Neutrophilic dermatosis associated with mycosis fungoides

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INTRODUCTION

An association between mycosis fungoides (MF) and neutrophilic dermatoses (ND) is rare. We describe a case of long-duration stage IIB MF developing pyoderma gangrenosum-like lesions and neutrophilic hidradenitis with histologic findings suggestive of necrotizing vasculitis.

Abbreviations used:

IFN-α:	interferon-alfa
MF:	mycosis fungoides
MTX:	methotrexate
ND:	neutrophilic dermatosis
PUVA-T:	psoralen–ultraviolet A therapy

CASE REPORT

We report the case of an 80-year-old woman with MF diagnosed 30 years previously after the appearance of a tumor on her right forearm which was treated with radiotherapy (initial stage IIB). In the following years, the patient periodically had plaques on the trunk and extremities. These plaques were controlled with psoralen–ultraviolet A therapy (PUVA-T). After 2 years in complete remission, she presented with a new tumor on the neck. Histologic examination confirmed tumoral MF without transformation to large cell. Disseminated disease was ruled out and chest, abdominal, and pelvic computer tomography demonstrated no pathologic findings. Serum lactate dehydrogenase levels were normal. Treatment with PUVA-T was initiated with good initial response for the first 3 months, then painful nodules developed on the upper lip, scalp, and legs that progressed rapidly toward ulceration (Fig 1). Skin biopsy of the scalp lesion found inflammatory infiltrate with predominance of neutrophils and eosinophils with associated neutrophilic hidradenitis. Biopsy of one of the leg nodules found syringotropic, atypical lymphoid infiltrate (Fig 2) with CD3 and CD30 positivity and foci of necrotizing vasculitis. The infiltrate was negative for CD4, CD7, CD8, CD20, CD56, Mum-1, and Epstein-Barr virus, and no large cells were present (Fig 3). The T-cell receptor gene rearrangement showed monoclonality. Cultures for bacteria, mycobacteria, and fungi were negative. Test results for viral hepatitis, human immunodeficiency virus, syphilis, antinuclear antibodies, antineutrophil cytoplasmic antibodies, and cryoglobulins were all negative. Protein electrophoresis showed no alterations. PUVA-T was discontinued, and treatment with prednisone, 30 mg/d, was initiated with rapid resolution of lesions of scalp and upper lip, but the leg lesions did not respond to treatment. Prednisone was increased to 45 mg/d with

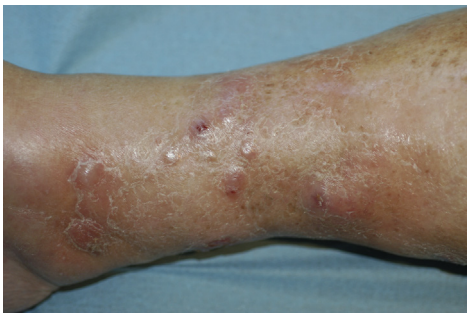

Fig 1. Painful nodules on the legs.

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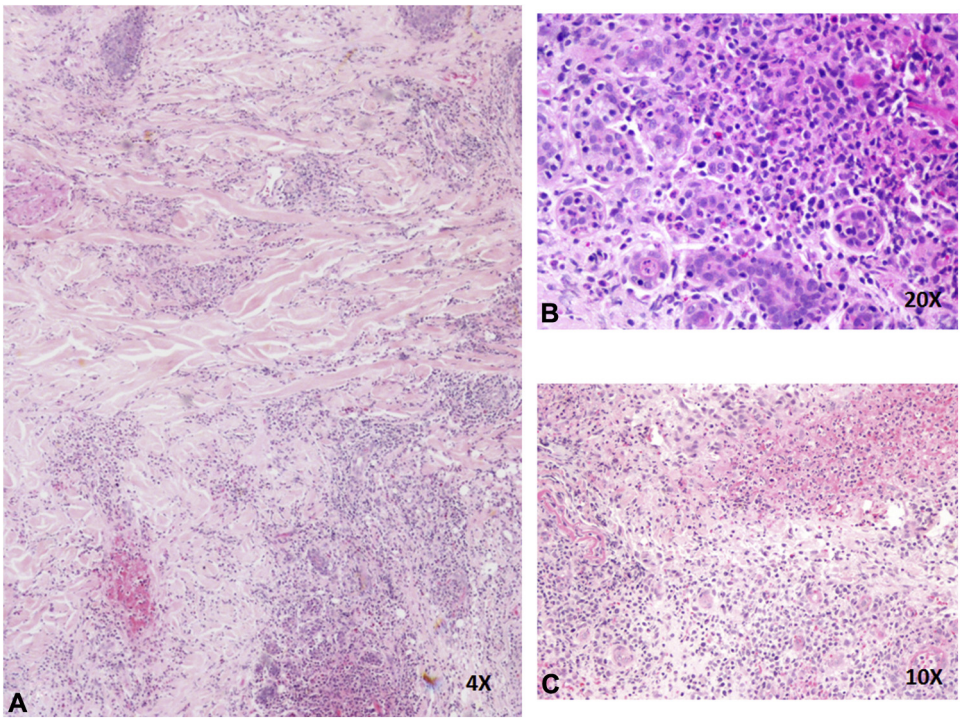

Fig 2. Neutrophilic dermatosis associated with atypical lymphoid infiltrate (**A**). Neutrophilic hidradenitis and syringotropic atypical lymphoid infiltrate (**B**). ND and necrotizing vasculitis (**C**). (Hematoxilin-eosin stain.)

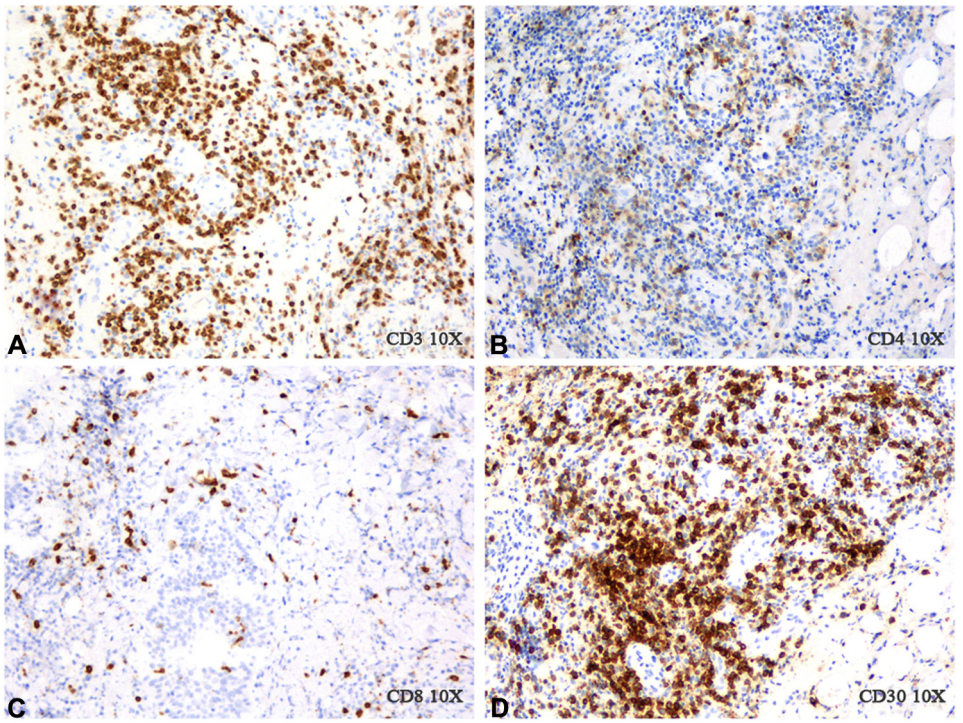

Fig 3. Atypical T lymphoid infiltrate. Immunohistochemical studies show expression of CD3 and CD30 (**A** and **D**) and loss of expression of CD4 and CD8 (**B** and **C**).

the addition of methotrexate (MTX), 20 mg once weekly. Disease progression continued with the appearance of new tumors on the legs, some ulcerated, clinically similar to lesions of pyoderma gangrenosum (Fig 4). Neutrophilia was evident in the blood count. Another biopsy of a tumoral lesion

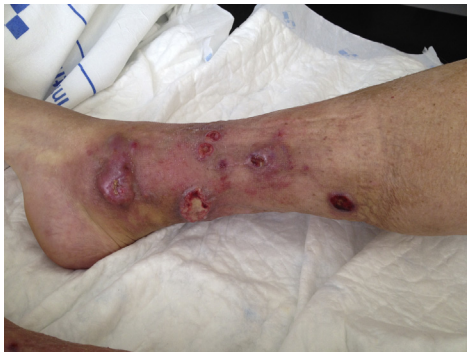

Fig 4. Evolution of the painful nodules into ulcerated tumors, some of them clinically similar to pyoderma gangrenosum.

of the leg found a predominantly neutrophilic inflammatory infiltrate with focal necrotizing vasculitis and neutrophilic hidradenitis. A companion atypical lymphoid infiltrate was evident. New total-body computer tomography scan found the presence of new masses in both adrenal glands, suggestive of metastases. A fine-needle aspiration biopsy of one of those lesions found the presence of atypical lymphoid cells. Pathologic lymph nodes were not found on clinical examination or in the tomography images. Immunophenotyping of peripheral blood T cells showed a monoclonal population < 5% $CD3^+$, $CD4^+$, and $CD8^-$. With the diagnosis of neutrophilic dermatosis associated with stage IVB MF, prednisone 40 mg/d was continued, the dose of MTX was increased to 40 mg/wk, and bexarotene 300 mg/d was added. However, the patient's status rapidly deteriorated. She subsequently died of acute respiratory failure 1 month after the diagnosis of the ND.

DISCUSSION

NDs are characterized by a neutrophilic inflammatory infiltrate in the absence of infectious disease. NDs may be associated with various systemic diseases including inflammatory bowel disease and rheumatic or hematologic diseases. Their relationship with lymphoproliferative disease is known, especially with acute leukemias.[1] However, to our knowledge there are only 5 reported cases of ND associated with MF (Table I).[2-4] The types of neutrophilic dermatoses described in these cases are diverse. There are cases of pyoderma gangrenosumlike lesions, neutrophilic hidradenitis, Sweet's syndrome, and exanthematous pustulosis. In our case, the patient had pyoderma gangrenosumlike lesions, neutrophilic hidradenitis, and associating histologic images suggestive of necrotizing vasculitis. The pathogenic mechanism that causes activation of neutrophils in these cases is unknown. A potential pathogenic role of interleukin-8, which has been shown to induce neutrophil recruitment and activation, and which can be secreted by CD30 cells, has been proposed.[2,5] Another possible cause could be the use of drugs such as IFN-alfa (IFN-α) that can act as an inducer of granulocyte colony-stimulating factor and neutrophils.[2] Two of the published cases also associated transformation to $CD30^+$ cells. We believe that the diagnosis of MF in these cases can be complex, as with pyogenic anaplastic variant $CD30^+$ cutaneous lymphomas. In these cases, the dense neutrophilic infiltration may mask the lymphoid infiltrate.[6] With the exception of the case presented by Aubin et al,[4] all cases, including ours, share a number of features already described by Franck et al[2]: (1) The development of neutrophilic dermatosis is associated with poor prognosis, and all patients died in an interval of between 6 weeks and 17 months. Interestingly, the final cause of death in all patients was acute respiratory failure, but we don't know whether neutrophils played some pathophysiologic role in the development of pulmonary involvement. (2) There was a lack of response to standard treatment of neutrophilic dermatosis. (3) There was syringotropism of atypical lymphoid cells in the histologic study. The pathophysiology of the association between MF and development of neutrophilic dermatosis, however, remains unknown. Both treatment with IFN-α and histologic transformation are causal theories postulated to date. We failed to establish the underlying cause because our patient did not receive treatment with IFN-α, and histologic transformation could not be demonstrated. We suggest that it is possible that this association has been the manifestation of a paraneoplastic phenomenon associated with advanced lymphoproliferative disease.

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Table I. Reported cases of MF associating ND

Case report	Sex/Age	TNM/Stage	Neutrophilic dermatosis	Possible etiology	Treatment	Evolution
Franck et al[2]	Male/35	T4N0M0/IIIA	Exanthematous pustulosis Neutrophilic hidradenitis	IFN-α	MTX Prednisone Colchicine RCT electro.	Death
	Male/68	T1N0M0/IA	Pyoderma gangrenosum Sweet syndrome Pustulosis. Neutrophilic hidradenitis	IFN-α $CD30^+$ transformation	MTX Prednisone Colchicine	Death
	Male/59	T3N0M0/IIB	Pustules over MF lesions.	IFN-α	Colchicine-Indometacin-Thalidomide Prednisone MTX CHOP Bexarotene	Death
Guillet et al[3]	Male/47	T3NxMx	Exanthematous Pustulosis.	G-CSF $CD30^+$ transformation	Corticosteroids Romidepsin	Death
Aubin et al[4]	Female/76	—	Sweet syndrome	Cytokines released by T cells	Corticosteroids	Resolution of the Sweet syndrome
Current case	Female/80	T3N0M1/IVB	Pyoderma gangrenosum Neutrophilic hidradenitis Necrotizing vasculitis	Progression	Prednisone MTX Bexarotene	Death

CHOP, Cyclophosphamide-hydroxydaunorubicin-oncovin-prednisone; *G-CSF*, granulocyte colony-stimulating factor; *MF*, mycosis fungoides; *MTX*, methotrexate; *ND*, neutrophilic dermatoses.

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