CLINCOPATHOLOGICAL CASE



Erythematous scaly patches and plaques on the trunk and extremities

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CLINICAL FINDINGS

A 42 year-old man presented with itchy skin lesions on the trunk and extremities lasting for 5 years duration. The condition started as an itchy dry patch on the abdomen then lesions started to increase in size and involved other areas on the trunk and spread to the proximal extremities with increased itching. There was no significant improvement with oral antihistamines and topical therapy including topical steroids, pimecrolimus and emollients. There was no previous history of similar lesions or other skin problems. The patient didn't complain from any systemic illness during this period and there was no family history of similar lesions.

Local examination of the skin revealed ill defined large erythematous scaly patches and plaques on the trunk and extremities. Trunk lesions were more located on the lower part of the abdomen around the umbilicus and flanks (Fig. 1). The lesions on the extremities were predominantly on the proximal parts specially the dorsal aspect of the thigh and gluteal region (Fig. 2). Old lesions were more pigmented, well defined and showed scaly elevated surface. Hair, nail and mucous membranes were not affected and showed no significant abnormalities.

Laboratory investigations showed mild elevation of liver enzymes and serum lipids while serum creatinine and hemoglobin were slightly lower than



Fig. 1 Large ill defined erythematous scaly patches on the abdomen and pubic region.



Fig. 2 Large ill defined scaly erythematous patches on the gluteal region and dorsal aspect of the left thigh.

normal. Chest x-ray and abdominal sonography were normal. Lymph node examination showed mild enlargement of inguinal lymph nodes on the right side with soft consistency and they were non tender and not attached to the underlying structures.

What is your clinical differential diagnosis?

Subacute dermatitis (discoid eczema or atopic dermtitis), psoriasis vulgaris, tinea corporis, chronic superficial dermatitis (parapsoriasis), and mycosis fungoides.

Pathological findings

An incision biopsy was taken from the periphery of the trunk lesion. It showed psoriasiform dermatitis with epidermal acanthosis and superficial perivascular inflammatory infiltrate. The epidermis showed mild elongation of the rete ridges while the horny layer showed mild hyperkeratosis with focal areas of parakeratosis. The dermis showed superficial perivascular inflammatory infiltrate that extended into the papillary dermis and epidermis (Fig. 3).

The inflammatory cells were composed mainly of lymphocytes with less number of histiocytes and sparse plasma cells and eosinophils. Few lymphocytes showed atypical morphology and nuclear pleomorphism. The epidermis showed focal infiltration with many lymphocytes with vacuolar alteration of the basal layer. Some lymphocytes spread into the mid-epidermis with formation of micro-abscess and others showed halo formation (Fig. 4).

The papillary dermis showed minimal melanin pigmentation with fibrotic collagen. Immunohistochemical staining showed positive staining for CD3, CD4 and CD45Ro in the majority of cells while small proportion of dermal lymphocytes showed positive staining for CD20. Other CD markers including CD8, CD30 and CD7 were negative. Epidermal lymphocytes were strictly positive for CD3 and CD4 (Fig. 5) and negative for CD8 and CD20.

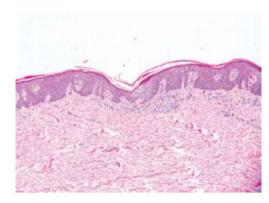


Fig. 3 Psoriasiform dermatitis with superficial perivascular lymphohistiocytic inflammatory infiltrate (H&E x100).

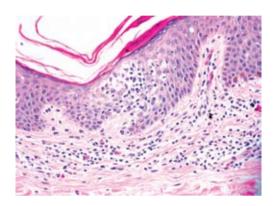


Fig. 4 Marked epidermotropism with formation of micro abscess and numerous halo cells in the epidermis (H&E x 400).

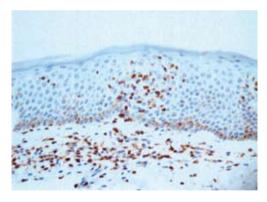


Fig 5 The epidermotropic cells are CD4+ lymphocytes (IHC x400).

DIAGNOSIS

Mycosis fungoides (cutaneous T-cell lymphoma)

COMMENT

Mycosis fungoides (MF) is a distinct form of cutaneous T-cell lymphoma which can be defined as

The clinicopathological challenges of patch-plaque stage of mycosis fungoides

Diagnosis	Clinical	Histological
Dermatitis (atopic)	Mostly since childhood The lesions predominate on the face and extremities Secondary bacterial infection is common May be associated with other atopic disorders (such as bronchial asthma)	Spongiosis is more prominent Exocytic lymphocytes is small and showed no halo around Vacuolar alteration of the basal layer is uncommon Parakeratosis is common The dermal infiltrate is superficial perivascular with few eosinophils.
Psoriasis (vulgaris)	 Dry, well demarcated plaques, usually covered with fine silvery scales Positive Auspitz sign Commonly involve the scalp, sacral region and extremities Nails and intertrigenous areas may be affected Psoriatic arthritis involving the terminal interphalangeal joints may be associated 	Acanthosis with regular elongation of the rete ridges Thinning of the suprapapillary epidermis Diminished to absent granular layer Confluent parakeratosis Presence of Munro microabscesses or small spongiform pustules Increased mitotic figures on the lower epidermis Dilated and tortuous capillaries in the dermal papillae
Fungal infection (epidermophytosis)	Large erythematous patches with central clearing Usually shows arcuate, annular or polycyclic scaly border Sometimes the lesions are more inflammatory with papulovesicular borders May be associated with grouped follicular pustules	Superficial perivascular lymphoid infiltrate with mild psoriasiform epidermal hyperplasia The horny layer may shows compact hyperkeratosis or sandwich sign (hyphae in between orthokeratotic and Parakeratotic keratin Neutrophils in the stratum corneum is a diagnostic clue
Chronic superficial dermatitis (small plaque parapso- riasis)	 Well-defined, round to oval patches with a fine 'cigarette-paper scale' Usually situated on the trunk and proximal parts of the extremities Usually have a reddish-brown color but may show a yellowish hue Mostly asymptomatic and persistent 	 Epidermal acanthotic with psoriasiform hyperplasia Spongiosis is focal and mild Focal parakeratosis or scale crust formation Superficial perivascular lymphohistiocytic infiltrate that extend into the papillary dermis Mild exocytosis of lymphocytes No interface changes and no atypical lymphoid cells
Lymphomatoid drug reactions	Associated with ingestion of drugs such as carbamazepine, griseofulvin, atenolol Solitary plaque, nodule or multiple lesions with a widespread distribution May spread to erythroderma	Band-like infiltrate in the dermis contains lymphocytes with atypical cerebriform nuclei There is usually a substantial histiocytic component, particularly in the nodular lesions Eosinophils and plasma cells are usually sparse or absent
Lymphomatoid papulosis (type B)	Crops of papules, nodules, and sometimes large plaques mainly on the trunk and proximal parts of the limbs Lesions spontaneously regress after several weeks or months, sometimes Resulting in atrophic scars Initially, the lesions are smooth but later they become necrotic, crusted, and ulcerated There is a predilection for females in the third and fourth decades of life	Uncommon pattern seen in 10% of cases Perivascular or band-like dermal infiltrate with epidermotropism The predominant cell types are small to medium sized lymphocytes with cerebriform nuclei Focal spongiosis in the epidermis, parakeratosis with neutrophils, ulceration and mitotic figures are common findings Some dermal fibrosis in resolving Lesions CD30+ cells are sparse
Adult T-cell leu- kemia/lymphoma, (papular stage)	Lesions are often widespread Erythematous patches, plaques, papules, and tumors May precede by non-specific skin lesions such as prurigo	The epiderm-al microabscesses may contain prominent apoptotic fragments The infiltrate sometimes conforms to a papular outline Other inflammatory cells are uncommon finding Atypical lymphocytes are sometimes seen in the lumina of blood vessels

a peripheral epidermotropic non-Hodgkin T-cell lymphoma of low grade malignancy. Although the etiology of MF still not established, the role of occupational, environmental agents and viral infections is rising in addition to the possible increased incidence with non-melanoma skin cancer, melanoma and lung cancer.¹⁻³

MF is a disease of late adulthood and the occurrence in children and young adults is rare. There is male predominance and there are differences in incidence among various racial groups. The tumor initially presents in the skin and shows clinical progression from one stage to another starting from patch to plaque then tumor stage. Lesions of MF tend to affect the lower part of the trunk and thigh, and breast in females. With progression of the disease to the entire body. In addition to face, scalp, palms and soles are also involved and may also spread to involve more than 90% of the body (erythrodermic MF).⁴

The non-classic clinical presentations of MF include a long list that consider MF as one of the major imitators of skin diseases and many subvariants were described in the literatures such as follicular, purpuric, granulomatous slack skin, hypopigmented, dyshidrotic, bullous, granulomatous, papular, syringotropic, hyperkeratotic, palmo-planter, leukodermic, annular and anetodermic.⁵

The histological diagnosis of MF is based on numerous subtle changes that can be present to some degree in other inflammatory and neoplastic cutaneous conditions. Although the histologic features of MF vary according to the clinical stage, there are significant diagnostic criteria including Pautrier microabscesses, haloed lymphocytes, allayment of lymphocytes along the basal layer, exocytosis of lymphocytes with hyperconvoluted nuclei and

disproportionate epidermotropism. Some of these criteria may be missed in the early stage and the diagnosis at this stage may form a challenge that needs a clinicopathological correlation.⁶⁻⁸

The immunophenotypical prototype of MF is CD2+, CD3+, CD4+, CD5+, CD45R0+, CD8-, CD30- and during progression of the disease, loss of CD7, CD2 and CD5 can occur. The neoplastic cells in MF express TH2 phenotype, which accounts for many systemic changes associated with MF due to production of a TH2-specific cytokine pattern (IL-4, IL-5 and IL-10) leading to variable constitutional manifestations such as fever and edema. 9,10

The staging of MF may be performed by two systems; TNM (tumor, nodes, and metastasis) classification and TNMB staging that include blood involvement. The value of this staging system is to distinguished patients with early stage IA/IB, to stratify lymph node incorporation, to assess the degree of peripheral blood involvement and to clarify the prognostic relevance of features such as folliculotropism and large cell transformation. Routine hematology and biochemistry studies should be performed for all cases while chest x-ray, CT scans, bone marrow aspirate and trephine biopsy are more required in advanced stages. The treatment of MF depends on constellation of factors including the age and general condition

factors including the age and general condition of the patient and the stage of the disease. Phototherapy (UVB, PUVA and UVA-1), immunotherapy (IFN-α, IFN-γ and IL-12, retinoids and topical chemotherapy (nitrogen mustard and carmustine) are different therapeutic modalities for early stages while chemotherapy, photopheresis, monoclonal antibodies and toxin therapy are usually preserved for late stages.¹³⁻¹⁵

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