Case Report

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Pathology Section

Sèzary Syndrome-A Rarely Seen Variant of Non-Hodgkins Lymphoma

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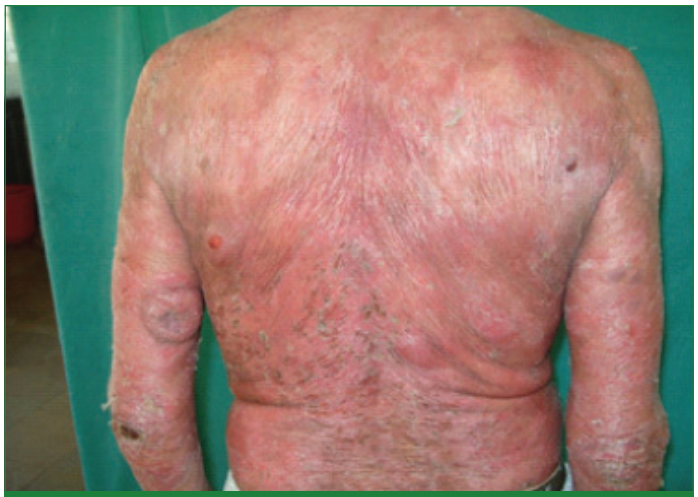
ABSTRACT

Cutaneous T-Cell Lymphomas (CTCL) is a group of T-Cell Non-Hodgkin's Lymphomas, originating from T-cells of skin associated lymphoid tissue. Mycosis fungoides is a specific type of CTCL derived from CD4+T-cells. Sèzary Syndrome (SS) is the leukemic counterpart of Mycosis fungoides and is defined by the triad of erythroderma, generalised lymphadenopathy and presence of clonally related neoplastic T-cells (Sèzary cells) in skin, lymph nodes and peripheral blood. In addition one or more of the following criteria are required: an absolute Sèzary cell count of at least 1000/cu.mm, an expanded CD4+T-Cell population resulting in a CD4/CD8 ratio of more than 10 and/or loss of one or more T-Cell antigens. Here, the authors report a case of 63-year-old male patient who fulfilled the criteria for diagnosis of SS. Clinically, the presentation of this lesion can be mistreated and misdiagnosed as chronic dermatitis or any psoariasiform lesion. If the patient fails to respond to treatment, then it prompts an extensive search for more serious disease along with thorough investigatory approach.

Keywords: Cutaneous, Erythroderma, Generalised lymphadenopathy, T-cell

CASE REPORT

A 63-year-old male presented to the Dermatology Outpatient Department (OPD) with history of pruritic skin lesions which were present since preceding 4 years. Patient complained of exacerbation of symptoms in the last 6 months. There was no history of any drug intake, allergy, diabetes mellitus, hypertension. On examination, the lesions were multiple and present more on the trunk and extremities (bathing trunk distribution) [Table/Fig-1a].

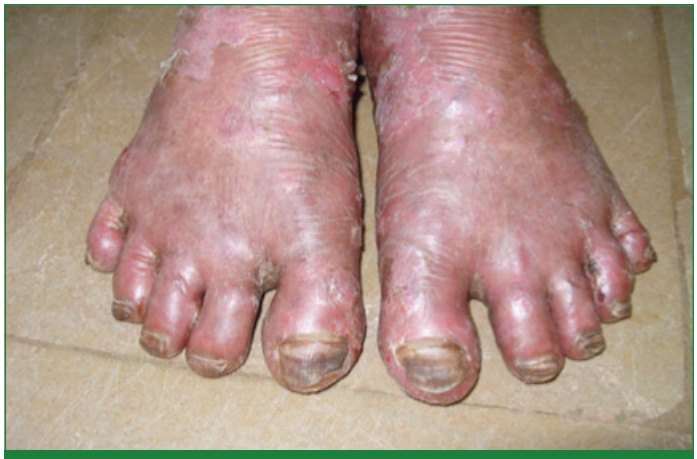


[Table/Fig-1a]: Clinical photograph showing multiple lesions-plaques, nodules, erosions and pustules on the trunk and extremities (Bathing trunk distribution).

They were in the form of plaques, nodules, erosions and pustules measuring from 3x3 cm to 7x5 cm in size. The plaques were erythematous with ill-defined margins. Nodules too were erythematous with many of them showing central ulceration. The face of the patient showed diffuse erythema. The palms and soles showed scaling. There was involvement of all the finger and toe nails with brownish discolouration [Table/Fig-1b].

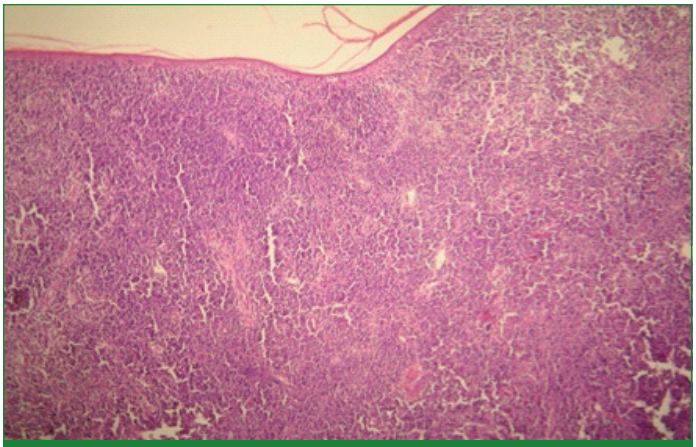
There was cervical, axillary and inguinal lymphadenopathy. The lymph nodes measured 2x3 cm in diameter, were firm, hard and non tender. Nothing abnormal was detected on chest X-ray and abdominal ultrasound.

Based on the clinical features, a differential diagnosis of Mycosis fungoides, fungal infection, allergic contact dermatitis, psoariasis and lepromatous leprosy were made. Patient was subjected to skin biopsy and blood examination. The skin biopsy revealed epidermis and dermis. There was a band like lymphoid infiltrate in the superficial dermis comprising of atypical cerebriform cells [Table/Fig-2a]. Some of the atypical lymphoid cells were seen to invade the epidermis (epidermotropism) [Table/Fig-2b,c]. Collections of these cells within the epidermis gave rise to Pautrier's microabscesses [Table/Fig-2d] which is a characteristic feature of Mycosis Fungoides/SS. The differential diagnosis on histopathology included eczema, psoariasis, non specific dermatitis, Lichen planus, Discoid lupus erythematosus, pseudolymphoma and parapsoariasis. However, the clear presence of atypical cerebriform lymphoid cells in the band like infiltrate along with epidermotropism and Pautriers microabscesses helped to rule out the other lesions as mentioned above.

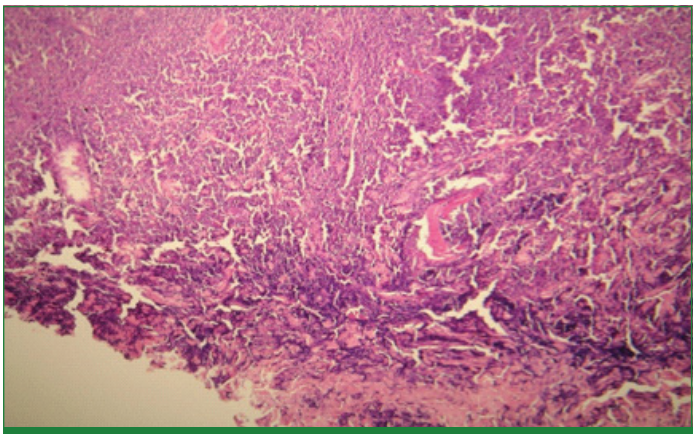


[Table/Fig-1b]: Clinical photograph showing brownish discolouration of toe nails with scaling.

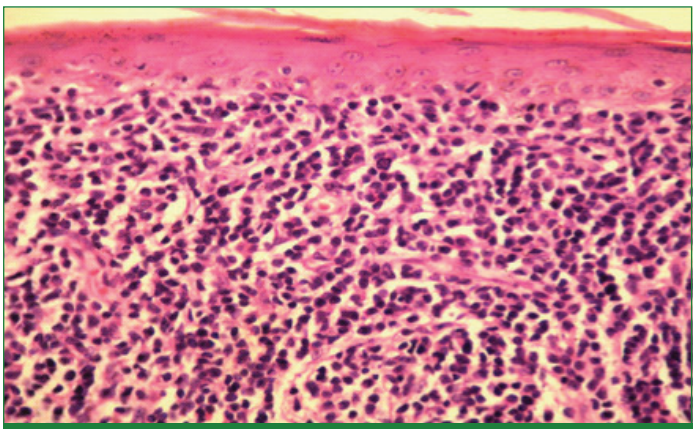
The complete haemogram revealed Hb 13.4 g/dL, total White Blood Cell (WBC) count 11,500/cumm, platelet count 2.2 lac/cumm. Differential count neutrophils-68%, lymphocytes-20%, eosinophils-01% and Sèzary cells-11%. Buffy coat revealed presence of circulating Sèzary cells with the more common small cell type (Lutzner Cell). The Sèzary cells had a non granular cytoplasm with the characteristic delicately convoluted, cerebriform nucleus with condensed chromatin and inconspicuous nucleoli [Table/Fig-3a,b].



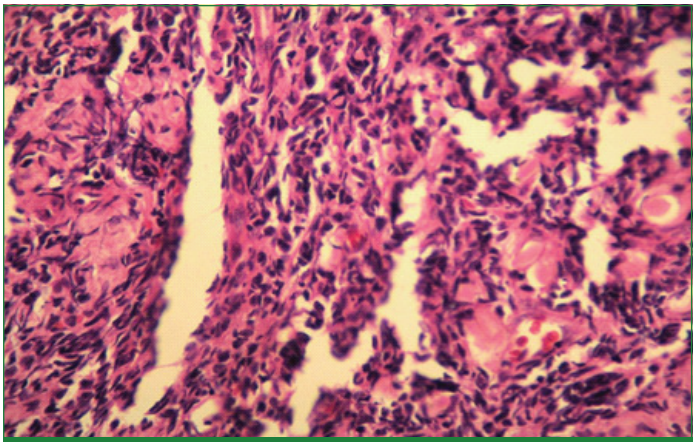
[Table/Fig-2a]: Microscopy showing band like lymphoid infiltrate in the papillary dermis (H&E X40).



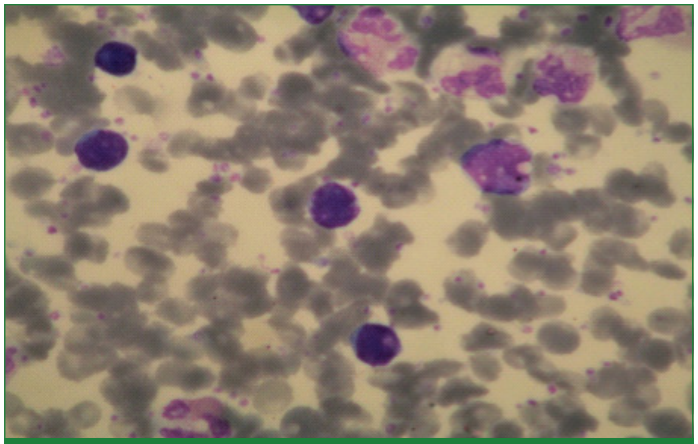
[Table/Fig-2b]: Microscopy showing atypical lymphoid cells invading the epidermis (Epidermotropism) (H&E X100).



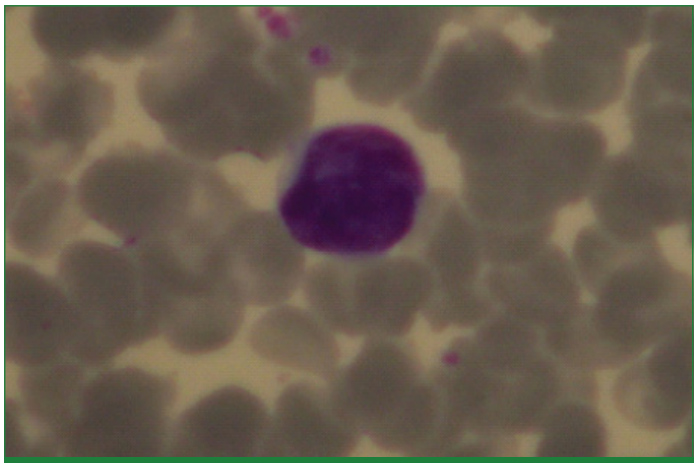
[Table/Fig-2c]: Microscopy showing lymphoid cells at the epidermo-dermal junction and some of them migrating to the epidermis as single cells. The cells showing cytologic atypia (H&E X400).



[Table/Fig-2d]: Microscopy showing Pautrier's microabscesses (H&E X400).



[Table/Fig-3a]: Peripheral smear showing Sèzary cells (Wright's stain X400).



[Table/Fig-3b]: Peripheral smear showing Sèzary cell with non granular cytoplasm, showing the characteristic delicately convoluted cerebriform nucleus with condensed chromatin and inconspicuous nucleoli (Wright's stain X1000).

The Red Blood Cells (RBCs) were normocytic, normochromic. Correlating the skin biopsy picture and the peripheral blood picture along with the clinical features, a diagnosis of SS was made. Patient was referred to a tertiary care Oncology centre and patient was lost to follow-up.

DISCUSSION

Primary cutaneous Lymphomas are a heterogenous group of T and B-cell Lymphomas present in the skin with no evidence of extracutaneous disease at the time of diagnosis [1]. According to series of reports from 1938-1940, Sezary observed the patients with erythroderma and very large number of abnormal cells in the blood. Later, he ascribed these to a new malignant cutaneous reticulosis, but related to Mycosis Fungoides [2]. SS is a rare disease and accounts for less than 5% of all cutaneous T-Cell Lymphomas. It is mainly seen in adults over 60 years of age and has a male predominance [3].

Clinical staging system for Mycosis Fungoides and Sèzary Syndrome as proposed by ISCL-EORTC includes [4]:

Stage I: Wherein the disease is confined to the skin with patches/papules/plaques <10% (Stage IA) or >10% (Stage IB) of the skin surface. No clinically abnormal lymph nodes.

Stage II: Skin involvement with patches/papules/plaques associated with early (N1-N2) lymph node involvement (Stage IIA) or skin involvement with one or more tumours (>1cm) (Stage IIB).

Stage III: Skin involvement with erythroderma, no or early (N1-N2) lymph node involvement and absent or low blood tumour burden (<1000/µL circulating Sèzary cells).

Stage IV: High blood tumour burden (>1000/µL circulating Sèzary cells) and/or extensive lymph node involvement (N3) or visceral involvement (M1) [4].

The present patient was in Stage IV (N3) considering his lymph nodes and blood involvement with Sèzary cells >1000/µL.

The SS is the leukemic variant of CTCL characterised by a triad of erythroderma, peripheral lymphadenopathy and presence of circulating atypical lymphoid cells (Sèzary cells) [5].

In terminal stages, all visceral organs may be involved, but, sometimes there is remarkable sparing of bone marrow and is found in advanced forms of the disease [3,6,7]. On immunopheno typing tumour cells are CD2+,CD3+TCRβ+ and CD5+. Most cases are CD4+ [3]. This is an aggressive disease with an overall survival rate of 10-20% at 5 years. Prognostic factors include the degree of lymph node and peripheral blood involvement [3]. Most patients die of opportunistic infections [3]. Since the overall prognosis is poor with few lasting remissions and responses, there has been an intense search for better treatment of the disease. The use of immunomodulators like interferons, the availability of new chemotherapeutic drugs and monoclonal antibodies has changed the course of the disease. While selecting therapy for patient with SS, few important principles should be kept in mind. Firstly, the initial choice of therapy must rely on relative burden of disease, impact on quality of life and rapidity with which the progression of disease is taking place. Disease Burden implied the degree of infiltration of skin, presence or absence of tumours in skin, lymphadenopathy extent, the relative burden of malignant circulating T-cells, the rate of increase in serum lactate dehydrogenase and rate of increase of peripheral WBC count [2]. The malignant T-cells produce soluble factors that result in endogenous immune suppression which leads to opportunistic infections; hence preservation of immune response is essential to prolong life. Therefore, use of immunomodulators like Interferon α, Interferon γ along with retinoids and/or extracorporeal photopheresis should be considered as initial treatment choices. Thus, combination or multimodality approach should be encouraged to achieve a higher response rate [2].

CONCLUSION(S)

SS is very rare and must be considered in the routine differential diagnosis when investigating a patient with erythroderma whose aetiology must be clarified. Proper and timely diagnosis is important so that therapy is initiated to improve the quality of life.

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