Primary malignant fibrous histiocytoma of the breast

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Summary. Clinical, light microscopic, electron microscopic and immunocytochemical features of 4 cases (3 women and 1 man) of primary malignant fibrous histiocytoma (MFH) of the breast are presented. The literature is reviewed and the diagnosis and treatment discussed. The good outcome is stressed and local excision or simple mastectomy recommended as appropriate treatment.

Key words: Malignant fibrous histiocytoma - Breast - Light microscopy - Immunocytochemistry - Electron microscopy

Introduction

The reported incidence of sarcomas of the breast varies from 0.24% to 3% of all malignant breast lesions (Khaïna et al., 1981). The majority have been classified as cystosarcoma phyllodes. In the remaining group of sarcomas, some belong to the group of postirradiation malignant fibrous histiocytoma (MFH) (Hardy et al., 1978; Tsuneyoshi and Enjoji, 1979; Langham et al., 1984; Vera-Sempere and Llombart-Bosch, 1984). Only 5 cases of primary MFH of the breast without a preceding fibroadenoma, phyllodes tumour or irradiation have been reported (O'Brien and Stout, 1964; Kobayashi et al., 1977; Langham et al., 1984; Vera-Sempere and Llombart-Bosch, 1984).

We present the clinical, light microscopic, electron microscopic and immunocytochemical features of 4 cases of primary MFH of the breast, a review of the literature and a discussion of the diagnosis and treatment.

Materials and methods

The files of the Norwegian Radium Hospital from 1958 to 1981 contain 30 cases of breast sarcomas. We reviewed the light microscopic sections and the medical records of all the cases and identified 4 as primary malignant fibrous histiocytomas. The criteria for selection were:

- Presence of typical storiform or pleomorphic growth pattern.
- Presence of spindle-shaped fibroblasts and larger pleomorphic histiocytic cells.
- Absence of an epithelial component.
- Absence of other mesenchymal components like lipoblasts, rhabdomyoblasts, etc.
- Cases were excluded in which the breast had been treated surgically and/or irradiated prior to the finding of a suspect MFH.
- Absence of skin involvement.
- Cases were excluded in which the tumour had developed in a preexisting phyllodes tumour.

An average of 10 haematoxylin and eosin-stained sections from formalin-fixed, paraffin-embedded material were studied in each case.

Immunocytochemical studies were performed on paraffin-embedded material using the avidin-biotin peroxidase complex method (Hsu et al., 1981), and using antibodies raised against α-antitrypsin, lysozyme, keratin and CEA (all from Dako Corp.).

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Further technical details are given in the article of Holm and co-workers (1985). Control studies included 1) incubation with normal rabbit IgG at the same concentration as the primary antibodies, 2) incubation with antibody preabsorbed with homologous antigen and 3) positive controls.

Material for electron microscopy was available in 2 cases (nos. 1 and 2). Fresh material had been fixed in a cacodylate-buffered mixture of 4% formaldehyde and 1% glutaraldehyde (McDowell and Trump, 1976), post-fixed in cacodylate-buffered 1% osmium tetroxide, dehydrated in graded ethanols and embedded in an Epon/Araldite mixture (Mollenhauer, 1964). Semithin sections were stained with toluidine blue and used for light microscopic orientation and ultrathin sections for electron microscopy were contrasted with uranyl acetate and lead citrate.

Two MFH tumours were excluded because of prior removal of cystic breast lesions of which no histological evaluation had been made.

Results

Case reports

1. A 77 year-old woman (parous 1) noticed a tumour in the left breast. Mastectomy was performed one month later and axillary lymph nodes removed. A well-circumscribed fleshy tumour was identified in the upper lateral quadrant of the breast. It measured 5 cm in diameter and had some solid grey areas. No lymph node metastases were found. The patient is still alive, without clinical signs of recurrence or metastases, 40 months later.

2. A 49 year-old woman (parous 1), was hospitalized with a well-circumscribed, grey-white tumour, 4 cm in diameter between the upper and lower medial quadrant of the left breast. Twelve months later a local recurrence, 11 cm in diameter, was removed and three months after this a simple mastectomy was performed due to another local recurrence measuring 3.5 cm in diameter. The patient is alive 9 years and 4 months after the primary surgical intervention and without clinical signs of recurrence or metastases.

Fig. 1. (Case no. 2). Spindle-shaped and polygonal cells in a typical storiform pattern. H.E. x 45

Fig. 2. (Case no. 2). Higher magnification of the tumour cells, H.E. x 280
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Fig. 3. (Case no. 4). Pleomorphic areas with numerous giant cells. H.E. ×45

Fig. 4. (Case no. 1). Overview electron micrograph of the tumour cells in abundant intercellular substance with bundles of collagen fibres. Uranyl acetate-lead citrate ×6,160
3. A 71 year-old unmarried woman was found to have a well-circumscribed tumour in the upper lateral quadrant of the left breast. The grey-white tumour measured 6 cm in diameter and was of an elastic consistency. A simple mastectomy was performed and postoperative irradiation given. Follow-up 6 years and 5 months after surgery showed no signs of disease. The patient died 3 years and 7 months later but autopsy was not performed.

4. A tumour was found in the upper medial quadrant of the left breast of a 66 year-old man and malignant cells in the aspiration biopsy led to an ablative and axillary lymphadenectomy, followed by irradiation 2 months later. Eighteen months later the patient died of a heart attack without clinical signs of local recurrence or metastases. Autopsy was not performed.

Light microscopy

All four lesions fell within the bounds of MFH. The cellular areas consisted of fascicles of spindle-shaped fibroblast-like cells and polygonal histioyte-like cells (Figs. 1, 2). The nuclei were pleomorphic and hyperchromatic with frequent mitoses. The mitotic rate varied from 2/10 high power field (HPF) (case no. 1) to >10/10 HPF (cases nos. 2 and 4). Areas with typical storiform pattern were present in all cases, but less differentiated areas giving a more pleomorphic appearance dominated in case no. 4 (Fig. 3). Myxoid areas with an Alcian-green positive matrix were seen in cases nos. 1 and 3. Foam cells and cells phagocytizing erythrocytes and hemosiderin were occasionally seen. Multinucleated giant cells were rather frequent in case no. 4. Epithelial structures were not present in any of the tumours. The tumour borders were sharp in cases 1 and 3 but not in cases 2 and 4. A typical intraductal carcinoma of comedotype was however present in the breast tissue next to the sarcoma in case no. 3.

Immunocytochemistry

All tumours contained cells that stained positively for lysozyme and a-antitrypsin. No immunoreactivity for CEA and keratin was detected. Keratin-positive cells were only seen in duct epithelium outside the tumours.

Electron microscopy

Histiocytic, fibroblastic and undifferentiated mesenchymal cells were seen, together with fibrohistiocytic cells having features of both fibroblasts and histiocytes (Fig. 4). The spindle-shaped fibroblastic cells were surrounded by varying amounts of collagen fibres. The histiocytes were polygonal or irregular in shape, and had an abundant cytoplasm with lysosomes, some fat droplets and a well-developed rough endoplasmic reticulum. Scattered condensations were seen along the cell membranes but no well-developed desmosomes.

Discussion

MFH is probably the most frequent soft tissue sarcoma in adults (Enzinger and Weiss, 1983). Its histogenesis is still unclear, but the cell of origin seems to be an undifferentiated pluripotent mesenchymal cell (Enzinger and Weiss, 1983). The tumour occurs not only in "classic" soft tissue regions - extremities and retroperitoneum - but also in the skeleton (Terashina et al., 1981; Capanna et al., 1984); lung (Spencer, 1977; Carter and Eggleston, 1980; Silverman and Coalson, 1983; Lee et al., 1984); vulva (Hensley and Friedrich, 1983); larynx (Canalis et al., 1975); conjunctiva (Delgado-Partida and Rodriguez-Trujillo, 1972); heart (Shah et al., 1978; Morinmoto et al., 1980; Harndam et al., 1981; Terashina et al., 1983) and the kidney (Klugo et al., 1974). Cases of MFH in the breast have also been published (O'Brien and Stout, 1964; Kobayashi et al., 1977; Hardy et al., 1978; Tsuneyoshi and Enjoji, 1979; Hamada et al., 1980; Langham et al., 1984; Vera-Sempere and Llombart-Bosh, 1984) but are extremely rare without prior existence of phyllodes tumour or prior irradiation to the gland. Only 5 cases have been published (O'Brien and Stout, 1964; Kobayashi et al., 1977; Langham et al., 1984; Vera-Sempere and Llombart-Bosh, 1984) before this report.

Diagnosis of primary MFH in the breast is rather difficult and we believe that all criteria listed in Materials and methods should be fulfilled. Postirradiation variants (Vera-Sempere and Llombart-Bosh, 1984) seem to have a more aggressive biological behaviour than primary ones and should therefore be classified separately.

A MFH arising in a phyllodes tumour (Hanada et al., 1980) metastasized and killed the patient 1 month after a simple mastectomy. In our study we excluded 2 cases which may have been primary MFHs but the cystic lesions had been removed without having been studied morphologically and the possibility of pre-existing phyllodes tumours could not be excluded. We feel that a tumour with the morphology of a MFH lesion that occurs in a phyllodes tumour belongs to the group of malignant phyllodes tumours and not to the primary MFHs of the breast.

Dermatofibrosarcoma protuberans with its typical storiform growth pattern can easily be confused with a MFH. It is locally invasive but only rarely gives rise to metastases (Lever and Schaumberg-Lever, 1983). This skin tumour can also infiltrate the breast parenchyma proper (Lattes, 1967; Norris and Taylor, 1968; Azzopardi, 1979) and whether it theri should be classified as dermatofibrosarcoma protuberans or as a MFH is an open question. As a already stated in the criteria for selection, there was no skin involvement in any of our cases.

Anaplastic carcinomas and spindle cell carcinomas may mimic sarcomas (Azzopardi, 1979; Kaufman et al., 1984) but immunostaining for keratin filaments and electron microscopy will usually reveal their true nature.

The fact that only 5 cases of primary MFH in the breast have been reported in addition to the present 4 cases,
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is probably not only a sign of their exclusivity but also reflects that they tend to be placed in portmanteau groups like stromal sarcoma and spindle cell sarcoma of the breast. Berg and co-workers (1962) promoted the term "stromal sarcoma" for all breast sarcomas except malignant phyllodes tumour, lymphosarcoma and angiosarcoma. They found a striking similarity both in histological pattern and in clinical behaviour in their 25 cases. Although the "stromal sarcoma" designation is still in use (Seemayer et al., 1975; Tang et al., 1979; Harris and Khan, 1983; Yeh et al., 1985), several studies have shown the benefit of splitting up breast sarcomas into several morphological groups such as osteogenic sarcoma (Smith and Taylor, 1969; Barnes and Pietszuka, 1977); rhabdomyosarcoma (Oberman, 1965; Elhence et al., 1972); leiomyosarcoma (Cameron et al., 1984; Nielsen, 1984) and angiosarcoma (Steingassner et al., 1965; McDivitt et al., 1967; Gulesserian and Lawton, 1969; Brennan, 1981; Merino et al., 1983). All seem to have a poor prognosis whereas the prognosis of primary MFH of the breast seems to be good. The observation time for the 5 cases reported in the literature was from 1 to 5 years, and only in 1 case (O'Brien and Stout, 1964) did a recurrence appear in the follow-up period. In our material, the observation time for cases nos. 1 and 2 was 40 months and 9 years and 4 months, respectively. Case no. 2 developed local recurrences after 12 and 15 months but later had no tumour manifestations. Case no. 3 had a 6 year 5 month follow-up without any signs of metastases or recurrence. She died 16 years and 5 months after the mastectomy. The male (case no. 4) died of a heart attack 18 months after the mastectomy. Axillary lymph node metastases were not observed in any of the cases. Our material thus confirms the good outcome for patients with primary MFH in the breast. None of the patients died with metastatic disease. We agree with those who think that local excision or simple mastectomy with or without removal of the pectoral muscle are appropriate forms of treatment (Oberman, 1965; Vera-Sempere and Llombart-Bosch, 1984).

In their series of 38 malignant fibrous xanthomas O'Brien and Stout (1964) included a storiform sarcoma occurring in the breast of a 70 year-old man. However, the possibility that this superficially located tumour involving skin and/or subcutaneous tissue might belong to the dermatofibrosarcoma protuberans group and not be a true MFH cannot be ruled out. Thus, case no. 4 in our series seems to be the first well-documented case of primary MFH of the male breast to be reported.

References


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