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SHORT COMMUNICATION

Neurolymphomatosis Associated with Erythrodermic Mycosis Fungoides

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Infiltration of the peripheral nervous system by neoplastic cells including non-Hodgikin's lymphoma is termed neurolymphomatosis (NL). Typical manifestations of NL include peripheral or cranial nerve neuropathy (1). Diagnosis of NL is difficult and requires nerve biopsy, and may be delayed for months or years after the onset of symptoms. Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma (CTCL), and is characterized by a prolonged clinical course that progresses over years through patch, plaque, and tumour stages. In MF, skin lesions become confluent and finally develop into erythroderma without blood involvement, termed erythrodermic MF (2). We report here an unusual case of NL associated with erythrodermic MF.

CASE REPORT

A 68-year-old woman presented with a 3-year history of diffuse skin dryness and erythema on the trunk and extremities. She was referred to our department because her symptoms were refractory to topical steroids. Physical examination revealed erythroderma and lymphadenopathy. Histological examination (Fig. 1) and the presence of identical T-cell clonality in skin and inguinal lymph nodes revealed a CTCL with node involvement. Laboratory tests demonstrated normal complete blood cell counts without circulating atypical cells and normal biochemical findings, except for soluble interleukin (IL)-2 receptor levels (1,130 U/ml; normal value 124–466 U/ml), lactate dehydrogenase (379 U/l: normal value 115–217 U/l), and thymus and activation-regulated chmokine (6, 284 pg/ml: normal value <450 pg/ml). Serological analysis for human T-lymphotropic virus infection was negative. Computed tomography (CT) scans and 18F-fluorodeoxyglucose-positron emission tomography scans did not show any visceral involvement. The patient was diagnosed with erythrodermic MF with stage IIIA disease (3) and was treated with psoralen plus ultraviolet A (PUVA) and interferon-alpha. One year after diagnosis, she developed numbness, pain and progressive weakness of the right finger and both legs, which rapidly made walking and standing difficult. A nerve conduction study and needle electromyography revealed axonal peripheral neuropathy in her lower extremities. Biopsy of the left sural nerve showed a loss of myelinated fibres, axonal degeneration and infiltration of CD3+ atypical T cells (Fig. 2). Identical T-cell clonality was revealed in the nerve biopsy by PCR analysis of T-cell receptor beta (Vβ/Jβ1,2, Vβ/Jβ2, Dβ/Jβ) and gamma (VγIf, Vγ10/Jγ) gene rearrangement. A diagnosis of multi-mononeuropathy secondary to neural infiltration of MF cells was established. Two cycles of systemic chemotherapy with cyclophosphamide (750 mg/m^2 Day 1), vincristine sulphate (1.4 mg/ m^2 Day 1), doxorubicin hydrochloride (50 mg/m^2 Day 1), and predonisolone (100 mg/body Day 1–5) (CHOP) improved muscle weakness, walking difficulty and cutaneous lesions, but CHOP therapy was discontinued because of drug-induced interstitial pneumonitis associated with use of filgrastim for agranulocytosis.

DISCUSSION

B cells are the predominant malignant cell types of NL, and occasional cases have been associated with T-cell

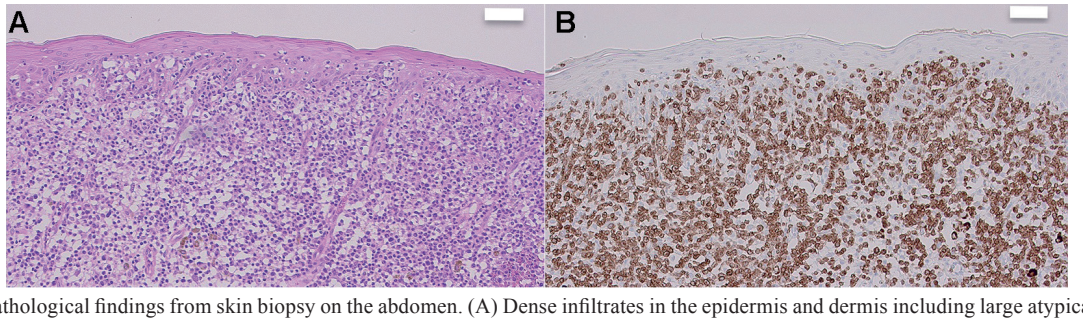

Fig. 1. Histopathological findings from skin biopsy on the abdomen. (A) Dense infiltrates in the epidermis and dermis including large atypical cells (*white bar* = 100 μm) (Hematoxylin and Eosin, original magnification × 100). (B) Infiltration of CD3$^+$ T cell into the epidermis and dermis (*white bar* = 100 μm) (Immunohistochemical staining for CD3, original magnification × 100).

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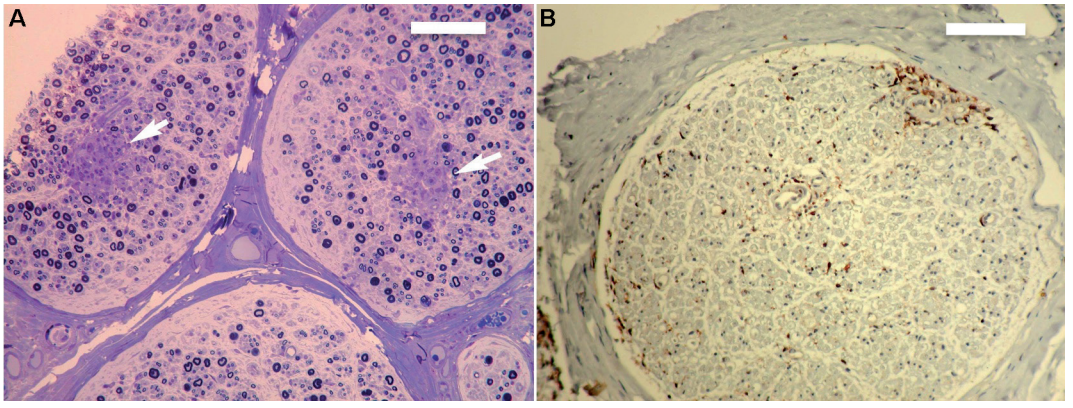

Fig. 2. Histopathological findings from sural nerve biopsy. (A) Loss of myelinated fibres, axonal degeneration and infiltration of atypical cells (*arrow*) (light microscopy, magnification × 10, *white bar* = 100 µm, transverse section of left sural nerve; Epon-embedded, semi-thin section, toluidine blue stain). (B) Infiltration of $CD3^+$ T cells into endoneurium (light microscopy, *white bar* = 100 µm, transverse section of left sural nerve; Immunohistochemical staining for CD3).

lymphomas (1). NL in MF is very rare (4) and, to our knowledge, this report is the first case of erythrodermic MF with NL proven by nerve histological examination. There is no known standard treatment for NL, but the majority of patients are managed by systemic chemotherapy (1). Clinical improvement has been observed in 46% of treated patients, although prognosis is poor (1). Because our patient's neuropathy progressed rapidly, she was treated with CHOP and experienced improvement in NL as well as cutaneous symptoms after treatment. This unusual case suggests that erythrodermic MF may be accompanied by NL exhibiting peripheral neuropathy, and that early treatment of NL associated with CTCL may improve neurological symptoms.

The authors declare no conflicts of interest.

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