Haematological malignancies presenting with skin manifestations

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Abstract

It is rare for a patient with haematological malignancy to initially present to a dermatologist with related skin manifestations. In this case series we describe 4 patients with haematological malignancies who presented to our unit over a 2 year period with related skin lesions. The skin manifestations described include leukaemia cutis, erythema nodosum, papular urticaria like lesions, generalized pruritus and exfoliative dermatitis. Increased awareness on these rare presentations should help early recognition of these treatable and potentially fatal conditions.

Introduction

It is not rare for patients with haematological malignancies to have cutaneous manifestations. These can occur due to various reasons. Infections and thrombocytopaenia due to bone marrow involvement can give rise to skin lesions. Cutaneous lesions can also result from direct infiltration of the skin by the tumour cells. Some specific skin manifestations occur as a part of a paraneoplastic syndrome. Patients may develop skin lesions following chemotherapy. However it is unusual for a patient with haematological malignancy to initially present with related skin manifestations. When it does occur, early recognition is vital in making a diagnosis and referring the patient for treatment.

Case report 1

A 46 year old female presented to the dermatology unit with asymptomatic reddish skin nodules over limbs and trunk for 2½ months, painful oral ulcers and gum bleeding for 2 months, and fever for 1 week.

On examination she was not pale, had ulcers on the lower lip, tongue and the buccal mucosa. There were erythematous skin nodules with depressed necrotic centers on the limbs and trunk (Figure 1). She had no lymphadenopathy or organomegaly.

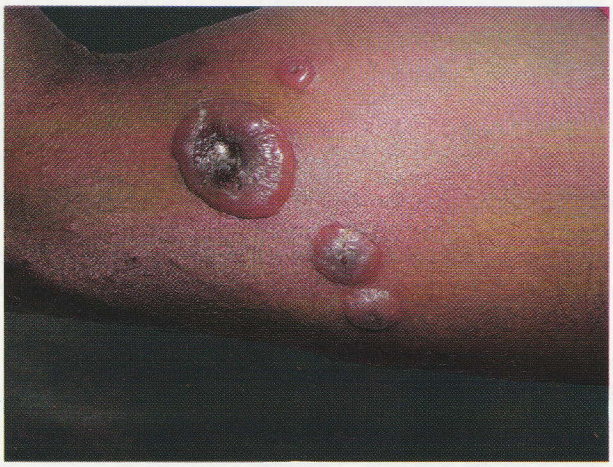

Figure 1. *Leukaemia cutis: Erythematous skin nodules with depressed necrotic centers.*

89% of the white cells in her blood picture appeared abnormal. There were blast cells with increased nuclear: cytoplasmic ratio and prominent nucleoli. The red cells and platelets were normal.

The histology of the skin nodule showed a heavy atypical mononuclear cell infiltrate in the upper and mid dermis. Some of these cells had cerebriform nuclei (Figure 2). The appearance was consistent with leukaemic or lymphomatous infiltration of the dermis.

The bone marrow examination showed a hypercellular marrow with depressed erythropoiesis. The granulopoiesis was markedly depressed, and more than 60% of cells were abnormal promyelocytes with hypogranular cytoplasm and bilobed nuclei (Figure 3). 90% of the abnormal cells showed Sudan Black positivity. The appearance was consistent with acute myeloblastic leukaemia (AML) – M3 variant (acute promyelocytic leukaemia).

This patient was transferred to Cancer Institute Maharagama for chemotherapy. She died of septicaemia following pneumonia prior to commencement of treatment.

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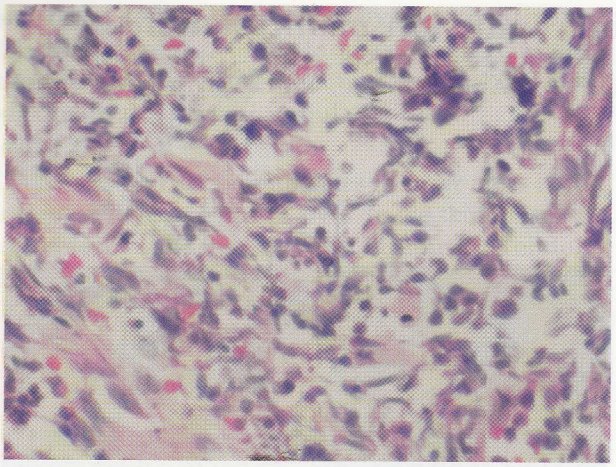

Figure 2. *Histological apperance of leukaemia cutis: atypical mononeuclear cells with cerebriform neuclei (H & E 40x).*

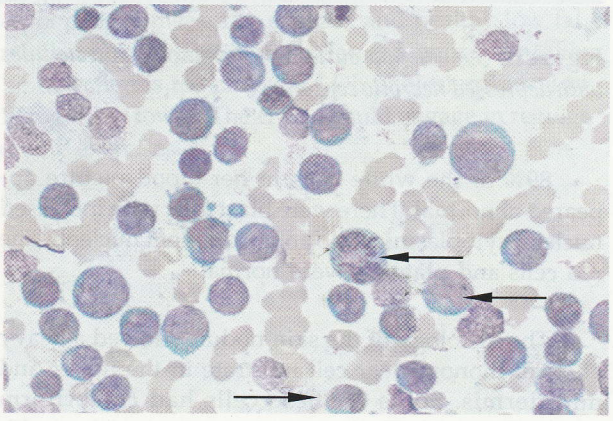

Figure 3. *Bone marrow appearance: abnormal promyelocytes with hypogranular cytoplasm and bilobed neuclei.*

Case report 2

A 27 year old male presented with recurrent painful skin nodules over the shins, trunk and upper limbs associated with malaise, fever and arthralgia. His previous skin biopsy was consistent with erythema nodosum. He also complained of recurrent painful orogenital ulceration for 6 months.

On examination he was pale, had deep apthoid oral ulcers and genital ulcers. There was no lymphadenopathy or organomegaly.

The possibility of Behcet's syndrome was considered at that stage.

Skin biopsy showed septal panniculitis with lymphocytic vasculitis.

His ESR was 100mm 1st hour. He had bicytopenia (Hb 9.8g%, MCV 107 fl, MCH 34pg, MCHC 32 g/dl; WBC 5000/mm^3, N-28%, L-44%, M-11%, E-1%; Platelets 132000/mm^3) and reticulocytosis (5.4%).

Blood picture showed normochromic and normocytic red cells, polychromasia, and occasional nucleated red cells. About 15% of the white cells were hypergranular promyelocytes. Platelets count was low.

Bone marrow biopsy revealed that more than 90% of total granulocytes were blast cells. The blast cells were positive for Sudan Black stain. Erythropoiesis and megakaryopoiesis were depressed. The marrow findings were consistent with acute myeloid leukaemia (AML M1).

Abdominal ultrasound scan was normal.

The patient was referred to the oncologist for chemotherapy.

Case report 3

A 76 year old lady had pruritic papules over her upper and lower limbs for 1 year. She had been treated for papular urticaria. She complained of anorexia and loss of weight for 3 months.

On examination she had papules and ulcerative nodules on the limbs and neck (Figure 4). She was pale, had generalized lymphadenopathy but no organomegaly.

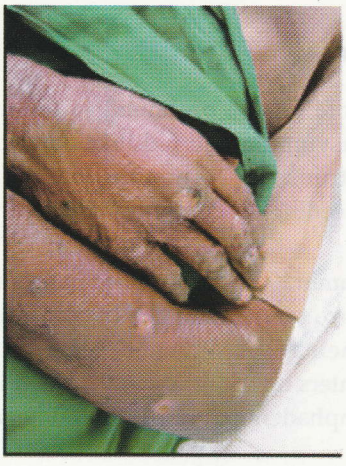

Figure 4. *Papules and ulcerative nodules on the hands and forearms of Case 3.*

Her ESR was 110 mm 1st hour. Haemoglobin was 10.2 g%, white cell count 11500/mm^3 (N-31%, L-52%, E-11%, M-4%) and the platelet count 184000/mm^3. Her blood picture showed mild lymphocytosis and small lymphocytes with clumped chromatin. Red cells and platelets were normal.

The chest radiograph and ultrasound scan of the abdomen were normal.

Her lymph node biopsy showed a fully effaced normal architecture. The node was infiltrated by small and intermediate sized lymphocytes, some showing prominent nucleoli. The appearance was suggestive of non-Hodgkin's lymphoma small and large cell type (intermediate grade in working formulation).

This patient died due to septicaemia during chemotherapy.

Case report 4

A 37 year old male who had generalized pruritus for 3 months was admitted with exfoliative dermatitis. On examination he was erythrodermic but did not have lymphadenopathy or hepatosplenomegaly.

His ESR was 65 mm 1st hour. His haematological investigations were as follows: Hb 11.1g/dl, WBC 9800/mm^3 (N-21%, L-76%, M-1%, E-1%), platelets 175000/mm^3; blood picture showed normochromic normocytic red cells, lymphocytosis with atypical cells, and normal platelets.

His skin biopsy showed an irregular acanthotic epidermis. There was no exocytosis. The dermis contained a moderately dense inflammatory infiltrate comprising lymphocytes (some were atypical) and histiocytes.

His bone marrow was consistent with non-Hodgkin's lymphoma.

Discussion

Within a 2 year period, we diagnosed 4 patients with haematological malignancy who presented primarily with skin lesions.

The first patient's presenting feature was leukaemia cutis due to skin infiltration by neoplastic cells. The underlying pathophysiology of this specific migration of leukaemic cells to the skin is poorly understood. There is evidence to suggest that in leukaemia cutis the presence of T cell related antigens on the surface of leukaemic cells may promote a specific tropism to the skin[1].

Leukaemia cutis is not a common cutaneous manifestation of leukaemias. Out of the different types, it occurs in increased frequency in acute myeloid leukaemias (13%)[1]. Of the 8 main types of acute myeloid leukaemias (M0 to M7), the subtypes M4 and M5 are known to cause leukaemia cutis commonly[1,2]. However, in most cases of leukaemia cutis the systemic disease precedes the cutaneous manifestations. AML M3 variant commonly presents with haemorrhagic diathesis due to thrombocytopaenia and disseminated intravascular coagulation[3]. It is unusual for it to present as leukaemia cutis as in our patient.

The histology of leukaemia cutis depends on the type of leukaemia but typically has minimal epidermal involvement with dermal leukaemic cell infiltrate predominantly around vessels and adenexial tissue.

The presence of leukaemia cutis is a poor prognostic sign. About 90% of patients with these skin lesions have extramedullary involvement[1], although it was not the case in our patient.

As leukaemia cutis is a cutaneous manifestation of a systemic disease, the treatment should be directed at the underlying haematological malignancy. All-trans retinoic acid is the specific treatment for AML M3 variant. Response to treatment is generally good if disseminated intravascular coagulation can be controlled[3].

Erythema nodosum is a rare but a known cutaneous manifestation of AML[1]. Patient in case 2 initially had erythema nodosum like lesions and criteria for diagnosis of Behcet's syndrome. Later his blood film and bone marrow findings showed evidence of AML M1. There are reports of Behcet's syndrome associated with solid tumours like lung and renal carcinomas as well as AML[4,5]. These erythematous nodules in AML usually show a leucocytoclastic vasculitis, but lymphocytic vasculitis (as in our patient) has also been reported[6].

Cutaneous eruptions simulating papular urticaria have long been described in leukaemias and lymphomas. Exaggerated hypersensitivity reactions to insect bites and intractable pruritus are recognized presentations of non-Hodgkin's lymphoma[7,8]. It is important to investigate appropriately and follow up these patients for development of underlying haematological malignancy.

Exfoliative dermatitis, also referred to as erythroderma, is an inflammatory disorder of the skin that may occur as an idiopathic entity or as a manifestation of various cutaneous or systemic

disorders, as well as after exposure to a number of drugs. The common causes are eczemas, psoriasis, and drug eruptions. Rarely it is caused by haematological malignancies such as acute and chronic leukaemia, lymphoma and myeloma[9].

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