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Case Report

Leukaemia cutis in a patient first presented with chronic plaque psoriasis

皮膚白血病發生於慢性斑塊型銀屑病患者一例

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A 56-year-old gentleman initially presented with chronic plaque psoriasis with partial response to topical treatment subsequently developed atypical cutaneous lesions over the thighs, which were atypical for psoriasis. Alternative diagnosis was suspected. Skin biopsy and further investigations established the diagnosis of leukaemia cutis and the underlying asymptomatic acute leukaemia. Clinical features of leukaemia cutis, its incidence, treatment and prognosis were discussed.

一名五十六歲男士初期患上慢性斑塊型銀屑病，在外敷治療後有部份改善，但其後大腿上長出與牛皮癬不符的皮損，在血液及切皮檢查後，確認為皮膚白血病並診斷出其隱藏的急性白血病。皮膚白血病的臨床表現，其發病率、治療及預後將一一討論。

Keywords: Acute leukaemia, chronic plaque psoriasis, leukaemia cutis

關鍵詞：急性白血病，慢性斑塊型銀屑病，皮膚白血病

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Case report

A 56-year-old male construction site worker presented with multiple itchy plaques over scalp and limbs for 6 months. He enjoyed good past health without any known drug allergy, and his family history was unremarkable. Moreover, he was a non-smoker and non-drinker.

At his first visit to our clinic, examination of skin demonstrated thickened, adherent plaques over scalp and well-demarcated erythematous plaques

over the back and lower limbs. There was no nail or joint abnormality. The overall clinical picture was suggestive of psoriasis, chronic plaque type, with 3% body surface area involvement. He was then prescribed aqueous cream, 5% cetirimide shampoo, elomet scalp application and combined synalar 0.025% cream with 2-4-2 ointment (salicylic acid 2%, coal tar solution 4% and precipitated sulphur 2%) as treatment.

Twelve weeks later, he was reviewed in our clinic for progress. He expressed some cutaneous improvement on the topical treatment. However, some non-specific cutaneous lesions (Figure 1) were noted over bilateral thighs, which were atypical for psoriasis.

In view of the atypical lesions, further clinical information was gathered. Patient denied any constitutional symptoms (e.g. fever, weight loss) and he enjoyed good health except for one episode of heat stroke at work. He had no travel, contact or trauma history before onset of the skin disease, and all his household members were well.

Skin biopsy and blood investigations were arranged to rule out differential diagnoses as listed below in Table 1.

Table 1. Differential diagnoses

Inflammatory	• Psoriasis • Discoid eczema / Prurigo nodularis • Arthropod bite reactions • Vasculitis / Pityriasis lichenoides et varioliformis acuta • Subacute cutaneous lupus erythematosus • Sweet syndrome
Infective	• Folliculitis • Deep fungal infection • Atypical mycobacterial infection
Neoplastic	• Adnexal tumour • Cutaneous lymphoma, tumour stage • Pseudolymphoma • Leukaemia cutis • Langerhans cell histiocytosis • Xanthogranuloma • Xanthoma • Cutaneous metastasis

Blood investigations revealed a marked anaemia (haemoglobin 7.7 g/dL) and neutropenia (WBC 1.4 x 10^9/L, neutrophil 0.1 x 10^9/L) with 3% atypical mononuclear cells, and elevated erythrocyte sediment rate 69 mm/hr, while liver and renal function tests and antinuclear antibody were unremarkable.

Skin biopsy showed focal pseudoepitheliomatous hyperplasia and a cellular infiltrate throughout the dermis and subcutaneous tissue with perivascular and periadnexal accentuation (Figure 2). The

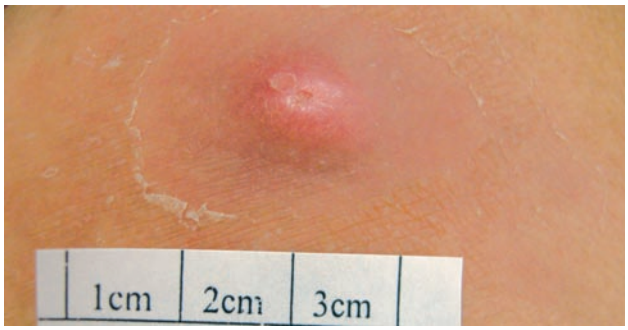

Figure 1. A 1 cm erythematous nodule with central umbilicated excoriation and a peripheral rim of hyperkeratosis with inner collarette scaling on the thigh of patient.

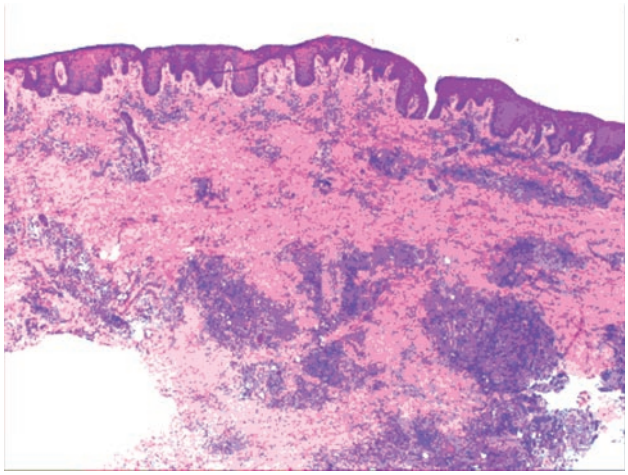

Figure 2. Low power view showing cellular infiltrate with periadnexal and perivascular accentuation, involving predominantly lower dermis and upper subcutis. The upper dermis is less involved and no epidermotropism is present.

cellular infiltrate was composed of large oval cells with occasional mitoses, some plasma cells and granulocytes (Figure 3). The large oval cells are atypical, with vesicular nuclei, prominent nucleoli, and small amount of amphophilic to mildly eosinophilic cytoplasm. Further immunohistochemical study confirmed those large oval cells were positive for leucocytes common antigen (LCA) and myeloperoxidase (Figure 4), but negative for cytokeratin (MMF116), S100, CD30, CD3 and CD20. Moreover, the skin biopsy was negative for both fungal and acid fast bacilli smear and culture. Overall, histological and immunohistochemical features are consistent with myeloid leukaemic infiltration.

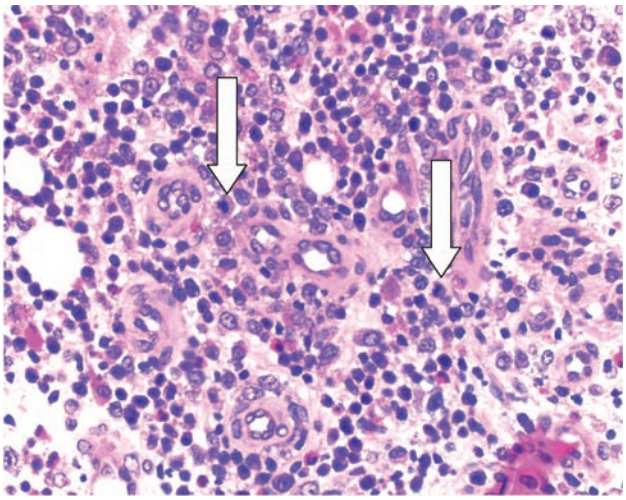

Figure 3. Higher power view shows that the infiltrate is composed of large atypical cells admixing with granulocytes. The atypical large cells are non-cohesive and possess irregular nuclei with prominent nucleoli. There is also appreciable amount of amphophilic cytoplasm. Mitosis is easily found in some areas (white arrow). The infiltrate is also rich in plasma cells in this field.

He was admitted for inpatient care for the marked anemia and neutropenia before the skin biopsy result was available. Bone marrow examination was performed and acute erythroid leukaemia (acute myeloid leukaemia (AML), M6) was found. The skin biopsy and clinical findings confirmed the diagnosis of leukaemia cutis.

Induction chemotherapy (Daunorubicin and Ara-C 3+7 regimen) was started after the diagnosis of AML and blood transfusion was also given. Unfortunately, the patient had rapid deterioration with multiple complications including sepsis, disseminated intravascular coagulation, forefoot gangrene and multi-organ failure, and succumbed within two months of establishing the diagnosis of AML despite intensive care.

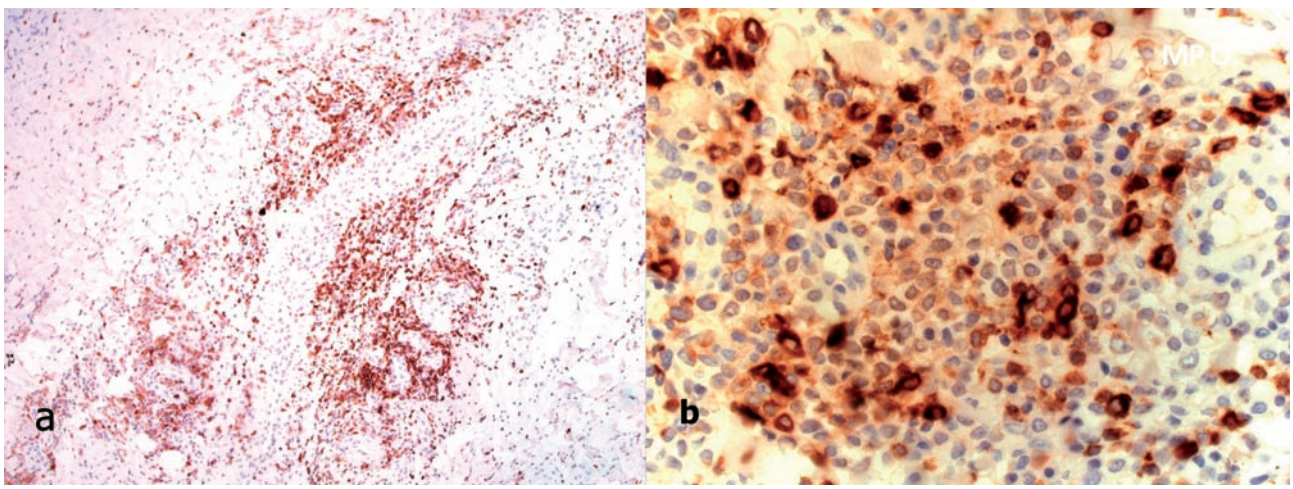

Figure 4. (a) The tumour cells are diffusely leucocytes common antigen positive, and (b) a small proportion of the large cells are positive for myeloperoxidase.

Discussion

Leukaemia cutis is a rare cutaneous eruption that may be difficult to diagnose and is usually associated with a poor prognosis. It is defined as 'the infiltration of neoplastic leukocytes or their precursors into the epidermis, the dermis, or the subcutis, resulting in clinically identifiable cutaneous lesions'.[1]

Apart from leukaemia cutis, there are other cutaneous manifestations of leukaemia as well, which can be categorized into 'disease-related' versus 'treatment-related' (Table 2).[2-4]

The typical lesions of leukaemia cutis are red-brown to violaceous, or plum papules and nodules, while indurated or haemorrhagic plaques, perifollicular acneiform papules, macules, ulcers, bullae,[5] and palpable purpura are less frequently seen. From previous case reports, other unusual manifestations of leukaemia cutis may also mimic stasis dermatitis,[6] erythema nodosum, erythema annulare centrifugum, pyoderma gangrenosum, urticaria, urticaria pigmentosum, guttate psoriasis, chronic paronychia, and macular erythema. The trunk and the lateral surface of the extremities are the sites of predilection for myeloid leukaemia, while face is more commonly involved in the lymphocytic leukaemia.[5]

For our patient presented in this case report, it is hard to conclude whether he had leukaemia cutis together with psoriasis, or leukaemia cutis presented initially as psoriasiform dermatitis before developing the non-specific lesions. Skin biopsy had only been performed on the non-specific lesion but not the psoriasiform plaques.

Though the lesions of leukaemia cutis were noticed first and led to the diagnosis of AML in this patient, his cutaneous disease could not be categorized as 'aleukaemic leukaemia cutis' or 'aleukaemia cutis' since the diagnosis of acute erythroid leukaemia was made very soon after the diagnosis of leukaemia cutis. Aleukaemic leukaemia cutis or aleukaemia cutis is defined as 'the presence of extra-medullary leukaemic cell infiltration in the absence of blood or bone marrow involvement before or within 1 month of diagnosis'. According to the literature, up to 7% of patients with leukaemia cutis have solely localised disease at presentation regarded as aleukaemic leukaemia cutis. On the other hand, leukaemia cutis may rarely signify or herald disease progression in a subset of patients with myelodysplastic syndrome to acute myelogenous leukaemia.[6]

Table 2. Cutaneous manifestations of leukaemia

Disease-related:	Treatment-related:
• Purpura and ecchymoses	• Adverse drug reactions including alopecia, stomatitis and some specific patterns secondary to chemotherapy:
• Gingival hypertrophy (acute monocytic and myelomonocytic leukaemia)	Acral erythema (hand-foot syndrome)
• Leukaemic vasculitis	Neutrophilic eccrine hidradenitis
• Opportunistic infections (particularly fungal and viral)	Cutaneous eruptions of lymphocyte recovery
• Intraepidermal vesicular eruptions mimicking transient acantholytic dermatosis (Grover's disease) and Hailey-Hailey disease	• Opportunistic infections (particularly fungal and viral)
• Reactive inflammatory process	• Acute or chronic graft-versus-host disease
• Acute leukocytoclastic vasculitis	
• Pyoderma gangrenosum	
• Sweet's disease	

Chronic benzene exposure is one of the well-known risk factors for leukaemia. This patient might have the potential risk of chronic benzene exposure through inhalation of vapour from benzene-containing products such as glues, paints or detergents at work.

Leukaemia cutis is associated with all types of leukaemia and has disproportionately high incidence in adult T-cell leukaemia (Table 3). The French-American-British classification divides AML into 8 main subtypes M0 to M7, based on the morphology and the state of differentiation of the leukaemic cells. Acute myelomonocytic leukaemia (AML-M4) and acute monocytic leukaemia (AML-M5) have the highest rates of skin involvement among all the subtypes and these rates are reported to be as high as 30%.

In leukaemia cutis, the histopathologic findings often show a diffuse monomorphous infiltration of leukaemic cells in the dermis and subcutis, with prominent single arraying of neoplastic cells between collagen bundles. Extensive involvement and distortion of skin appendages and vessels are characteristic as well. One cannot rely on skin biopsy findings alone to determine the type of leukaemia, which has to be confirmed by the more reliable cytochemical and cytomorphologic studies of bone marrow and peripheral blood smear.[7,8]

Several studies have demonstrated that, in the presence of leukaemia cutis, the disease course of AML or chronic myelogenous leukaemia (CML) would be aggressive and the length of survival would be short as demonstrated in our case. Kaddu et al showed an average survival time to be 7.5 months in AML and 9.4 months in CML.[7] Another study by Baer et al revealed that of 18 patients with leukaemia cutis in AML, 90% had other sites of extramedullary involvement, including meningeal involvement in 6 patients.[9] In a smaller case series by Shaikh et al, all 5 patients with AML had a median survival of only 12.5 weeks after they were diagnosed to have leukaemia cutis.[10] Skin infiltration in chronic lymphocytic leukaemia (CLL) is relatively rare. A case series of 42 patients with leukaemia cutis reported by Su et al showed that the longest survival was found in the group of CLL with a mean survival of 16 months among these 16 patients. A literature review from 1965-2001 reported an overall survival rate of 6% at 2 years in AML patients with leukaemia cutis compared with 30% in those without leukaemia cutis.[1,8]

Treatment for leukaemia cutis is directed at eradicating the leukaemic clone by using systemic chemotherapy, and the treatment regimen is determined by the subtype of leukaemia and the patient's tolerance. Under certain circumstances, such as resistant or recurrent skin disease, local treatment in the form of electron beam therapy may be used.

In conclusion, leukaemia cutis is a rare cutaneous disease which can be associated with any type of leukaemia and is regarded as a poor prognostic

Table 3. Incidence of leukaemia cutis in various leukaemia in the United States [adopted from reference 1]

Type of leukaemia	Incidence in the United States	Percentage of patients with leukaemia cutis (%)
Acute myeloid leukaemia (AML)	2.5 cases per 100,000 population	13
Acute lymphocytic leukaemia (ALL)	1.3 cases per 100,000 population	3
Chronic myelogenous leukaemia (CML)	1-2 cases per 100,000 population	2-8
Chronic lymphocytic leukaemia (CLL)	2.3 cases per 100,000 population	8
Hairy cell leukaemia	0.6-2.9 cases per 1,000,000 population	8
Adult T-cell leukaemia	Extremely low	40-70

sign. Due to its rarity and varied clinical morphology mimicking other more common dermatoses, skin biopsy and blood tests are required to establish the diagnosis of leukaemia cutis.

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