Skin Vasculitis with Direct Vessel Infiltration by Leukaemic Cells: A Case Report

Sir,

Different skin manifestations have been described in patients with leukaemia (1–4). These are classified into two main types: those caused by tumour cell localization in the skin and those appearing as a skin reaction to leukaemia (leukaemids). The former may appear clinically as erythematous-papulo-nodular, or less frequently as bullous, ulcerative or erythrodermic lesions (2, 5). Leukaemids, on the other hand, may show the clinical features of other skin diseases, including psoriasis, lichen ruber planus, annular erythema, rosacea, xanthomas, urticaria or vasculitis (1, 3, 6, 7). Finally, Sweet's syndrome and pyoderma gangrenosum may also herald leukaemia (8–9).

A patient with acute myeloid leukaemia and cutaneous lesions on the perineal and inguinal fold was observed recently. These lesions were clinically diagnosed as *p. gangrenosum*. However, a histological examination showed them to be characterized by massive dermo-hypodermic leukaemic cells infiltration. Moreover there were histologic signs indicative of "leukaemic vasculitis" (10–11).

CASE REPORT

A 68-year-old woman presented with multiple ulcerated nodules, ranging in diameter from 1 to 3 cm, localized on the perineal-inguinal area. Some of these lesions had a necrotic centre (Fig. 1), others were surrounded by pustule-like microvesicles.

The patient had suffered from type 2 diabetes mellitus and high blood pressure for 10 years. Two years earlier, she had undergone right mastectomy and chemotherapy with cyclophosphamide, methotrexate and fluorouracil for stage II invasive ductal breast cancer. In the same period, she was also found to be suffering from chronic renal failure. Two months before our observation, acute myeloblastic leukaemia (type M2-FAB classification) had been diagnosed.

When admitted to our department, the general condition of the patient was severely compromised to the point of contraindicating chemotherapy. Routine laboratory investigations showed the following results: anaemia (Hb = 7.6 g/dl), thrombocytopenia (10,000/mm^3) and leukopenia (2,000/mm^3) with 90% of myeloblastic elements, hyperglycaemia (440 mg/dl) and hypercreatininaemia (2.33 mg/dl). Total body computer tomography scan and abdominal sonography were negative.

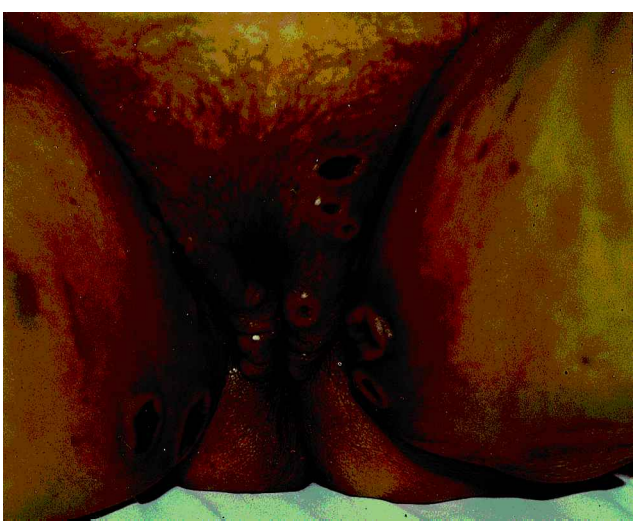

Fig. 1. Ulcerated nodules with necrotic centre on the perineal–inguinal area of the patient.

The clinical aspect of the lesions suggested the following differential diagnosis: pyoderma gangrenosum, leukaemic skin infiltration or skin metastasis from an internal tumour.

Histologic examination of a perineal nodule showed epidermic ulceration with dense dermal infiltration of tumour cells between collagen bands and adjacent structures (Fig. 2). Blood extravasion endothelial cell swelling, fibrinoid degeneration of vessel walls, local damage of endothelial cells and infiltration of the vessel wall by leukaemic cells were evident (Fig. 3). Immunohistochemical and enzymocytochemical tests showed that tumour cells inside the vessel wall were positive for naphtol-ASD-chloroacetate esterase (Fig. 4) and lysozyme, negative for CD45(LCA), CD45RO(UCHL-1),CD3, CD20(L-26),CD43(Leu-22), CD68(KP-1) and cytokeratin (12).

A diagnosis of leukaemic vasculitis from neoplastic cell infiltration was made (10–11). The patient died 2 weeks later owing to deterioration of her general condition.

DISCUSSION

In patients with leukaemia, skin manifestations are usually clinically unspecific. Therefore, histologic examination is essential in order to give a correct diagnosis, especially in lesions determined by the direct localization of skin tumour cells. In these cases, the histological pattern is specific. On

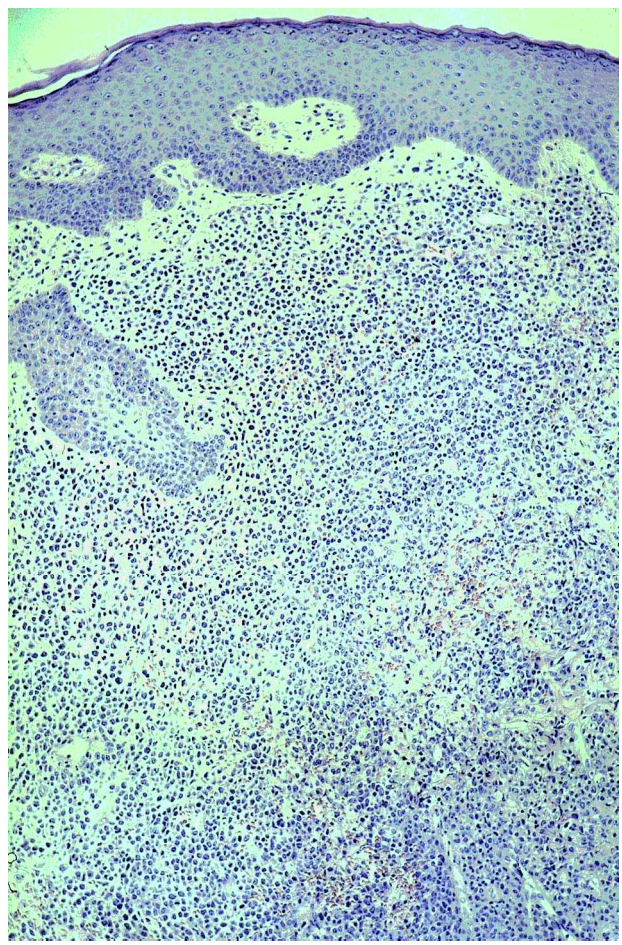

Fig. 2. The dense dermal infiltrate is composed of mononuclear cells with several erythrocytes outside the vessels (haematoxylin and eosin staining; 25 ×).

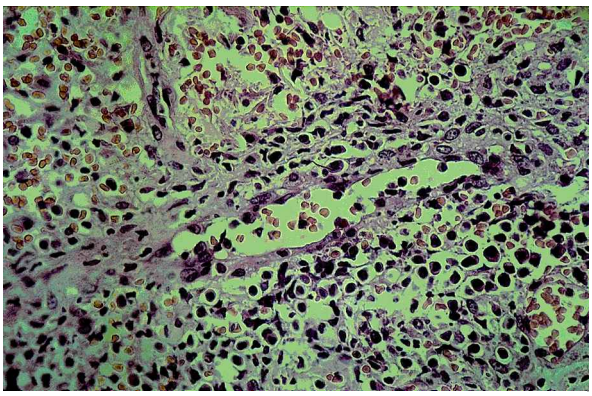

Fig. 3. Infiltration of the vessel wall by leukaemic cells with endothelial cell swelling and focal damage of endothelium (haematoxylin and eosin staining; 40 ×).

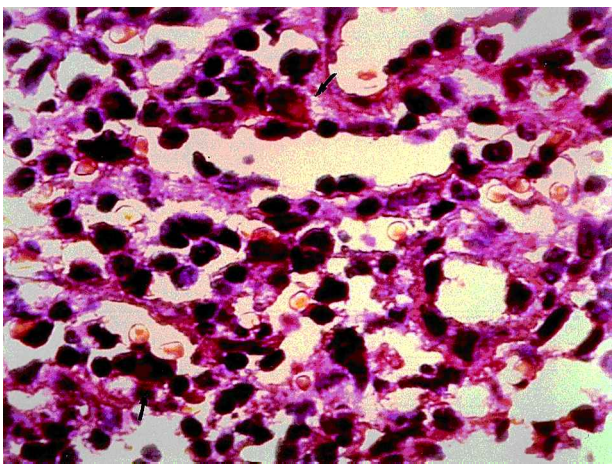

Fig. 4. Leukaemic cells inside the vessel wall (*arrows*) are positive for naphtol-ASD- chloroacetate esterase (40 ×).

the other hand, in skin lesions reactive to leukaemia, otherwise known as leukaemids, the histological aspect is not specific and, clinically, may mimic other disorders such as psoriasis, lichen ruber planus, annular erythema and rosacea (2, 3, 6).

In most cases, the diagnosis of leukaemia has already been made when skin lesions appear. In fact the skin is rarely involved before leukaemia becomes clinically symptomatic. Also, in the patient we observed, the skin lesions appeared about 2 months after the diagnosis of acute myeloid leukaemia and clinically resembled pyoderma gangrenosum.

Pyoderma gangrenosum is a skin disorder that is often associated with various internal diseases, including leukaemia. Generally it is histologically characterized by infiltration of granulocytes and lymphocytes with vascular damage (9).

In this case, the skin infiltrate was formed almost exclusively by tumour cells with morphological and enzymocytochemical features typical of myeloid cells.

The clinical aspect of skin lesions in our patient could be due to either tumour infiltration of the dermis (nodular aspect) or vasculitis induced by neoplastic cells infiltrating vessel walls. The latter hypothesis is confirmed by signs of fibrinoid degeneration of the vessel walls and the discovery of red blood cells outside the dermal vessels. This so-called leukaemic vasculitis was recently described by Jones et al. (10). These authors reported on 6 patients with skin lesions showing histologically signs of vasculitis. They distinguished between low-grade and high-grade leukaemic vasculitis. Low-grade lesions were characterized by small vessel injury with endothelial swelling, red blood cell extravasation and focal fibrin deposition. High-grade lesions showed necrotizing vasculitis with luminal obliteration, extensive fibrin deposition and leukocytoclasia. According to this classification, our case could be considered as a low grade leukaemic vasculitis (10, 11). We find this case significant because of its peculiar clinical and histological findings. This is another indicative case how the skin may be an area where infiltration by tumour cells from other organs should be considered as a negative prognostic sign. In fact, our patient died 2 weeks after the appearance of skin lesions.

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