

CASE REPORT

# Invisible Mycosis Fungoides: Not to be Missed in Chronic Pruritus

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## ABSTRACT

**Introduction:** Pruritus without visible dermatoses may be the first manifestation of hematological malignancies such as Hodgkin disease, chronic lymphocytic leukemia and mycosis fungoides (MF) and may precede the definitive diagnosis by weeks to years.

**Case Report:** We present a case of 'invisible' MF associated with chronic generalized pruritus in an elderly patient.

**Conclusion:** Our case highlights the importance of performing skin biopsies in patients with chronic unexplained pruritus, especially in the absence of cutaneous lesions. This can prompt the clinician to consider possible underlying malignancy, such as 'invisible' MF.

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## INTRODUCTION

Pruritus is a prominent symptom of many skin diseases and is also frequently present in hematological malignancies such as Hodgkin disease and occasionally in chronic lymphocytic leukemia and mycosis fungoides (MF) [1, 2]. Hepatobiliary malignancies are also a rare cause. In some cases, pruritus without visible dermatoses may be the first manifestation of such diseases and may precede the definitive diagnosis by weeks to years [2].

We present a case of 'invisible' MF associated with chronic generalized pruritus in an elderly patient. Informed consent was obtained from the patient for being included in the study.

## CASE REPORT

An 80-year-old female presented with a 15-month history of persistent pruritus affecting the arms, back, torso and anterior lower limbs without any obvious dermatoses.

She suffered periods of severe attacks of pruritus, which occurred in waves approximately every few weeks. There were no clear-cut causes for the exacerbations, no worsening with heat and she did not drink alcohol. She was requiring fexofenadine and diazepam each evening to get to sleep. She denied fevers, night sweats or weight loss.

Her past medical history included non-insulin dependent diabetes, hypertension, hypercholesterolemia and glaucoma. She had asthma and allergic rhinitis but denied any history of eczema. There was no known history of any drug allergies. Her regular medications were amlodipine, indapamide, metformin and simvastatin. She had been recently trialed off gliclazide in case this medication had contributed to her pruritus. She was taking regular salbutamol for her asthma. The patient was also using the following ocular drops for her glaucoma: brimonidine, brinzolamide and bimatoprost.

Physical examination was grossly unremarkable with no palpable nodes, no palpable spleen and her skin looked generally dry but normal in appearance with no visible dermatoses present. With an atopic background, it was thought the patient could potentially have some subtle eczema and so was treated with topical steroid ointment, 2% menthol cream and an emollient.

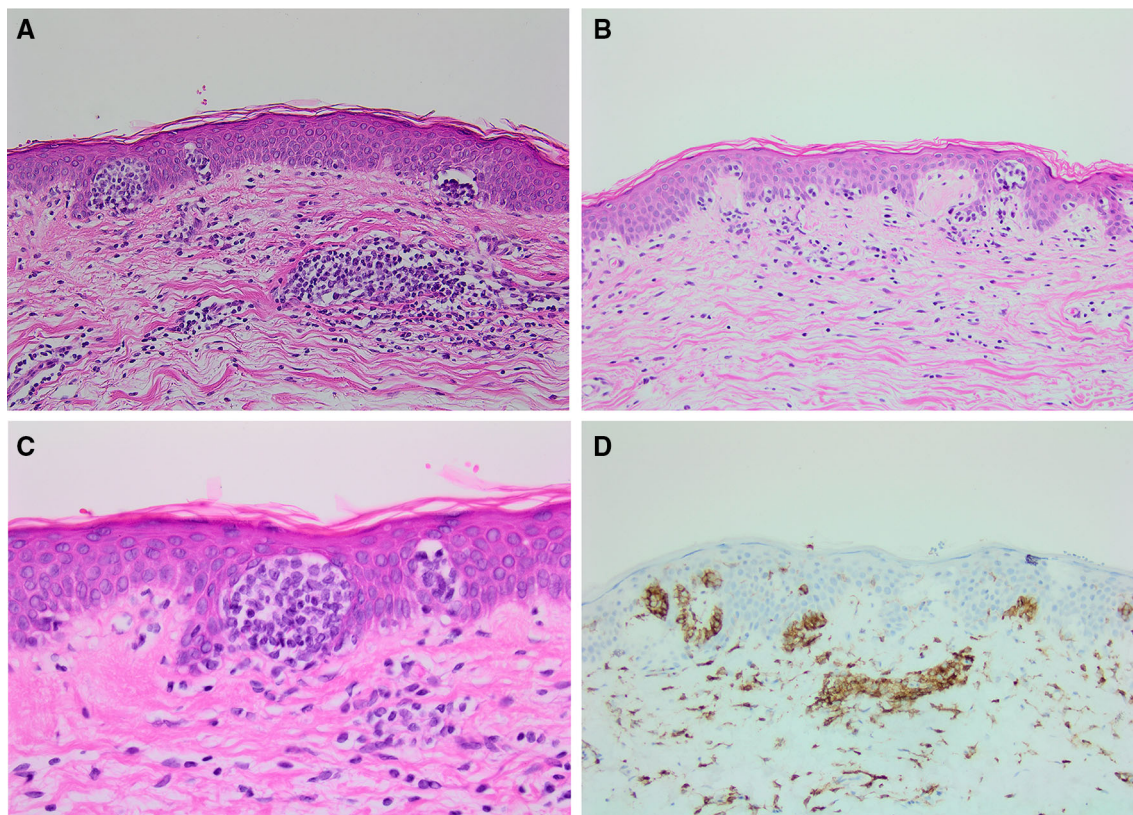
Several weeks later, the pruritus had not resolved and thus further investigations were undertaken. Initial bloods demonstrated a normal full blood count, liver function and erythrocyte sedimentation rate, but she had minor renal impairment. Uric acid was mildly elevated at 0.44 mmol/L. Antibody studies showed an intercellular substance antibody titre of 40 (reference <10) and a basement membrane antibody of <10 (reference <10). Subsequent chest X-ray, abdominal ultrasound and other blood tests were unrevealing.

As a result of these normal tests, two punch biopsies from normal-appearing skin on the abdomen were taken (Fig. 1). Histology showed acanthosis with several collections of lymphocytes in the basal layer forming small Pautrier microabscesses (Fig. 2a). Epidermotropism was also evident (Fig. 2b). The superficial dermis showed fibrosis with a perivascular infiltrate of lymphocytes, some of which had hyperchromatic nuclei. On deeper levels, some of the lymphocytes appeared large and atypical with apoptotic lymphocytes also present (Fig. 2c). Immunophenotyping showed the majority of cells to be CD4 positive (Fig. 2d). There was some loss of CD7 and only rare CD30-positive cells. The immunofluorescence was negative. These results were consistent with a finding of CD4-positive MF.

Subsequent peripheral blood analysis confirmed the presence of Sezary cells (absolute number of circulating Sezary cells was 30 per  $\mu\text{L}$ ). Peripheral blood surface



**Fig. 1** Clinical photograph demonstrating absence of cutaneous lesions and site of biopsies



**Fig. 2** a Histology showing Pautrier Microabscesses (H&E, 20 $\times$ ). b Epidermotropism (H&E, 20 $\times$ ). c Atypical lymphocytes (H&E, 40 $\times$ ). d Immunophenotyping showing CD4 positivity (20 $\times$ ). *H&E* Hematoxylin and eosin stain

markers detected an abnormal T cell population with CD2, CD3, CD4 and CD5 positivity and CD7, CD25 negativity. Human T-lymphotropic virus type 1 and 2 antibodies were negative. Bone marrow biopsy showed a very occasional cell with Sezary morphology and normal numbers of lymphocytes. T cell receptor (TCR) gene rearrangement analysis revealed positive TCR–Beta rearrangement but negative TCR–Gamma rearrangement. The patient was initially commenced on prednisone 10 mg daily and methotrexate 5 mg weekly in combination with folic acid. She was also commenced on topical menthol ointment for the pruritus. The methotrexate was titrated up to 20 mg weekly for a trial of therapy for 8 weeks, while the prednisone was weaned to 3 mg daily. This resulted in some improvement in the pruritus.

Unfortunately, more recently she has developed methotrexate-induced mucositis and raised liver function tests, necessitating cessation of the methotrexate.

## DISCUSSION

Mycosis fungoides is the most common form of cutaneous T cell lymphoma and represents approximately 50% of all lymphomas arising primarily in the skin [1, 2]. Cutaneous lesions can be divided morphologically into patches, plaques, and tumors, and this clinical morphology is used to classify the disease into three clinical stages accordingly [2]. The clinical course can be protracted over years and commonly manifests as generalized or localized pruritus with associated dermatoses. However,

very rarely MF can be clinically occult in the setting of pruritus as demonstrated in our case and has been termed ‘invisible’ MF [3, 4]. It is the significant association of generalized pruritus with potential underlying malignancy that can lead to diagnostic uncertainty and should therefore prompt clinicians to perform investigations to exclude systemic involvement.

‘Invisible’ MF has been previously reported in four cases [3–6]. Two cases occurred as incidental findings in asymptomatic patients [3, 4]. The other case reports described two patients in their 70s, who initially presented with generalized long-standing pruritus with no visible cutaneous lesions of MF [5, 6]. In our case, the only manifestation of MF in the patient was chronic pruritus and it was only after taking biopsies from pruritic, normal-appearing skin that a definitive diagnosis could be made.

## CONCLUSION

Our case highlights the importance of performing skin biopsies in patients with chronic unexplained pruritus, especially in the absence of cutaneous lesions. In particular, more attention should be given to elderly patients who complain of persistent pruritus, which should prompt the clinician to consider possible underlying malignancy, such as ‘invisible’ MF.

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**Compliance with ethics guidelines.** Informed consent was obtained from the patient for being included in the study.

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