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LEUKAEMIA CUTIS IN A PATIENT WITH ACUTE MYELOGENOUS LEUKAEMIA: CASE REPORT

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SUMMARY

Leukaemia cutis is a specific lesion of leukaemia in which there is leukaemic cell deposit in the skin. There are few reports of this condition in our environment. Several mechanisms have been postulated for the pathogenesis of the disease. One of which is the tissue selective homing of a unique sub-population of malignant clone of cells. The presence of leukaemia cutis does not seem to worsen the prognosis as the acute myeloid leukaemia is an equally lethal disease. The fatality of the disease is compounded by the unavailability of the right regimen in our patient. This paper documents a case of leukaemia cutis in a patient initially diagnosed to have AML who developed skin lesion in remission. A skin biopsy was found helpful in diagnosing the first sign of relapse in a patient in haematological remission.

INTRODUCTION

Leukaemia cutis is one of the cutaneous manifestations of leukaemia. It is a specific lesion of leukaemia in which there is leukaemic cell infiltration into the epidermis, dermis or sub-cutis, resulting in clinically identifiable lesions(1,2).

The term leukaemia cutis embraces all skin infiltration by leukaemic cells of the granulocytic, monocytic and lymphoid leukaemias in contrast to granulocytic sarcoma which is specific for myelogenous leukaemia. Well documented reports of cutaneous tumour deposit dates back to the earliest part of last century when the initial description were mainly in the myelogenous leukaemias, hence the term granulocytic sarcoma of the skin was used by most workers(3,4). The term granulocytic sarcoma is more appropriate for these tumours rather than the previous term chloroma. The reason being that the green colour (hence chloroma), seen with extramedullary tumour deposits is not present in all tumours, and similar cutaneous tumour deposit has subsequently been described in other forms of leukaemia. Monocytic leukaemia, chronic lymphocytic leukaemia and chronic granulocytic leukaemia are most commonly associated with leukaemic infiltrations of the skin, with a reported incidence of 10-50%, 6-10% and 5.5% respectively(5). Granulocytic sarcoma is more common among children, with a particularly high incidence in congenital leukaemia (6). Leukaemids on the other hand result from immunological responses to the presence of tumour antigens and on histology(7), lesions in leukaemids do not contain leukaemic cells. Leukaemids occur more frequently than leukaemia cutis.

There had not been any known racial or ethnic predilection for leukaemia cutis. The diagnosis is often difficult to make from routine haematoxylin-eosin stain as this is usually inadequate to characterise the cells, except in a situation in which the patient has already developed overt leukaemia(8). Cytochemical stains particularly immunoperoxidase are usually necessary to characterise cells in situations where the diagnosis is not so obvious(9). However, with the aid of monoclonal antibodies, leukaemia cutis has been found to occur more frequently than previously thought. Treatment is directed towards the leukaemic process. Due to the rarity of leukaemia cutis, it is not surprising that there are very few reports of this condition in our environment. We therefore report a case of leukaemia cutis in a 28 year old patient with acute myeloid leukaemia in whom the skin lesion developed three months after the leukaemia was diagnosed.

CASE REPORT

A 27-year old male physician working in a private hospital was apparently well until three weeks prior to admission when he noticed he was bleeding from the gum, associated with joint pains and fever. These symptoms he concealed to himself until when he developed cough, breathlessness and pedal oedema. He was then rushed to the emergency room of our teaching hospital by the wife. General examination showed an acutely ill-looking man, febrile, severely pale, with sub-conjunctival haemorrhage, proptosis and blindness. He was also bleeding from the gum. He had generalised lymphadenopathy, bilateral pitting pedal oedema, tender, smooth and soft hepatomegaly of 10cm below the costal margin. The spleen was not palpable. The cardiovascular system showed evidence of anaemic heart failure. Full blood

count on admission revealed a PCV of 15%. WBC-45000/mm³, and a platelet count of 40,000/cu mm.

Peripheral blood film review showed, leukocytosis with 90% myeloblast and promyelocyte with Auer rods, marked neutropenia and thrombocytopenia. Bone marrow aspiration confirmed acute myeloid leukaemia (AML), FAB class M₂ morphology. He was resuscitated with red blood cell concentrate and platelet transfusion. He also had broad spectrum antibiotics, even though blood culture yielded no growth.

The patient could not afford the standard DAT regime comprising of daunorubicin, cytosine arabinoside plus 6-thioguanine. In addition these drugs were not easily available in the country at the time the patient presented. He was therefore treated with a cheaper regimen for the first cycle. The regimen used consisted of cyclophosphamide, vincristine, cytosine arabinoside and prednisolone (COAP) as a 14 day cycle. During the cycle he regained his vision but had severe leucopaenia with occasional myeloblast on the peripheral blood film. He also developed oral candidiasis, which was treated with oral nystatin drops, with good response. By the time he was due for the 2nd cycle of chemotherapy, the local branch of the National Medical Association (NMA) had received a report of the patient's inability to procure drugs. The NMA consequently donated daunorubicin, oncovin and cyclophosphamide for his treatment which he received for the second cycle as a 21 day regime. Full blood count during the resting phase of the cycle was PCV-24%, WBC 4,900/mm³, (a differential of N-70%, lymphocyte 25%, monocyte 2%). The platelet count was 281,000/mm³. The patient subsequently went into remission with a bone marrow blast of <5%. By the 3rd month post diagnosis, he developed tender firm subcutaneous nodules on the skin of the lower limb (Figure 1) which subsequently became generalised, though the peripheral blood film showed normal differential count. Associated with this skin nodules were excruciating joint pain and stiffness. A presumptive diagnosis of kaposi sarcoma was entertained due to the prevalence of HIV in sub-Saharan Africa. However the retroviral screening was negative. The histology of the biopsy specimen of the skin nodule revealed infiltration of the dermis and sub-cutaneous tissue by myeloblasts, myelocytes, band forms, and neutrophils. The histological diagnosis of the skin nodules was leukaemia cutis. A repeat bone marrow aspiration showed 15% myeloblast and reduced megakaryocyte population. Based on the above a diagnosis of bone marrow relapse of the AML with leukaemia cutis was made.

Figure 1

Nodular eruptions on the lower limbs



A re-induction course of cytotoxic drug was instituted consisting of COAP. Following this course of chemotherapy, the patient became less dependent on blood products. His peripheral blood film gradually mimicked that of chronic granulocytic leukaemia. There was also a steady decrease in size and number of the skin nodules until it completely cleared from the skin. With this marked improvement in the patient's clinical state he requested for the outpatient management, declining further admission.

At five months after the diagnosis of AML was made, he was brought back to the emergency room in a poor clinical state and in obvious respiratory failure. He died almost immediately despite resuscitative measures.

DISCUSSION

The lesions of leukaemia cutis may be localised and appear benign. They may present as macules, plaques or nodules and may mimick sarcoidosis or lupus vulgaris. On the other hand lesions may be extensive, erythematous, haemorrhagic, pruritic and tender. Diffuse infiltration of skin of the face, eyebrows, and cheeks may produce the leonine facies seen in lepromatous leprosy. The presence of bullae and ulcers may suggest underlying chronic lymphocytic leukaemia. Cutaneous lesion of acute leukaemia tends to affect the face and extremities, as was the case of our patient. Mucous membrane involvement is common in monocytic leukaemia. What may appear to be some haemorrhage under the skin may actually be due to cutaneous deposits of leukaemic cells. The morphology of the cells in the marrow or peripheral film usually correlates with the cells in the skin as was observed in our patient. Cellular infiltrates of cases with chronic lymphocytic leukaemia shows the presence of small lymphocytes whereas, lymphoblasts are found in acute lymphoblastic leukaemia and immature granulocytes in acute and chronic granulocytic leukaemia. Monocytes are present in cutaneous deposits in monocytic leukaemia. A retrospective study showed that 55% of patients developed the skin lesion after the leukaemia had been diagnosed, as was the case in our patient.

Thirty eight per cent had skin involvement at the time the leukaemia was diagnosed, and 7% had aleukemic leukaemia cutis (ALC)². This term, ALC, is used when leukaemic cells are absent in the peripheral blood film but can be found in non-haemopoetic tissue, such as the skin. It has been suggested that this aleukemic phase may be the leukopenic phase of the disease and careful examination of the blood smear may actually reveal abnormal cells. Other terms that have been proposed for aleukemic leukaemia cutis include true histiocytic lymphoma, lymphoma like presentation of leukaemia(2).

The pathogenesis of leukaemia cutis remains unclear. It has been suggested that it may occur as a result of dissemination of the leukaemic cells i.e. cutaneous metastasis. Other researchers have ascribed

it to an overspill phenomenon as it occurs more often in individuals with high white cell count. None of these explain the aleukaemic cutis in which leukaemic cells are not found in the peripheral blood film on light microscopy.

In another respect, it has been reported that the infiltration of the skin by leukaemic cells may persist or get worse even when the peripheral blood film or bone marrow picture has improved with treatment(9,10). There are reports of leukaemic infiltrates in areas of trauma or in typical lesions of inflammatory cutaneous conditions without relapses in the peripheral blood film or bone marrow of some patients(10,11). The various scenarios have led to speculations that surface antigens on malignant myeloid cells may be involved in the pathogenesis of specific cutaneous infiltrates. The infiltrates may probably occur as a result of tissue selective homing of a unique sub-population of malignant clone of cells and this may also be responsible for leukaemic infiltrates in other sites such as the orbit, oral mucosa and pharynx much as with the Maltomas(9). Electron beam therapy may be added to chemotherapy as adjunct therapy to the cutaneous infiltrates. In some patients, lesions may undergo spontaneous remission(12,13). It had always been presumed that involvement of the skin is associated with poor prognosis but recent evidence suggests that the appearance of leukaemia cutis does not necessarily herald poor prognosis(14,15).

This case report serves to highlight leukaemia cutis complicating AML in an adult, a very uncommon finding. In addition this case also serves to highlight the problems in the management of the acute leukaemias in a poor economy, unavailability of cytotoxic drugs for the treatment of AML and late presentation.

It is recommended that non-governmental organisations should be involved in assisting in the management of patients with malignancies who cannot afford drugs.

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