Acute myelomonocytic leukaemia presenting as xanthomatous skin eruption

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SUMMARY A case of acute myelomonocytic leukaemia (AMMOL) is reported in which skin infiltration with xanthomatous nodules was the presenting feature. The histological, including ultrastructural, appearances are described.

Skin and mucosal infiltrates are a well recognised feature of the monocytic leukaemias. We report a case of AMMOL which presented with xanthomatous skin nodules, a form of leukaemic skin infiltration not previously reported.

Case report

A 44-year-old man presented in October 1980 with multiple yellowish skin nodules on the anterior and posterior trunk and limbs (Fig. 1). The lesions were not painful or pruritic and had been present for six weeks. There were no other symptoms or significant previous complaints and no family history of disordered lipid metabolism. The lesions were absent on the palms, soles, tendon sheaths and buttocks and there was no gingival hypertrophy. There was no lymphadenopathy, hepatosplenomegaly, sternal tenderness, bruising or bleeding. Haemoglobin was 8:0 g/dl, white cell count 22:7 x10⁹/1 and platelet count 62:0 x10⁹/1. Blood film revealed 40% blast cells. Repeated attempts at marrow examination resulted in dry taps, but a trephine biopsy (Jamshidi needle, 11 gauge, regular adult size) from the posterior iliac crest provided material for trials from which a diagnosis of AMMOL (M4) was made, according to the criteria of the French-American-British (FAB) Cooperative Group.¹

Chest x-ray and ECG were normal. Total cholesterol (fasting) was 2:9 mmol/l (normal range 4:1–7:4). Total triglyceride (fasting) was 0:95 mmol/l (normal range 0:1–8). Lipoprotein electrophoresis was normal.

Induction chemotherapy was commenced comprising daunorubicin, cytosine arabinoside and thioguanine. After four full induction courses of this therapy bone marrow remission was achieved in December 1980. Although the xanthomatous lesions diminished in number and size they did not entirely disappear. Repeated estimations of serum lipids revealed no abnormality. Skin infiltration again became prominent and was partly haemorrhagic (Fig. 2) after the completion of two courses of consolidation chemotherapy consisting of daunorubicin, cytosine arabinoside and thioguanine. Peripheral blood examination on this occasion exhibited blast cells of similar morphological appearance to that of the initial presentation. The patient died suddenly before further chemotherapy could be instituted. Permission for post-mortem examination was not granted.

Prior to the initiation of antileukaemic therapy, two of the skin lesions were biopsied. Biochemical analysis revealed a high concentration of triglycerides

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but only small amounts of cholesterol. Histological examination of both specimens showed a light perivascular cellular infiltrate in the upper dermis. A few plasma cells could be recognised, but it was not possible to categorise the majority of cells which exhibited nuclear pleomorphism, mitotic activity, and variable amounts of amphophilic/eosinophilic cytoplasm with occasional granules. A discrete nodule comprising a cellular aggregate infiltrating the collagen bundles of the mid and lower dermis was found in the first biopsy. The overall impression was of a xanthomatous lesion, with several unusual features. The majority of the cells had large, irregular, pale nuclei with nucleoli and abundant basophilic foamy cytoplasm (Fig. 3) resembling macrophages. Mitotic figures were prominent.

A smaller number of multinucleate giant cells with similar nuclear and cytoplasmic features were present. In addition, scattered throughout the lesion, were cells with large rounded nuclei, some distinctly nucleolated and with scanty eosinophilic cytoplasm resembling myeloid precursors (Fig. 4). A number of these cells were Sudan black- and chloracetate-positive. Occasional mast cells, mature lymphocytes, mature eosinophils and eosinophil myelocytes were present.

Ultrastructural studies revealed closely packed cells with complex interdigitating surfaces, the cell membranes being in close apposition but lacking adhesion specialisations (Fig. 5). The cytoplasm was abundant and contained a number of organelles including fat vacuoles, single membrane-bound granules consistent with lysosomes, mitochondria, short profiles of rough and smooth endoplasmic reticulum and randomly disposed microfilaments (Fig. 6). The nuclei were large with a variable degree of infolding and prominent nucleoli with some segmentation interconnected by fine chromatin strands (Fig. 7). A little heterochromatin with peripheral margination was present.

Discussion

Extramedullary tissue infiltration by leukaemic cells is a well recognised and typical manifestation of the monocytic leukaemias. Such infiltrates, particularly of the skin and gingival mucosae were present in approximately one third of a recent intensively studied group of 45 patients with AMMOL or with acute monocytic leukaemia (AMOL). The wide variety of dermatological manifestations which may be found in the monocytic and other leukaemias is detailed in the monograph of Bluefarb. These include a large number of non-specific cutaneous
Fig. 5  Xanthoma cells showing complex interdigitation of adjacent cell membranes. × 9500.

Fig. 6  Fat vacuoles (f) and lysosomes (arrow) in a xanthoma cell. × 16 000.

Fig. 7  Nucleus of cell from xanthomatous lesion showing nucleolation and lobulation. The two lobes are interconnected by a fine chromatin strand. The scanty heterochromatin is marginated. Cytoplasm is abundant with fat vacuoles (f). × 3500.
features such as pruritus, exfoliative dermatitis, hyperpigmentation, erythema multiforme and bullous pemphigoid. Leukaemic lesions may take the form of solid papules or tumours macroscopically indistinguishable from infiltrates seen in the malignant lymphomas. The lesions in the monocytic leukaemias, however, tend to be large and purple or "plum" coloured and frequently ulcerate. As in the case we describe, skin tumours tend to spare the face. Skin lesions may antedate haematological expression of leukaemia by a variable period so that a wide differential diagnosis may be considered in such patients. Even at biopsy a leukaemic origin cannot definitely be assigned except in the case of chloroma (granulocytic sarcoma), the only localised tumour pathognomonic of leukaemia.

Our case presented with xanthomatous skin lesions, a form of skin infiltration we believe has not hitherto been described. No evidence of a systemic disorder of lipid metabolism was found. A diagnosis of AMMOL was made on the basis of Romanowsky and cytochemical stains of the tails of marrow obtained at bone marrow biopsy. Auer rods were not seen but the cytochemical pattern of Sudan black positivity combined with positive alpha-naphthyl acetate and naphthol-AS-D chloracetate esterases was clearly evident.

The light microscopic appearances of the xanthomatous nodules showed a degree of cellular pleomorphism and mitotic activity which suggested neoplasia rather than a diagnosis of eruptive xanthoma or infective granuloma. In addition, there was evidence of granulocytic infiltration in the presence of eosinophil myelocytes and Sudan black- and chloracate-positive cells scattered amongst the xanthoma cells.

Electron microscopy also demonstrated an infiltrate consisting predominantly of lipid containing macrophages but was of special value in showing absence of specialised intercellular junctions, indicating a non-epithelial origin of the tumour. In occasional cells cytoplasmic electron-dense granules suggested the presence of early myeloid precursors but several other features similar to those described by Glick and Horn, in peripheral blood and marrow, suggested the presence of monocytes and promonocytes; the latter characterised by large indented nuclei with prominent nucleoli, numerous free ribosomes and many short segments of rough endoplasmic reticulum. O'Brien, Catovsky and Costello have shown that monoblasts contain a previously undescribed small lysosomal granule characterised by presence of acid phosphatase activity and lack of myeloperoxidase activity, a useful ultrastructural differentiation feature between monocytic and granulocytic precursors. At the time of relapse, the xanthomata became more prominent on our patient but it was not possible to rebiopsy the lesions of obtain fresh tissue imprints for further cytochemistry because of the patient's sudden death.

It is possible only to speculate that the leukaemic monoblasts in our patient were capable of phagocytosing lipid to a degree which led to xanthomatous nodule formation in the skin. Permission for post-mortem examination was not granted so that it is impossible to know if organs other than skin were infiltrated. The "xanthomata", although diminished in size and number, remained evident during the two-month marrow remission. It appears likely that they provided a "sanctuary" for leukaemic cells during this period.

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References


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