Histol Histopath (1986) 1: 27-32

Histology and Histopathology

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 excisioo or simple mastectomy recommended as appropriate treatment.

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

Introduction

The reported incidence of sarcomas of the breast varies from 0.24% to 3% of all malignant breast lesions (Khaiina 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).

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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.).

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% osmiurn tetroxide, dehydrated in graded ethanols and ernbedded in an Epon/Araldite mixture (Mollenhauer, 1964). Semithin sections were stained with toluidine bluc and used for light microscopic orientation and ultrathin sections for electron microscopy were contrasted with uranyl acetate and lead citrate.

Two MFH turnours 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 turnour, 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 interventiori and without clinical signs of recurrence or metastases.

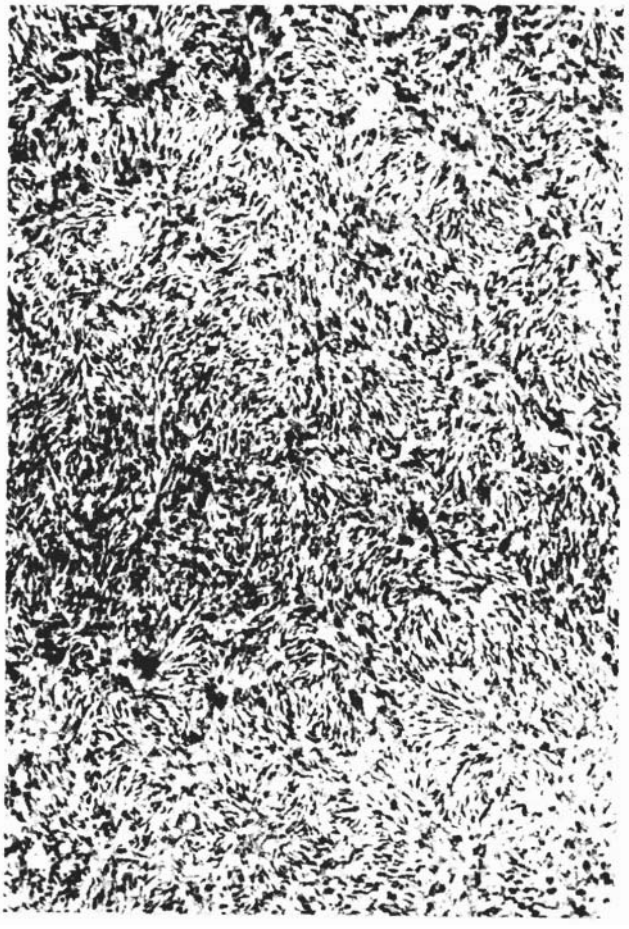

Fig. 1. (Case no. 2). Spindle-shaped and polygonal cells in a typical storiform pattern. H.E. x 45

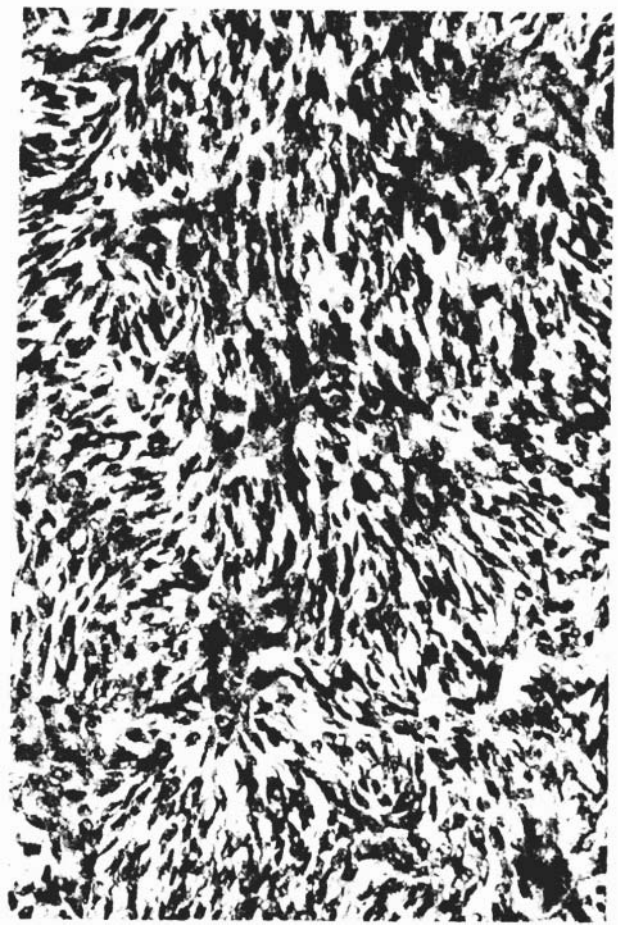

Fig. 2. (Case no. 2). Higher magnification of the tumour cells. H.E. x 280

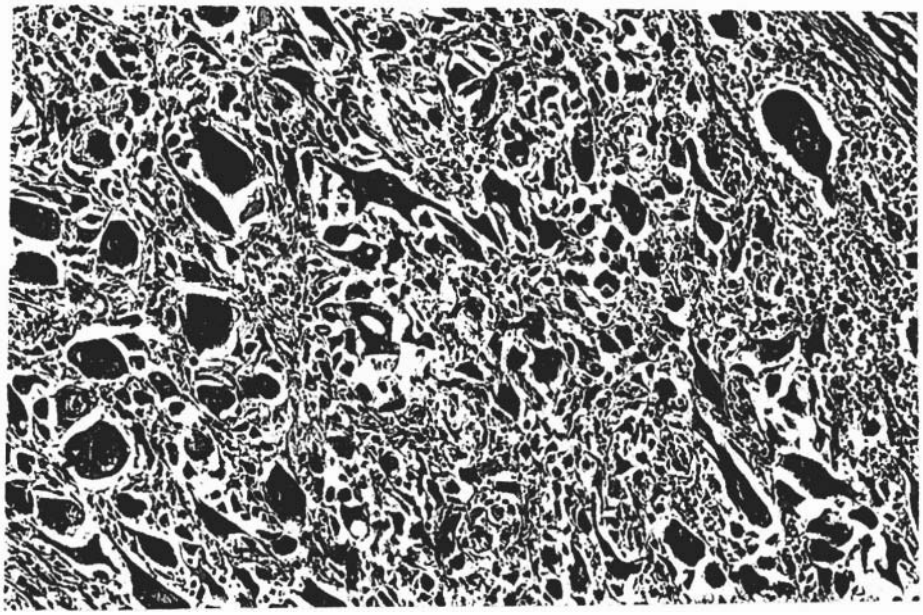

Fig. 3. (Case no. 4). Pleomorphic areas with numerous giant cells. H.E. ×45

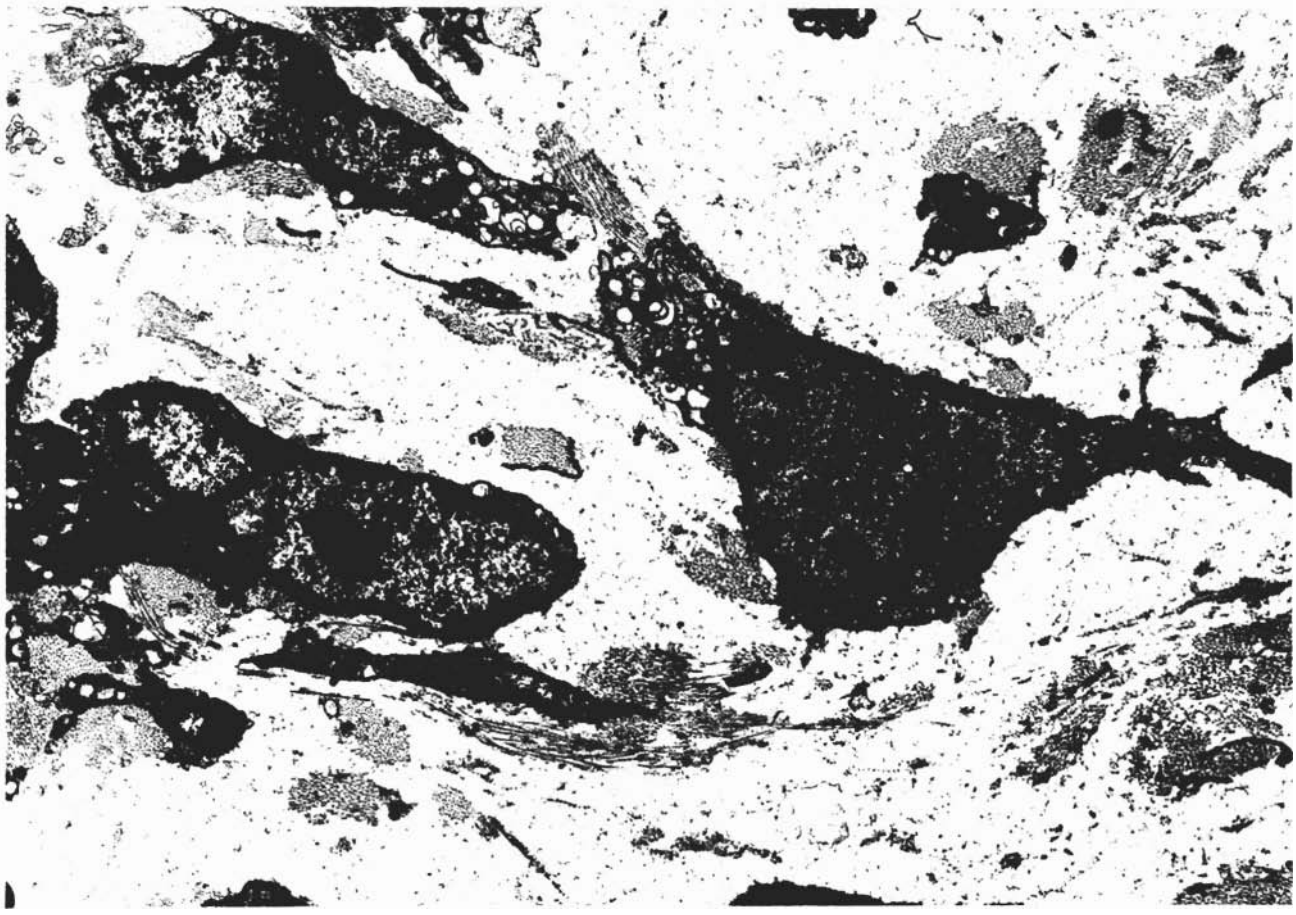

Fig. 4. (Case no. 1). Overview electron micrograph of the tumour cells in abundant intercellular substance with bundles of collagen fibres. Uranyl acetatellead citrate ×6,160

3. A 71 year-old unrnarried woman was found to have a well-circumscribed turnour in the upper lateral quadrant of the right breast. The grey-white turnour rneasured 6 cm in diameter and was of an elastic consistency. A simple rnastectorny 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 rnonths 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 rnan and rnalignant cells in the aspiration biopsy led to an ablatio and axillary lyrnphadenectorny, followed by irradiation 2 months later. Eighteen rnonths 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 histiocyte-like cells (Figs. 1, 2). The nuclei were pleomorphic and hyperchromatic with frequent mitoses. The mitotic rate varied frorn 2/10 high power field (HPF) (case no.1) to >10/10 HPF (cases nos. 2 and 4).

Areas with typical storiforrn 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 hernosiderin were occasionally seen. Multinucleated giant cells were rather frequent in case no. 4. Epithelial structures were not present in any of the tumours. The turnour borders were sharp in cases 1 and 3 but not in cases 2 and 4. A typical intraductal carcinonia of comedotype was however present in the breast tissue next to the sarcoma in case no. 3.

Immunocytochernistry

All turnours contained cells that stained positively for lysozyrne and a,-antitrypsin. No immunoreactivity for CEA and keratin was detected.

Keratin-positive cells were only seen in duct epithelium outside the turnours.

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 histocytes were polygonal or irregular in shape, and had an abundant cytoplasrn with lysosomes, sorne fat droplets and a well-developed rough endoplasmic reticulum. Scattered condensations were seen along the cell rnembranes but no well-developed desrnosornes.

Discussion

MFH is probably the most frequent soft tissue sarcoma in adults (Enzinger and Weiss, 1983). lts histogenesis is still unclear, but the cell of origin seems to be an undifferentiated pluripotent mesenchyrnal cell (Enzinger and Weiss, 1983). The tumour occurs not only in "classic" soft tissue regions -extremities and retroperitoneurn- but also in the skeleton (Terashinia et al., 1981; Capanna et al., 1984); lung (Spencer, 1977; Carter and Eggleston, 1980; Silverrnan and Coalson, 1983; Lee et al., 1984); vulva (Hensley and Friedrich, 1983); larynx (Canalis et al., 1975); conjunctiva (Delgado-Partida and Rodríguez-Trujillo, 1972); heart (Shah et al., 1978; Morirnoto et al., 1980; Harnada et al., 1981; Terashirna 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; Langharn et al., 1984; Vera-Sernpere and Llombart-Bosch, 1984) but are extremely rare without prior existence of phyllodes tuniour or prior irradiation io 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-Bosch, 1984) before this report.

Diagnosis of prirnary 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-Bosch, 1984) seern to have a more aggressive biological behaviour than prirnary ones and should therefore be classified separately.

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

Dermatofibrosarcorna protuberans with its typical storiform growth pattern can easily be confused with a MFH. It is locally invasive but only rarely gives rise to rnetastases (Lever and Schaumberg-Lever, 1983). This skin turnour can also infiltrate the breast parenchyrna 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 already stated in the criteria for selection, there was no skin involvernent 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,

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 Pietruszka, 1977); rhabdomyosarcoma (Oberman, 1965; Elhence et al., 1972); leiomyosarcoma (Cameron et al., 1984; Nielsen, 1984) and angiosarcoma (Steingaszner 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.

Acknowledgernents. We acknowledge with thanks the skillful technical assistance of Inga Finseth, Ellen Hellesylt, Liv Inger Háseth, Mette Myre and Elisabeth Ernilsen Molsted.

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Accepted September 19, 1985