CD8-positive Mycosis Fungoides Masquerading as Pyoderma Gangrenosum

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Abstract
Mycosis fungoides (MF), a primary cutaneous T-cell lymphoma, accounts for <1% of non-Hodgkin lymphomas. The diagnosis of classic MF is based on a constellation of typical clinical presentation, histopathology, immunohistochemistry, and T-cell monoclonality detected by molecular studies. Rarely, atypical clinical presentation may occur. The typical immunohistochemical phenotype is, CD2 +ve, CD3 +ve, CD5 +ve, CD4 +ve, and CD8 – ve. Here, we report a rare case of CD8 +ve MF in a 43-year-male patient who was clinically diagnosed as pyoderma gangrenosum initially. The atypical presentation and rarity of such case have prompted this report.

Key Words: CD8+, mycosis fungoides, pyoderma gangrenosum

Introduction
Mycosis fungoides (MF) and Sézary syndrome comprise approximately 53% of primary cutaneous lymphomas.[1] MF usually appear as erythematous scaly patches or plaques. Rarely, atypical clinical presentations can occur. One such condition is pyoderma gangrenosum. Typical histopathologic picture in MF is the presence of a dense infiltrate of atypical lymphocytes in the dermis with epidermotropism (presence of atypical lymphocytes in epidermis). Immunophenotyping shows expression of CD4+ antigen, though CD8+ and double negative CD4-/CD8− variants have been described. Hence, these cutaneous lymphomas mimic other skin conditions both clinically and histologically, posing a diagnostic challenge to the dermatologists and the pathologists.

Case Report
A 43-year-old man presented with large areas of atrophic, wrinkled and dyspigmented skin, mainly distributed over his buttocks and ventral aspect of both thighs extending up to the popliteal fossa. The lesions initially started as superficial pustules which subsequently broke down to form well-defined, extremely painful ulcers. Initially, they were small in size, which gradually coalesced with each other to form large, bizarre-shaped ulcers. These lesions first appeared 20 years back. He was diagnosed as pyoderma gangrenosum clinically and started on a tapering dose of oral prednisolone along with regular local dressing; which is continuing till date. At present, the patient approached us with the complaint of emergence of new lesions over his trunk, for the last 6 months. Family history and drug history were unremarkable. General examination was within normal limits except for the presence of pallor and icterus. No lymphadenopathy was noted. Cutaneous examination revealed large atrophic scars with thinned and wrinkled skin, measuring approx. 17 cm × 13 cm, mainly distributed over his buttocks [Figure 1] and ventral aspect of both thighs even extending up to the popliteal fossa. Speckled areas of hyperpigmentation and depigmentation were observed within the lesions. Routine serum biochemistry was unremarkable; except for the presence of reduced hemoglobin and elevated bilirubin levels. Peripheral blood smear was normal, without any atypical Sézary-like cell. The lesion on the left buttock was subjected to punch-biopsy. Histopathological examination revealed stratified squamous epithelium

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with hyperkeratosis, acanthosis, and basal cell degeneration. The upper dermis was diffusely infiltrated by the monomorphic population of atypical, small to medium-sized lymphoid cells with cerebriform nuclei. Epidermotropism was observed [Figure 2]. Histologically, a diagnosis of cutaneous lymphoma was made, favoring MF. Immunohistochemistry showed CD8+, CD3+, CD2+, TIA1+, CD20−, CD4−, CD5−, CD30−, CD56−, CD7−, granzyme B−. The MIB-1 labeling index was <5% [Figure 3]. The final diagnosis was CD8+ MF. Bone marrow aspiration was performed for staging of the tumor. The aspirate and biopsy showed focal deposit of atypical lymphoid cells, suggestive of metastatic involvement of the bone marrow. The whole body positron emission tomography (PET) scan revealed active Space occupying lesions (SOLs) in segment VI and VII of liver and focal involvement of the spleen [Figure 4]. At present, the patient is on follow-up and doing satisfactorily.

Discussion

MF is the most common primary cutaneous T-cell lymphoma (CTCL), occurring in old adults, with a 2:1 male predominance.[2] The most common site of involvement is photoprotected regions such as the trunk and body folds.[3] MF generally presents in the form of patch, plaque, tumor or nodule.[3] Nashan et al. performed a literature review on clinical presentations of MF.[4] They found that MF can mimic more than fifty different clinical entities. They mentioned unusual and newly described variants comprising of hyperpigmented, hypopigmented, urticarial, bullous, solely papular, pustular, and hyperkeratotic variants. Other clinical impressions included purpura pigmentosa, vasculitis, and pyoderma gangrenosum.[4] Our case mimicked pyoderma gangrenosum. Till date, there is only a single report of CD8+ MF mimicking pyoderma gangrenosum[5] in the English literature, to the best of our knowledge. However, there are few reports of other CTCLs resembling pyoderma gangrenosum. One case was natural killer T-cell lymphoma and other MF in a case of ulcerative colitis.[6,7]

Figure 1: Clinical photograph revealing large atrophic scars with thinned and wrinkled skin, distributed over buttocks. Speckled areas of hyperpigmentation and depigmentation are observed within the lesions

Figure 2: Stratified squamous epithelium showing diffuse dermal infiltration of atypical, small to medium-sized cells with obvious epidermotropism (H and E, ×100) inset shows lymphoid cells with cerebriform nuclei (H and E, ×400)

Figure 3: Immunohistochemistry showed CD8+, CD3+, CD2+, CD20−, CD4−, CD5−, CD30−, CD7−, granzyme B −ve (DAB chromogen, ×400)

Figure 4: Whole body positron emission tomography-computed tomography findings suggestive of active metastatic space occupying lesion in liver with multiple simple cysts and focal involvement in spleen
Investigators have proposed several histologic criteria to distinguish MF from other inflammatory and neoplastic cutaneous conditions. Parameters suggesting a diagnosis of MF included atypical intraepidermal lymphocytes surrounded by halos, Pautrier’s microabscess, exocytosis, disproportionate epidermotropism, epidermal lymphocytes larger than dermal lymphocytes, hyperconvoluted intraepidermal lymphocytes, and lymphocytes aligned within the basal layer. Characteristically, the lymphocytic infiltrate is helper T-cell phenotype of CD2+, CD3+, CD5+, CD4+, TCRβ+, and CD8−. Rarely, it is suppressor/cytotoxic CD8+. A feature which is helpful to differentiate between CTCLs and benign reactive lymphoid hyperplasia of the skin is a loss of the T-lineage antigens CD2, CD3, CD5, and CD7 that occurs in neoplastic T-cell lymphomas.

Berti et al. studied 17 cases of CD8+ CTCL and found that nine cases showed the clinical and histological features of well-defined types of CTCL, included as separate entities in the EORTC classification for primary cutaneous lymphomas. This group included two cases with MF-like lesions, two cases of pagetoid reticulosis, two cases of lymphomatoid papulosis, two cases of CD30+ primary cutaneous large T-cell lymphoma, and one case of panniculitis-like sub-CTCL. The other eight cases formed a homogeneous group showing a distinctive set of features, not consistent with that of other well-defined types of CTCL. The clinical characteristics of these included presentation with generalized patches, plaques, papulonodules, and tumors mimicking disseminated pagetoid reticulosis; metastatic spread to unusual sites and an aggressive course.

In our case, other CTCLs were ruled out by a combination of clinical, histological, and immunohistochemical findings. Our patient reported a long indolent course of 20 years. On histology, atypical convoluted cerebriform lymphoid cells in the dermis with epidermotropism were observed. The immunohistochemical findings were CD8+, CD3+, CD2+, TIA1+, CD20−, CD4−, CD5−, CD30−, CD56−, CD7−, and TDT−, granzyme B−ve. The MIB-1 labeling index was <5%. The finding of loss of CD4 and CD5 antigens and positivity with CD8 antigen were consistent with the diagnosis of CD8+ MF.

Extracutaneous dissemination in MF is observed in <10% of patients with patch or plaque disease and in 30–40% of patients with tumors or generalized erythrodermatous involvement. The most commonly involved organs are lung, spleen, liver, and gastrointestinal tract. Patients with the extracutaneous disease at presentation involving either lymph nodes or viscera have a median survival of <1.5 years. In our case, the patient had a remitting course for almost 20 years, with recent extracutaneous spread to bone marrow, along with PET scan showing multiple liver deposits. However, the patient is continuing the same treatment and is clinically stable.

This case is being reported to highlight one of the most atypical clinical presentations of CD8+ MF on rare occasions; the first such report from India. Thus, skin biopsy and immunohistochemistry are essential tools to arrive at the correct diagnosis in such cases.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**What is new?**

Mycosis Fungoides may rarely present as pyoderma gangrenosum.

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