positive, implying a T cell lymphoproliferative disorder (Figs. 4, 5, and 6).

The patient thereafter complained of ipsilateral triceps weakness for which an MRI of the brachial plexus was performed. The MRI demonstrated diffuse nodular thickening of the left brachial plexus, suggesting metastatic disease (Fig. 7). All MR images were obtained on a 1.5-T Siemens Magnetom Symphony scanner (Erlangen, Germany).

A few months later, the patient presented with left leg weakness for which an MRI of the sacral plexus was obtained. It demonstrated a similar appearance to the nerves

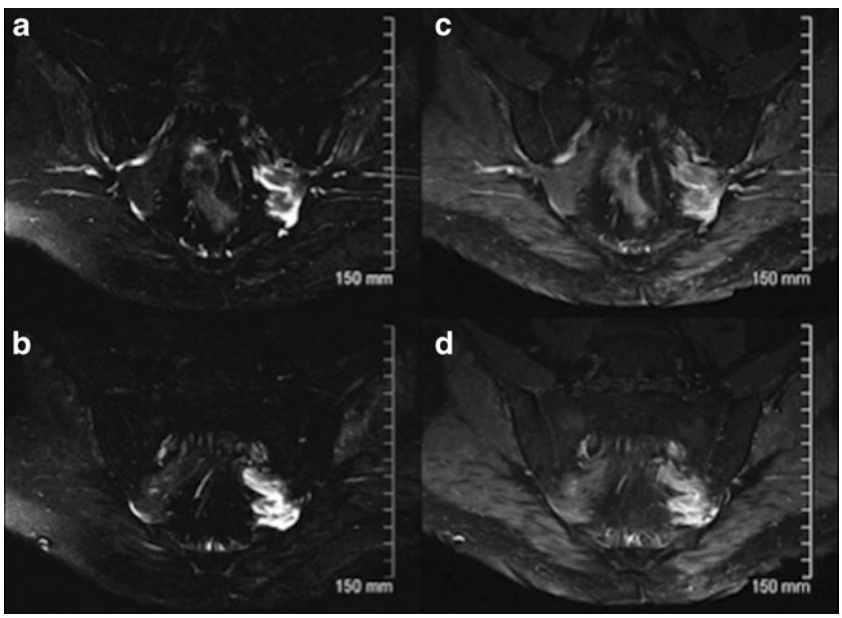

Fig. 8 Four coronal oblique images of the sacrum demonstrating abnormally high T2 signal intensity and nodular enhancement of the nerve roots of the left sacral plexus. **a**, **b** TSE T2 FS W sequences -T2 Neurogram (TR 2780, TE 102). **c**, **d** TSE T1 FS W sequences post-contrast (TR 715, TE 12)

along the left brachial plexus (Fig. 8). Radiotherapy was performed for symptomatic relief.

The patient was transferred to a palliative care facility and passed away shortly thereafter secondary to aspiration pneumonia.

Discussion

Mycosis fungoides is the most common form of cutaneous T cell lymphoma [1, 3–5]. The disease incidence is approximately 6.4 per million persons, with higher incidence in males over females and blacks over caucasians [6]. The disease is relatively indolent with less than 20 % of cases advancing beyond the cutaneous phase. If the disease progresses, it manifests as skin nodules and reactive regional lymphadenopathy. Further progression leads to actual tumoral metastasis to regional lymph nodes and eventually spread to the lungs, spleen, liver, and rarely to the central nervous system [4].

The overall rate of direct neurologic complications from cutaneous T cell lymphoma is 2–14 % [7–9] with leptomeningeal spread being the most common manifestation. Involvement of the peripheral and cranial nerves has been reported in only a handful of cases in the English literature. Among the most commonly sited cases are Bezier et al. [1] with the underlying pathology being Sézary syndrome, a leukemic form of mycosis fungoides; Peris et al. (1998) [3], where a 29-year-old male with mycosis fungoides presented with rapidly progressive neurolymphomatosis that became fatal in 7 months; and finally Atiq et al. (1992) [2] presented a case of an older patient who completely recovered from their neurolymphomatosis.

It is important to distinguish peripheral neurolymphomatosis from other neurologic disorders in patients with lymphoma as the treatment and prognosis differ significantly. Peripheral neurolymphomatosis is defined by direct lymphomatous infiltration of the peripheral and/or cranial nerves or their roots. This can be difficult to differentiate from other clinical entities such as tumoral invasion of the epidural space, paraneoplastic syndromes, Guillain-Barré syndrome, and neuropathy related to radiation and/or chemotherapy. These other entities should be considered first as they are much more common compared to lymphocytic infiltration [10–12].

Clinical manifestations of neurolymphomatosis are variable and largely depend on the extent of involvement of the nerve. Initially, the symptoms are often subtle and not recognized by the patient. However, as the disease progresses, patients can develop pain, foot drop, plexopathy, mononeuritis multiplex, radiculopathy, and cranial nerve palsies, depending on the nerve involved. Disease progression is often variable, but is typically indolent and limited to a single nerve. Concurrent CNS disease is found in up to 26 % of cases [2, 3, 8, 10, 11].

There are no clear guidelines for the diagnosis of neurolymphomatosis from cutaneous T cell lymphomas. Much of what is understood is extrapolated from B cell lymphoma data as that disease process is much more prevalent [10].

MRI may be helpful in the diagnosis of neurolymphomatosis. Nerve or nerve root enlargement with or without enhancement are the most common findings. These findings are best viewed on coronal T1W and STIR sequences. Areas of nodularity can also be seen and can have hyperintense signal on fluid sensitive sequences [11, 13, 14]. Unfortunately, these findings are not specific(only 40 %) for neurolymphomatosis and can be seen in other entities [11, 13].

PET/CT has also been used as a diagnostic modality for the detection of neurolymphomatosis. Although there has not been a series reporting the efficacy of this modality, Gan et al. (2010) extrapolated data from malignant peripheral nerve sheath tumors demonstrating a sensitivity of 89–100 % [10]. The less-than-perfect sensitivity is thought to be related to the volume of disease and the resolution of PET/CT. Several case reports of peripheral lymphomatosis on PET/CT imaging reported intense FDG18 uptake in the involved nerve and/or nerve roots. These are often in a linear distribution along the expected path of the nerves [14–18].

The use of ultrasound for making the diagnosis has been only anecdotally described in the literature. In several case reports, US has been used to exclude a compressive lesion or to target abnormal nerves for biopsy [19, 20].

Conflicts of interest The authors declare no conflicts of interest.

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