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Myeloid metaplasia of the breast

A lesion which clinically mimics carcinoma

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Summary. The authors report a case of myeloid metaplasia of the breast presenting as a tumor mass with homolateral axillary lymphadenopathy. The lesion was clinically misinterpreted as a breast cancer and developed in an elderly woman 8 years after the diagnosis of primary myelofibrosis was made. Immunohistochemical and ultrastructural studies confirmed the haematopoietic nature of the proliferating cells. The differential diagnosis from other breast lesions is discussed.

Key words: Myeloid metaplasia – Primary myelofibrosis – Breast-tumor – Giant cells

Introduction

Myeloid metaplasia (MM) of the breast is a rare entity, as is its presentation in the form of a tumor mass (Dieterick 1925; Brannan 1927; Glew et al. 1973; Brooks et al. 1980). We wish to report such an occurrence in an elderly woman with primary myelofibrosis (PM) which was clinically misinterpreted as a breast cancer.

Case report

A 68-year-old female was admitted to the Policlinico S. Orsola, Bologna University, in January 1982 because of a nodule in the upper, outer quadrant of the left breast associated with an enlarged homolateral axillary lymph node. In February 1974 she had been hospitalized due to fever, weight loss and splenomegaly. At that time, complete blood count was as follows: haemoglobin 11.7 g/100 ml; reticulocytes 3.5%; platelets 433,000 ml and WBC 24,000 with 58% neutrophils, 4% eosinophils; 5% lymphocytes, 2% monocytes, 16% metamyelocytes, 13% myelocytes and 2% myeloblasts. Blood smear showed 1% erythroblasts and aniso-poikilocytosis with teardrop-shaped red cells. Multiple aspirations of the bone marrow were unsuccessful.

A marrow biopsy revealed a pattern consistent with PM without osteosclerosis. Radio-iron kinetic studies showed a rapid disappearance of the injected isotope with an uptake into

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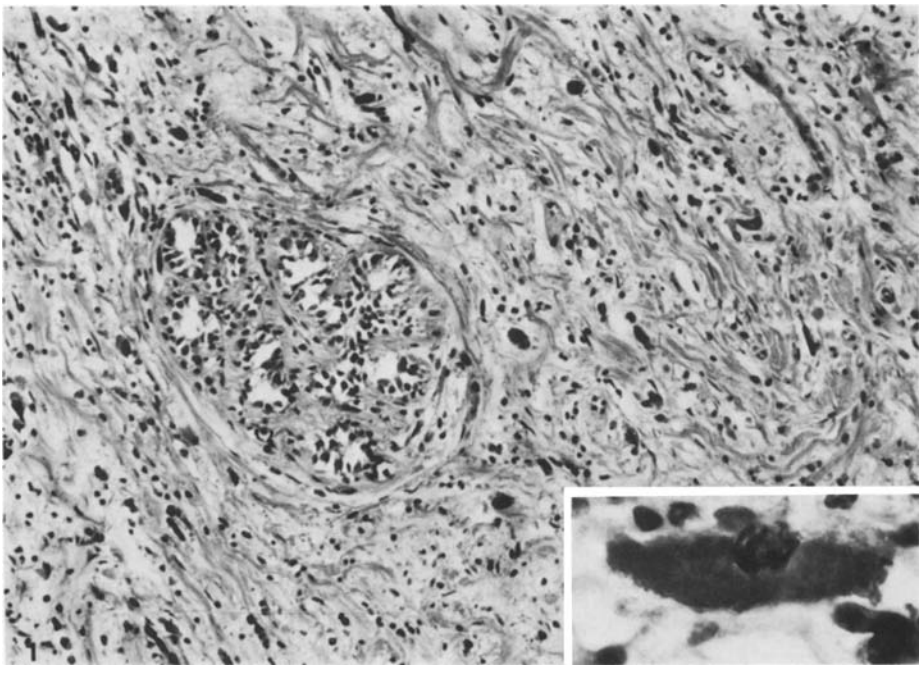

Fig. 1. The stroma of the mammary gland is infiltrated by haematopoietic elements with numerous megakaryocytes (H.E. × 135.3). *Inset:* immunoperoxidase staining for Factor VIII-related antigen in the cytoplasm of megakaryocytic cells (× 1,353)

the spleen and liver but not into the bone marrow. Reduction of spleen and liver radioactivity in the days following the injection and the red-cell radio-iron incorporation demonstrated extramedullary haematopoiesis. No treatment was instituted. The patient did well for five years. However in 1980 progressive symptomatic splenomegaly required radiotherapy to the spleen (800 rad).

At the time of her last admission to the hospital laboratory data were similar to those observed in 1974.

The breast nodule and enlarged axillary lymph node were excised. Macroscopically the breast mass was firm, irregularly ovoid, gray-white and measured 1.8 × 1 × 1 cm. The axillary lymph node was enlarged and white on cut-section.

Material and methods

Sections of Carson-fixed, paraffin-embedded breast and lymph node tissues were stained according to the following methods: H&E; Giemsa; PAS with and without diastase-digestion; Alcian blue/PAS and naphtol-ASD-chloroacetate esterase reaction (Leder stain).

An immunohistochemical investigation for Factor VIII related antigen (F VIII RAg) was performed employing a modified PAP-technique, as previously described (Pileri and Rivano 1983). In particular, the primary antiserum anti-F VIII RAg, raised in rabbit (DAKO, Code AO82) was diluted 1 :1250, while swine anti-rabbit IgG serum (DAKO, Code Z196) and rabbit PAP-complexes (DAKO, Code Z113) were applied at a dilution of 1 : 50 and 1 : 100, respectively. Controls of the specificity of the antisera and method were carried out.

For electron microscopy some Carson-fixed blocks were post-fixed in 1% osmium tetroxide and embedded in epoxy resin (Araldite). Ultrathin sections were stained with uranyl acetate-lead citrate.

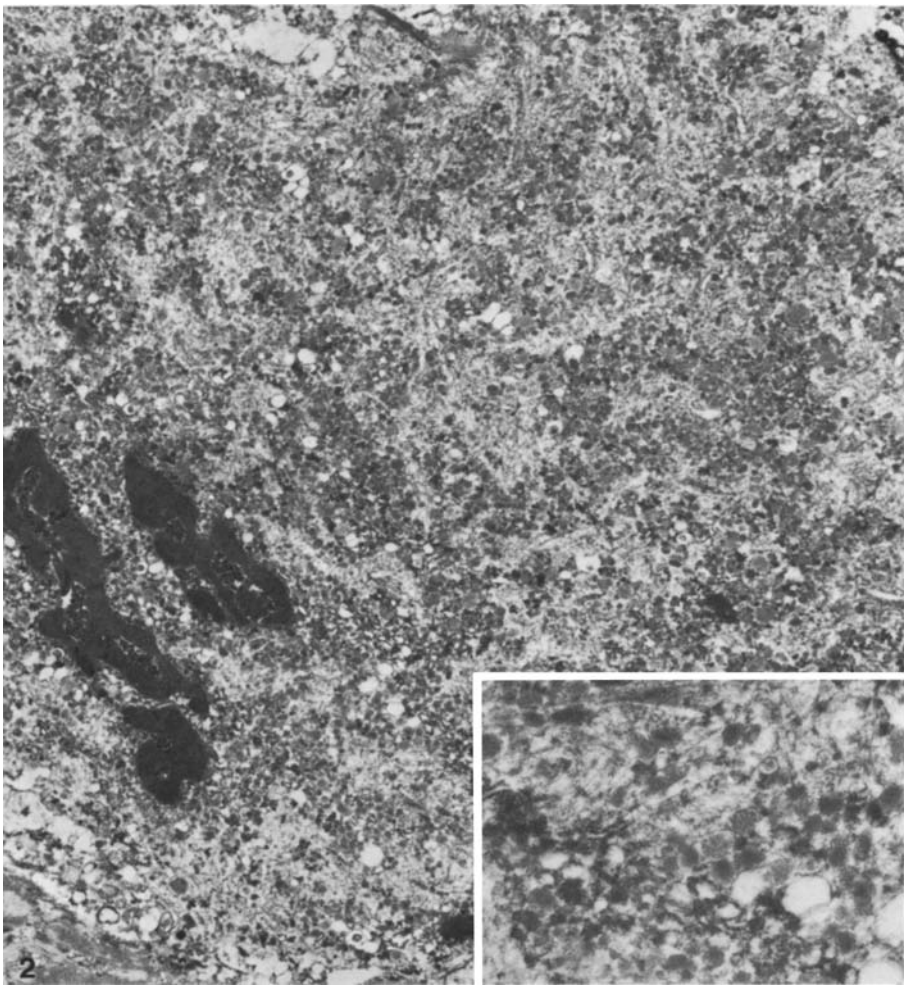

Fig. 2. Megakaryocytes showing numerous cytoplasmatic granules (×5,600). *Inset:* "bull's-eye" appearance of the megakaryocytic granules (×14,400)

Results

Microscopically the breast lesion consists of dense fibrotic tissue infiltrated by haematopoietic elements often arranged near or within the blood vessels. Numerous large hypercromatic and multinucleated megakaryocytes are seen (Fig. 1). Myeloid cells and, more rarely, erythroid elements are easily recognized. Eosinophilic myelocytes and rare granular blast cells of the myeloid series are better identified with the Leder stain. F VIII RAg is demonstrated by the PAP technique in the cytoplasm of megakaryocytes (Fig. 1, inset). The normal architecture of the axillary lymph node is almost entirely replaced by dense fibrous tissue and a cellular proliferation similar to that observed in the breast.

The electron microscopic studies show that the cellular infiltrate consistes of erythro-myeloid haematopoietic elements and megakaryocytes. The latter have multilobulated electron-dense nuclei and cytoplasm containing numerous specific granules intermingled with vesicles of the demarcation-system (Fig. 2). Segregation of platelets is not evident.

Discussion

Extramedullary tumor-like masses in patients with PM more often present themselves as multiple nodules involving several organs and tend to develop in the latter stages of the disease (Dieterick 1925; Bouroncle and Doan 1962; Beckman and Oehrle 1982). Brooks et al. (1980) reported a case of MM, which occurred as an isolated growth in the breast and was the only sign of the disease requiring treatment.

The case here reported was clinically misinterpreted as a malignant lesion because of the presence of both a breast mass and regional lymph nodal enlargement. The histological pattern, however, met the diagnostic criteria of MM; electron microscopy and immunohistochemistry confirmed the haematopoietic nature of the proliferating cells.

MM of the breast must be differentiated from several stromal and epithelial lesions as well as from other haematologic disorders. Leukaemic infiltrates and chloroma do not exhibit a mixed proliferation of elements belonging to the granulocytic-, erythroid- and megakaryocytic-series (Rappaport 1966; Pascoe 1970; Sears and Reid 1976). Non-Hodgkin's lymphomas and pseudolymphomas (Mambo et al. 1977; Navas and Battifora 1977; Fisher et al. 1979; Lin et al. 1980) consist of lymphoid cell-lines easily distinguishable from those of MM. A diagnosis of Hodgkin's disease may be excluded by the lack of Reed-Sternberg cells, in spite of the presence of multinucleated giant cells intermingled with granulocytes. Elements showing megakaryocytic features may be helpful in the differential diagnosis from inflammatory fibrous histiocytoma (Asirwatham and Pickren 1978).

In benign spindle cell tumor of the breast (Toker et al. 1981) the proliferating cells are quite different from those observed in MM. In fact, the former displays only spindle- or stellate-shaped cells, which ultrastructurally correspond to fibroblasts, myofibroblasts, smooth muscle cells and undifferentiated mesenchymal elements.

Multinucleated giant cells have been observed in several categories of mammary tumors (Factor et al. 1977). In most of these cases the differential diagnosis from MM is quite easy. Occasionally, however, electron microscopy and/or immunohistochemistry may be required to differentiate metaplastic giant cells from megakaryocytes. Giant cells and myelocytes are also seen in mastitis; in such an occurrence, the presence of lymphocytes, plasma cells and foreign-body material in or around them makes the diagnosis easy.

Finally, the benign lesion of the breast described by Rosen (1979) and characterized by multinucleated stromal giant cells must be taken into consideration. The absence of elements of the erythroid, myeloid- and megakaryocytic-series, however, allows the exclusion of the possibility of MM.

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