Acute myelogenous leukaemia with bilateral mammary gland involvement

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SUMMARY A 34-year-old woman developed acute myelogenous leukaemia in the course of pregnancy and, after delivery of a normal baby, developed multiple bilateral breast masses composed of myelogenous tissue.

Leukaemic tumefaction in soft tissues, especially the breast, has rarely been described. In two extensive necropsy studies of the metastatic pattern of human leukaemias,1 2 breast involvement was found in only two of a combined total of 472 cases of acute myelogenous leukaemia (AML). We present the case of a 34-year-old woman with AML, diagnosed in the course of pregnancy, who developed bilateral leukaemic breast infiltrates during final remission. The literature concerning such granulocytic sarcomas, as they have been termed by Rappaport,3 of the breast is briefly reviewed.

Case report

A 34-year-old woman presented with AML in July 1977, in the 27th week of her fourth pregnancy. Complete remission followed a single induction course of chemotherapy combining thioguanine, cytosine arabinoside, and daunorubicin in the regimen recommended by Gale and Cline in 1977.4 As we have reported elsewhere, a normal male infant was delivered in October 1977.5 The patient remained well on regular consolidation chemotherapy until August 1978 when she noted multiple bilateral breast masses which appeared over a period of a few days. A bone marrow aspirate taken 10 days before the breast masses were noted had shown less than 10% blasts. Full blood count and blood film ordered by her general practitioner were normal. He discontinued oral anovulant therapy without obvious change in the breast masses. One week later the patient was referred to hospital for excision biopsy. Histology will be discussed with the post-mortem findings. On admission bone marrow aspirate revealed early relapse of AML (20% blasts). Complete relapse rapidly ensued. Attempts to induce further remission using chemotherapy were followed by profound, irreversible pancytopenia. During this period the breast lumps diminished in size but remained palpable. The patient died of culture proven staphylococcal septicaemia in September 1978 after developing extensive pelvic sepsis resistant to antibiotic therapy.

Postmortem examination revealed diffuse infiltration of both liver (4000 g; normal 1440-1680 g) and spleen (500 g; normal 155-195 g) with immature myeloid precursors resembling myeloblasts. There were multiple, discrete, circumscribed nodules in both breasts similar to the excised surgical specimen. The tissue removed measured 2.5 × 2 × 1 cm. It was of firm consistency, partly haemorrhagic, and of a dark greenish colour. Addition of hydrogen peroxide intensified the green colour. Microscopic examination revealed circumscribed cellular areas arranged around ductules (Fig. 1). The constituent cells were loosely adherent to each other and resembled early myeloid precursors. Eosinophil myelocytes were prominent. Ductular epithelium was preserved (Fig. 2). Myeloperoxidase staining of touch preparations of unfixed material from breast biopsy demonstrated a positive reaction.

Electron microscopy (Fig. 3) failed to reveal any evidence of specialised intercellular junctions. Many cells contained prominent, mainly spherical, mem-

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Fig. 1  Periductal cellular infiltrate with preservation of ductular epithelium. (Haematoxylin and eosin original magnification × 100).

Fig. 2  Non-cohesive infiltrate of cells which closely resemble early myeloid precursors. Normal ductule included. (Haematoxylin and eosin original magnification × 400).
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brane-bound granules consistent with primary myeloid granulation.

Discussion

Solid tumour metastases in the breast are exceptionally uncommon. In 1972, Hajdu and Urban\(^6\) suggested an overall incidence of 1-2%. Isolated case reports have appeared of breast involvement in the leukaemias, in chronic granulocytic leukaemia (CGL),\(^7\) in acute lymphatic leukaemia (ALL),\(^8\)-\(^10\) and in chronic lymphocytic leukaemia (CLL).\(^11\)\(^12\) We have been able to find the following reports\(^13\)-\(^23\) in cases definitely classified as AML.

In 1912, Simon\(^13\) described a chloroma appearing as a malignant tumour of the breast. Chloroma, a term of long usage, signifying a green-coloured tumour composed of myelogenous tissue, was described by Turk\(^24\) in association with AML early this century. The green pigment, due to myeloperoxidase, is not always present, and many other terms and classifications have been proposed which have lost their descriptive implications.\(^25\) The most appropriate single description of these myeloblastic tumours is probably granulocytic sarcoma.\(^3\)

Review of the cases of granulocytic sarcoma of the breast so far reported reveals an exclusive female incidence with the exception of a patient described by Geelhoed et al.\(^10\) with testicular feminisation syndrome maintained on oestrogen therapy. Most affected females have been of child-bearing age (range, 3 months to 49 years), raising the possibility that high oestrogen levels might promote breast involvement with leukaemia. In addition, our patient received exogenous oestrogen in oral anovulant therapy following pregnancy. However, oestrogen does not appear to be a major factor in pathogenesis in view of the rarity of granulocytic sarcoma of the breast and the relative frequency of AML in young women.

The appearance of granulocytic sarcoma of the breast does not appear to be related to myeloid tumour mass. Some cases have antedated\(^10\) or coincided with\(^18\) diagnosis of AML. Another\(^17\)

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**Fig. 3** Electron micrograph of cellular infiltrate showing cells with irregularly shaped nuclei containing margined condensed chromatin. Prominent nucleoli and membrane-bound cytoplasmic granules are also present. (Postmortem breast tissue original magnification × 9620).
occurred in remission and preceded relapse, as in the case we have described. However, overall duration of survival does not appear significantly shorter for patients with AML who develop granulocytic sarcoma.1

Correct histological diagnosis is based on identification of the characteristic granulocytic sarcoma cells. Typically, they appear loosely arranged in periductular groups with preservation of ductular epithelium. The presence of eosinophil myelocytes should alert one to the granulocytic nature of the constituent cells. Auer rods and Reider cells may occasionally be identified in sections. However, tissue imprints taken from fresh biopsy material and stained, with Romanowsky stains best demonstrate cellular detail. Cytochemical methods such as myelo peroxidase staining may be applied to such preparations and provide useful evidence of a myelogenous origin of the cells. Such origin is further supported by use of the naphthol-as-chloroacetate esterase staining method on formalin-fixed, cryostat-prepared tissue sections.26 Electron microscopy is of value in revealing cytoplasmic electron dense granules characteristic of early myeloid precursors. In addition, absence of specialised intercellular junctions indicates the non-epithelial nature of the tumour cells.

Despite the characteristic histological appearances, there is scope for misdiagnosis, and granulocytic sarcoma of the breast may be more common than the few case reports in the literature might suggest. Some cases have been initially misdiagnosed as fibroadenoma or reticulum cell sarcoma10 and cystosarcoma phyllodes.25 Wrong diagnosis is most likely in cases where the breast mass antedates expression of AML, and breast biopsy is superfluous in a patient with multiple bilateral breast nodules and a known AML. However, single nodules occur with equal frequency, and it is our opinion that biopsy should be performed in all such patients, needle biopsy being the least invasive procedure. Only then may it become possible to establish the true incidence of this unusual cause of a breast mass.

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