

Sézary syndrome

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Summary

A 69-year-old female of recurrent erythroderma of few months duration, treated by a panel of specialties: pulmonologist, nephrologists, rheumatologist, endocrinologist and gastro-enterologist. She was receiving multiple drugs and initially diagnosed as drug reaction. The patient was thoroughly investigated; however, the tests done were inconclusive. It was a story of failure and frustrations: the patient was over-cared and treated by many consultants while the concept of integrated medicine was lacking. Over care was given but a true and sound medical diagnosis was not provided until the case was referred to a dermatologist just to repeat local medications. On examination several papules were found on the trunk together with enlargement of the peripheral lymph nodes. A biopsy was done but the result was non-specific spongiotic dermatitis. No immunophenotyping was done at that stage. Through the charts of CBC the diagnosis of Sézary Syndrome was suspected. In addition to elevated lymphocytic count the peripheral lymphocytes were almost hyperchromatic and convoluted. Immunophenotyping showed CD3+ve, CD4+ve, CD5+ve, CD7+ve, CD8-ve, CD10-ve, CD19-ve, CD20-ve; the diagnosis was verified and the patient received in UK later a proton beam therapy.

Introduction

Sézary syndrome (SS) is defined historically by the triad of erythroderma, generalized lymphadenopathy and the presence of neoplastic T cells (Sézary cells) in skin, lymph nodes and peripheral blood.^{1,2} In a recent report of the International Society for Cutaneous Lymphomas (ISCL) criteria recommended for the diagnosis of SS include one or more of the following: an absolute Sézary cell count of least 1000 cells per mm³, demonstration of immunophenotypical abnormalities (an expanded CD4+ T-cell population resulting in a CD4/CD8 ratio more than 10, loss of any or all of the T-cell antigens CD2, CD3, CD4 and CD5, or both); the demonstration of a T-cell clone in the peripheral blood by molecular or cytogenetic methods.³

It is acknowledged that Sézary syndrome is part of a broader spectrum of erythrodermic CTCL, and those alternative staging systems for assessment of

the degree of peripheral blood involvement in these erythrodermic CTCL have been proposed.⁵⁻⁷

However, until the results of an ISCL study investigating the clinical validity of these proposals are available, demonstration of a T-cell clone (preferably of the same T-cell clone in skin and peripheral blood) in combination with one of the above mentioned cytomorphological or immunophenotypical criteria are suggested as minimal criteria for the diagnosis of SS to exclude patients with benign inflammatory condition simulating SS.⁸

Case report

A 69-year-old female presented with severe intractable pruritus and recurrent erythroderma of few months duration (fig 1,2). She was treated by a panel of consultants: pulmonologist, nephrologist, rheumatologist, endocrinologist, gastroenterologist and dermatologist. She was also receiving multiple drugs (Tenormin, Warfarin, Klacid, Zocor, Femtrix, Singulair and antihistamines). She was initially diagnosed as drug reaction. The skin lesion was only in the form of erythema, which extended over few weeks to cover almost the whole body. The patient was admitted to hospital and the panel of consultants held several meetings they started systemic steroids the condition showed partial response however the pruritus was still stubborn.

This case was a typical example of diagnostic failure and frustrations that come across our practice. Though the patient was over-cared and treated by many consultants the concept of integrated medicine was missing. It is possible that everyone depends upon others or perhaps because the result of first skin biopsy report ruled out the possibility of lymphoma.

The patient was thoroughly investigated on both occasions; however, the tests done especially the skin biopsy (fig3) were inconclusive. In addition to elevated lymphocytic count the peripheral lymphocytes were almost hyperchromatic and convoluted. Immunophenotyping showed CD3+ve, CD4+ve, CD5+ve, CD7+ve, CD2-ve, CD8-ve, CD10-ve, CD19-ve, CD20-ve; CD4:CD8 ratio was 12.6 and the absolute count of convoluted abnormal Sezary cells was 1390 cell/cmm (fig4).

Histopathology showed Fig 5 H&E section, x20 magnification. The pathologic picture was confusing

it mimics Pityriasis Lichenoides acuta, perivascular lymphocytic infiltration and mild degree of exocytosis rather than frank epidermotropism. The original diagnostic triad of Sézary syndrome was verified. Other features of typical Sézary syndrome as alopecia, onychodystrophy and palmoplantar hyperkeratosis were absent. Three signs paved the way for the diagnosis of Sézary syndrome: the eruption of papules over the trunk which was associated with generalized lymphadenopathy and absolute lymphocytosis more than 1000 cell per cmm. The diagnosis was coined according to the criteria of

the International Society for Cutaneous Lymphomas (ISCL) criteria and the patient was referred to oncologist for further evaluation and management.

Discussion

Sézary syndrome is a rare disease and occurs exclusively in adults. It is characterized by erythroderma, which may be associated with marked exfoliation, oedema and intense pruritus. It is considered the leukemic phase of primary cutaneous T cell lymphoma, classified by EORTC and WHO as an aggressive lymphoma. Lymphadenopathy, alopecia, onychodystrophy, and palmoplantar hyperkeratosis are



Fig 1 The patient first presentation with erythroderma

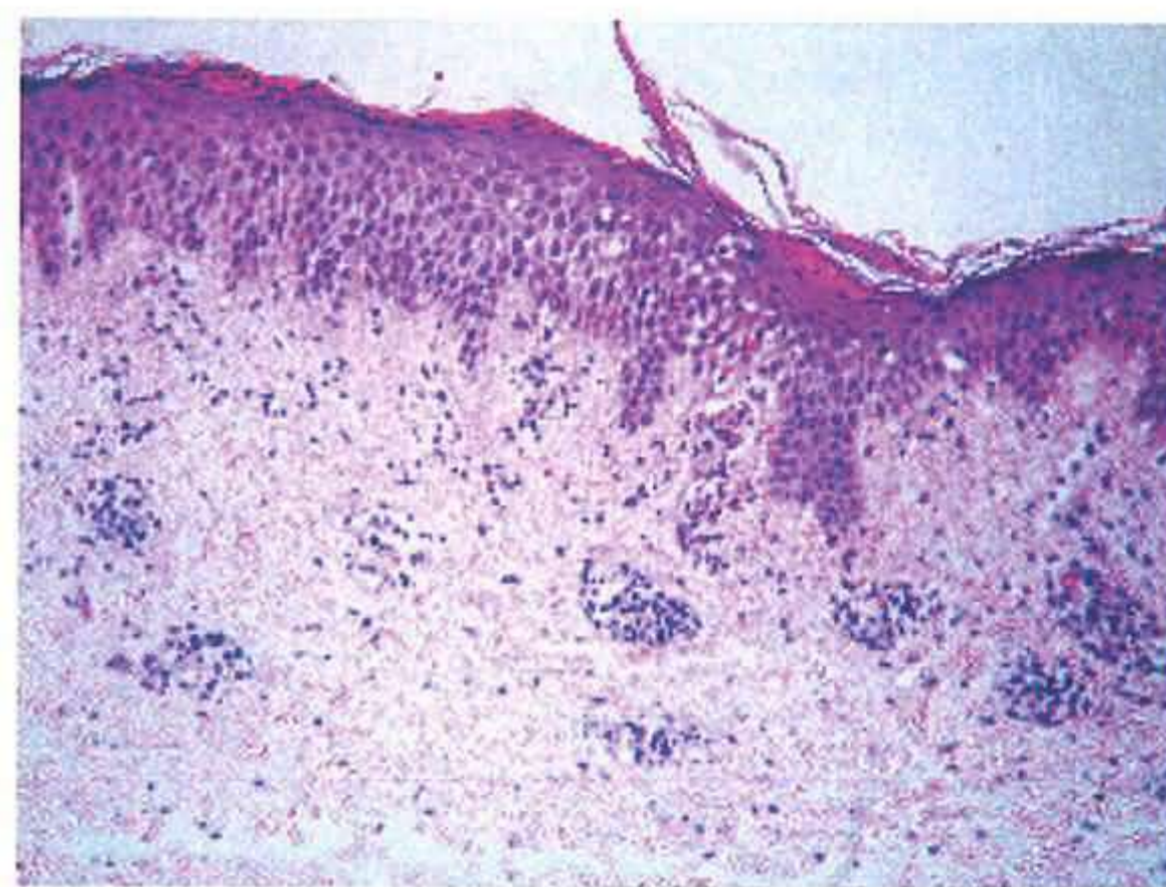


Fig 2 H&E section, x20 magnification. The pathologic picture was confusing it mimics Pityriasis Lichenoides acuta, perivascular lymphocytic infiltration and mild degree of exocytosis rather than frank epidermotropism

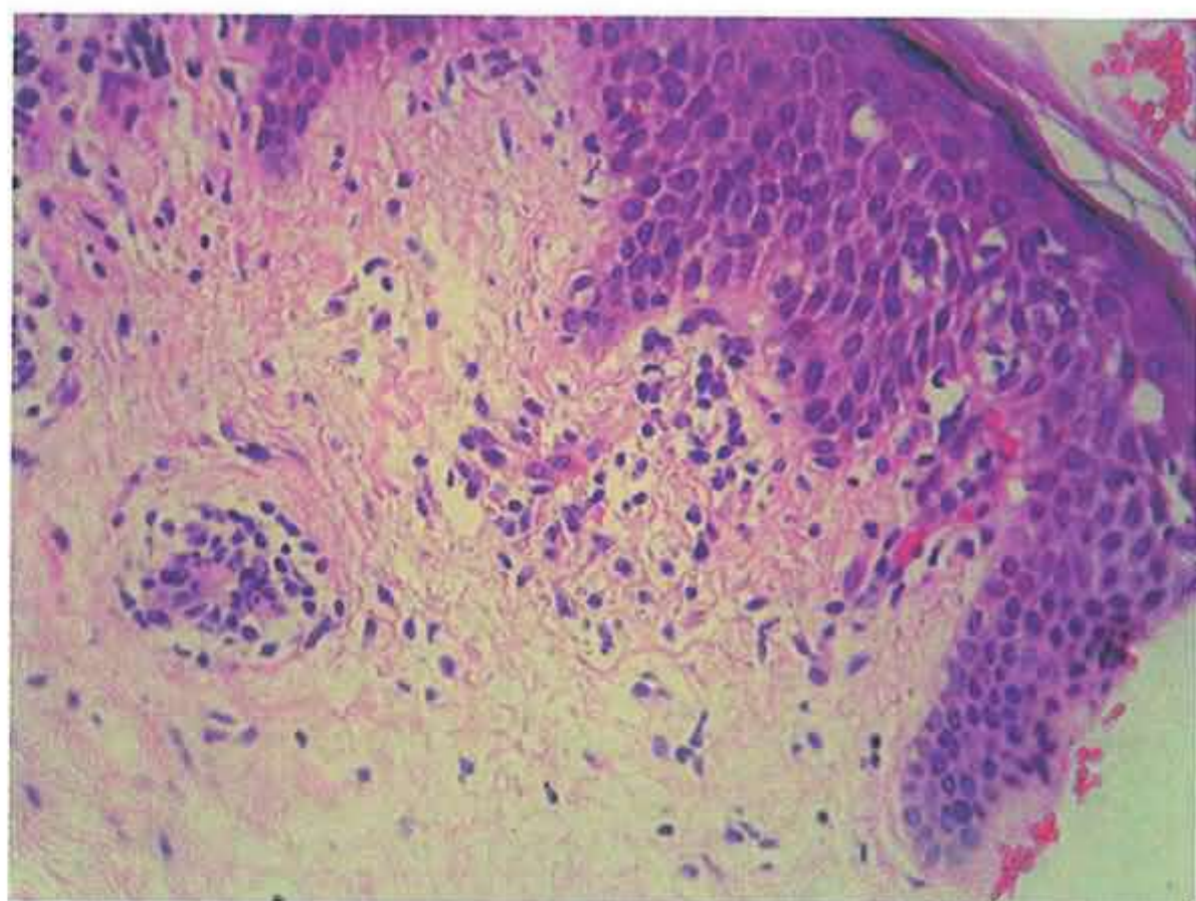


Fig 3 H&E section, x40 magnification. A close up view of the previous section showing perivascular infiltrate and extravasated RBCs in dermis and epidermis. Epidermis showed mild exocytosis.

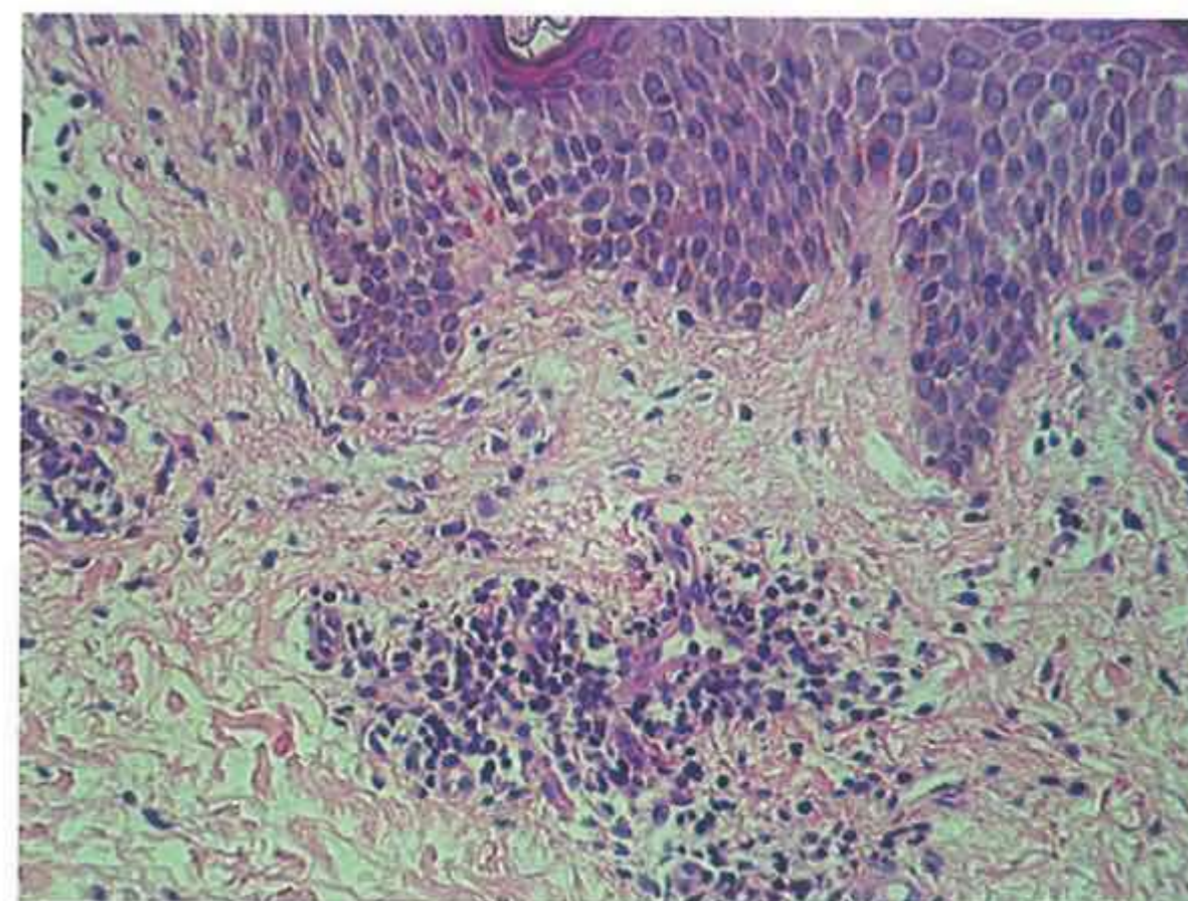


Fig 4 H&E section, x40 magnification showing the main pathognomonic features vasculopathy and RBCs in the epidermis.

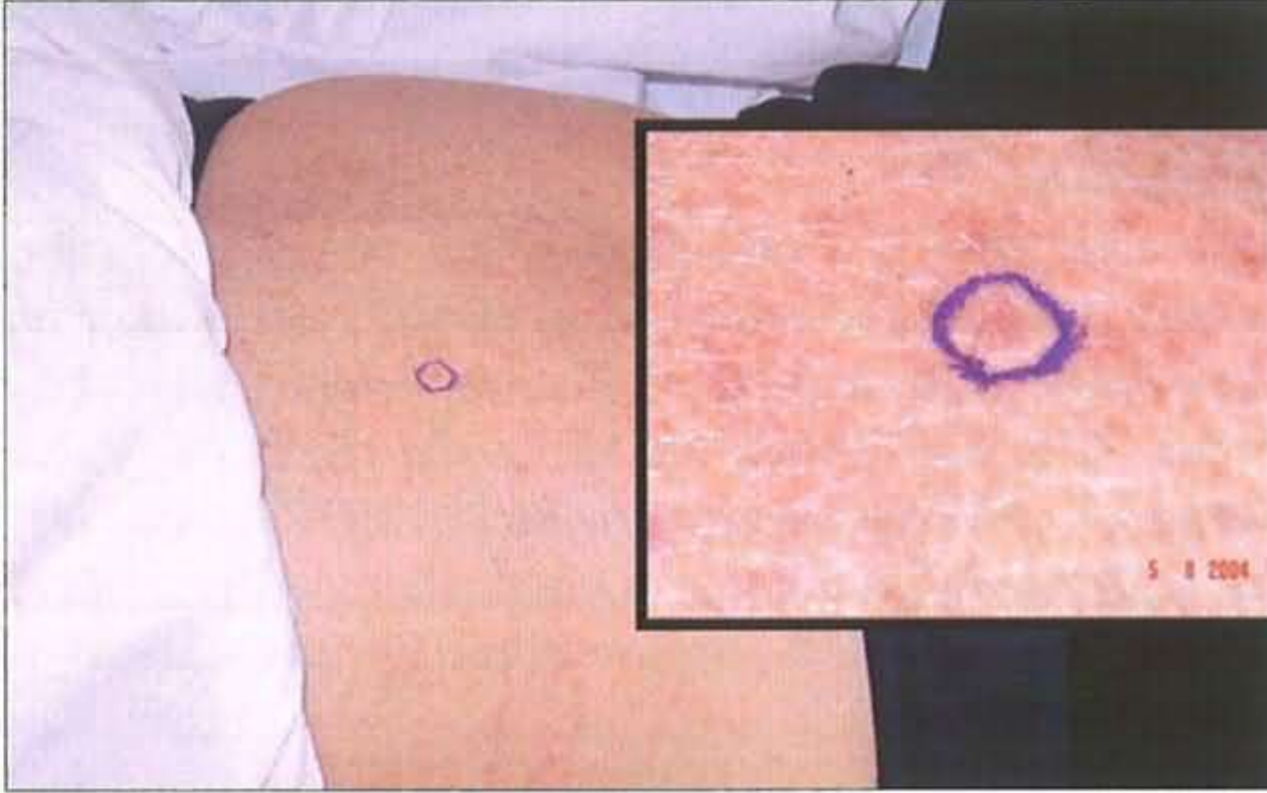


Fig 5 The clinical picture after initial steroid therapy changed, *small scaly papules appeared on the trunk.*

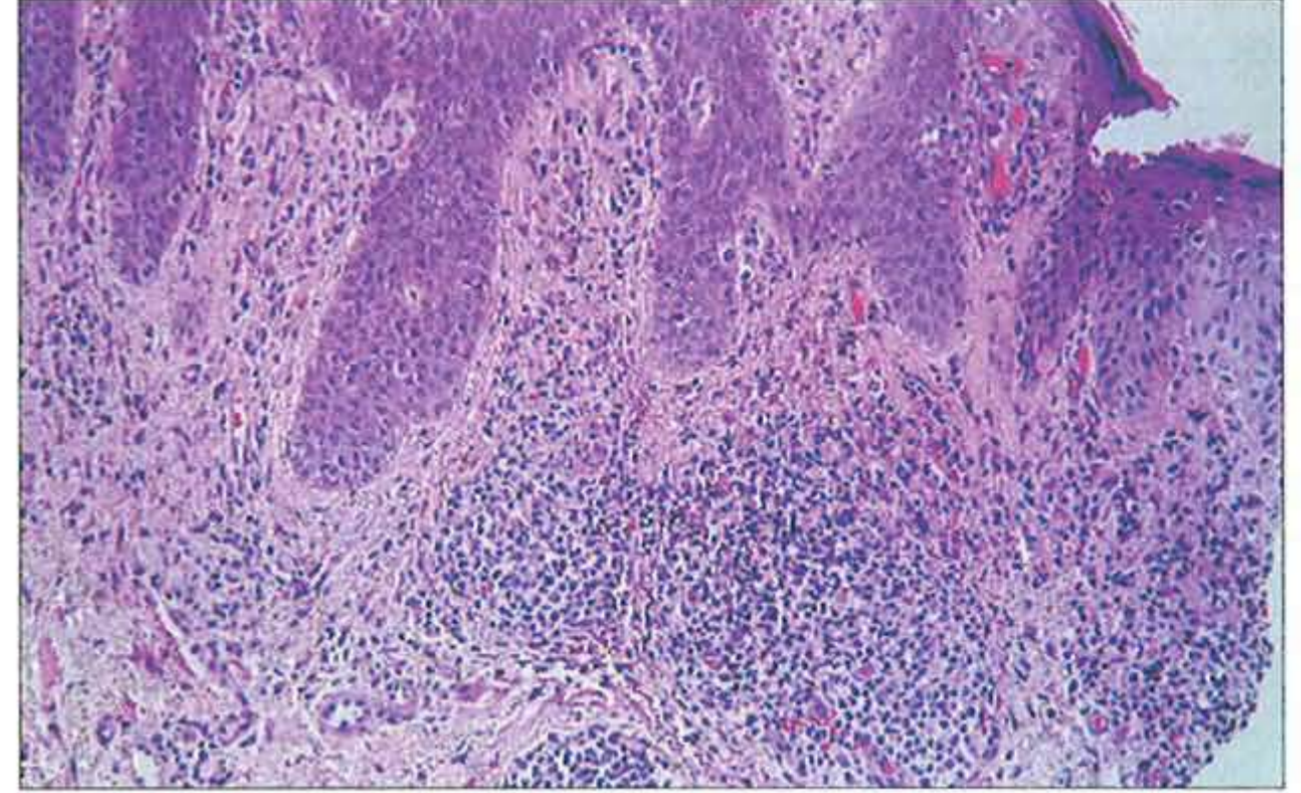


Fig 6 H&E section, x20 magnification showing psoriasisiform epidermis and dense perivascular lymphocytic infiltrate.

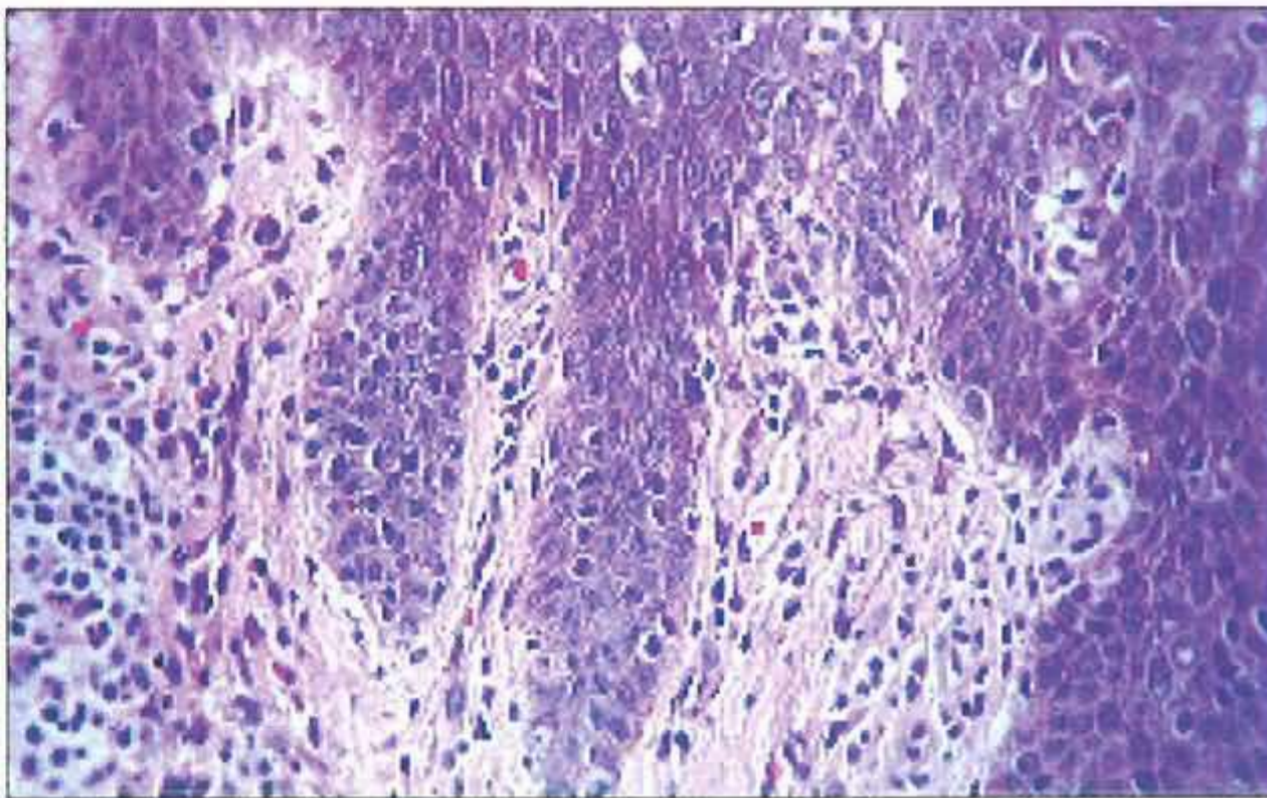


Fig 7 H&E section.

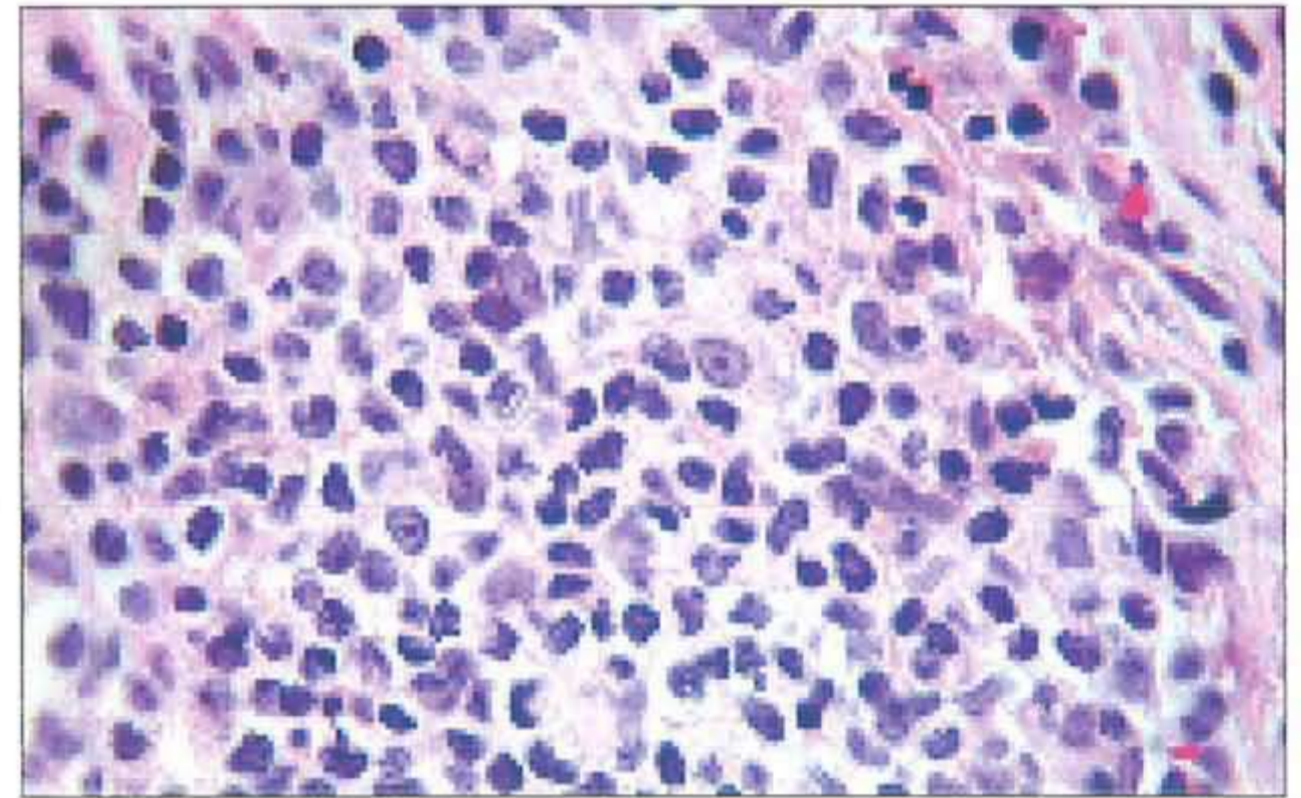


Fig 8 H&E section, with x100 oil immersion lens showing Sézary cells in the dermis.



Fig 9 The lymphocytic count of the patient: absolute lymphocytosis was a herald for diagnosis.

common findings. The age of onset is usually over 65 with male to female ratio of about 1:1.7.^{3,4,9}

“Nondiagnostic dermatitis may precede the overt clinical picture”; this is the exact words of Willemze et al., in 1997 in their initial paper about EORTC classification.² In this case the first biopsy was interpreted as picture of pityriasis rosea with no evidence of lymphoma. Later it was interpreted by another dermatopathologist as pityriasis lichenoides and the possibility of lymphoma was not excluded. Really, early cases of mycosis fungoides always have difficulties in clinico-pathological correlation.^{8,10}

Erythroderma in Sézary is not usually associated with plaques but in this case the evolution of macules into papules was alarming in addition to the size, site and shape of the papules. The erythroderma changed its picture as regards the vivid bright red colour and oedema of the skin under the effect of systemic corticosteroids. Later after more than 10 weeks of therapy, the remains of erythroderma were only exfoliation and minute, discrete flat-topped and brownish-red papules. These papules represent clearly the evolution of plaque stage from a patch stage.

In comparison between the two sections we found in the second one more hyperplastic epidermis (psoriasisiform) and massive perivascular infiltrate of frank abnormal Sézary cells. It is also noticed that epidermotropism is less pronounced compared to Mycosis fungoides.¹¹

Pruritus is the presenting symptom in most cases of cutaneous lymphomas.^{2,5,7} Pruritus is quite nonspecific, nonetheless; when intractable and not responding to conventional therapy the possibility of lymphoma should be raised among other causes of pruritus. The full clinical picture of Sézary syndrome was lacking at the time of presentation even with florid Sézary syndrome in the peripheral blood and in skin, the signs were masked by systemic corticosteroids except for pruritus.

In conclusion, we reported a case of Sézary syndrome which is a rare primary cutaneous T cell lymphoma, it is estimated that every twenty cases of Mycosis fungoides there is one case of Sézary syndrome. It presents with erythroderma, lymphadenopathy and abnormal neoplastic lymphocytes in the peripheral blood. Initial biopsy may be inconclusive and misleading. Other methods for diagnosis should be considered and approached for proper diagnosis.

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