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Myofibroblastoma of the breast with diverse histological features

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Abstract We report two cases of myofibroblastoma with unusual pathological features, in a 66-year-old woman and a 49-year-old man. Both tumours were unilateral, grossly nodular and well circumscribed, but not encapsulated. The lesions were made up of bipolar spindle cells arranged in fascicular clusters separated by bands of hialinized collagen; one included several islands of mature cartilage next to fat cells. The other contained atypical mononucleated and multinucleated giant cells. No mitotic figures were observed. Immunohistochemically, both tumours showed strong and diffuse cytoplasmic staining for vimentin and CD 34 and focal positivity for alpha-smooth muscle actin, and both were negative for cytokeratins, CD 68, Ham 5, 6, Mac 387, and S-100 protein. Desmin was positive in one case. Ultrastructural study revealed populations composed of fibroblastic cells without signs of myofibroblastic differentiation in one case; the second featured abundant undifferentiated mesenchymal cells with myofibroblastic differentiation. Both patients remain disease-free 38 and 36 months after lumpectomy.

Key words Myofibroblastoma · Benign mesenchymal breast tumours · Myofibroblastoma of the breast

Introduction

Myofibroblastoma, an uncommon benign mesenchymal tumour of the breast, was first described by Wargotz et al. in 1987 [18]. A similar lesion had been reported 7 years before by Toker et al. [17], who named it benign spindle-cell tumour. Begin [1] found smooth muscle cells but no myofibroblasts in this tumour on electron microscopy, so he proposed the name myogenic stromal tumour.

Recently, Damiani et al. [3] have included myofibroblastoma of the breast in the group of solitary fibrous tumours, on the grounds of histological and immunohistochemical similarities. Microscopically, myofibroblastoma of the breast presents as a mesenchymal tumour that is well demarcated from adjacent parenchyma, lacks epithelial breast elements and is composed of bundles of spindle cells separated by prominent collagen bands. Initial reports described a male predominance [12], but it is now clear that female persons are also affected [5].

This report describes two cases of myofibroblastoma of the breast with diverse histological patterns, featuring lobules of hyaline cartilage in one case and abundant cells with pleomorphic nuclei in the other, illustrating the diagnostic pitfalls of this rare tumour.

In a 66-year-old woman, who presented after noting enlargement of her right breast several months earlier (case 1). Mammography revealed a well-circumscribed mass occupying all the lower external quadrant of the breast. Lumpectomy was performed.

The other case was in a 49-year-old man, who had a right subcutaneous mastectomy for right-sided gynaecomastia of several years, duration (case 2). No breast lump was palpable.

Materials and methods

The excised tumours were fixed in buffered formalin and embedded in paraffin. Sections were routinely stained with haematoxylin-eosin.

Immunohistochemical studies were performed on formalin-fixed, paraffin-embedded tissues using the avidin–biotin peroxidase (ABC) method. Primary antibodies against the following antigens were used: vimentin (monoclonal, Amersham, Little Chalfont, UK; diluted 1:40), desmin (polyclonal, Bio-Science, Emmenbrucke, Switzerland; 1:50), α-smooth-muscle actin (monoclonal, Dakopatts, Glostrup, Denmark; 1:50), low-molecular-weight cytokeratin (CAM 5.2) (39 and 43 kDa, monoclonal, Becton-Dickinson, Mountainview, Calif. 1:1), S100 protein

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(polyclonal, Dakopatts; 1:200) and haematopoietic progenitor cell antigen, CD34 (monoclonal, Becton-Dickinson; 1:25). Appropriate positive and negative control experiments were also performed.

Formalin-fixed material was processed for electron microscopic study.

Results

Case 1

Macroscopically, a 9×5 cm elastic whitish mass with yellowish areas was found (Fig. 1).

Microscopically, the tumour was composed of monomorphic spindle cells arranged in bundles, intermingled with thick collagen fibres (Fig. 2); it was well demarcated from the adjacent breast tissue but not encapsulated. Tumour cells had elongated nuclei with sparse chromatin and no conspicuous nucleoli. No mitosis or nuclear pseudoinclusions could be seen. There were highly cellular areas and mostly sclerotic areas. There was abundant fat tissue among spindle cells. Islands of myxoid tissue composed of stellate cells, with central differentiation to mature cartilage, could be seen (Fig. 3). Such islands were usually close to areas of fat tissue.

The spindle cells showed strong membrane positivity for CD 34 and diffuse cytoplasmic positivity for vimentin. Smooth-muscle actin immunostaining was seen in isolated cells.

Tumour cells were uniformly negative for desmin, cytokeratins and S-100 protein, except for cartilage islands, in which chondroid cells were positive for S-100 protein.

On electron microscopy, spindle cells were seen to have fibroblastic features with bland nuclei and moderate amounts of cytoplasmic organelles, featuring numerous profiles of rough endoplasmic reticulum. No myofibroblastic features were seen.

Case 2

Upon section, a 2×2-cm whitish tumour with a smooth surface was found, which was sharply demarcated from the adjacent breast parenchyma.

Microscopically, the tumour was composed of bundles of spindle cells separated by thick collagen bands. The lesion was hypercellular, featuring abundant pleomorphic cells throughout the tumour; those had one or more hyperchromatic nuclei with irregular nuclear membrane and conspicuous nucleoli and ample globular and intensely eosinophilic cytoplasm (Fig. 4). No mitosis or areas of necrosis were seen. The remaining cells had elongated monomorphic nuclei with bland chromatin.

Blood vessels were prominent, surrounded by abundant collagen. No fat tissue was seen. The lesion was demarcated from the adjacent breast tissue, with no breast ducts or lobules within the tumour.

The immunohistochemical profile of the tumour included intense membrane positivity for CD 34 in both spindle and pleomorphic cells, generalized cytoplasmic positivity for vimentin and focal positivity for desmin and smooth-muscle actin. Pleomorphic cells stained most strongly for desmin. They were uniformly negative for cytokeratins (AE1-AE3), S-100 protein and histiocytic markers (CD 68, Ham 5, 6 and Mac 387).

Ultrastructurally, the tumour cells had large numbers of organelles and an irregular nuclear membrane, and occasional pseudoinclusions were seen. Focally, some cells had subplasmalemmal filaments with dense bodies, poorly defined cell junctions and pinocytic vesicles. The ultrastructural features of pleomorphic cells and of the remaining tumour cells were similar.

Discussion

Myofibroblastoma of the breast is an uncommon tumour composed of monomorphic spindle cells among collagen

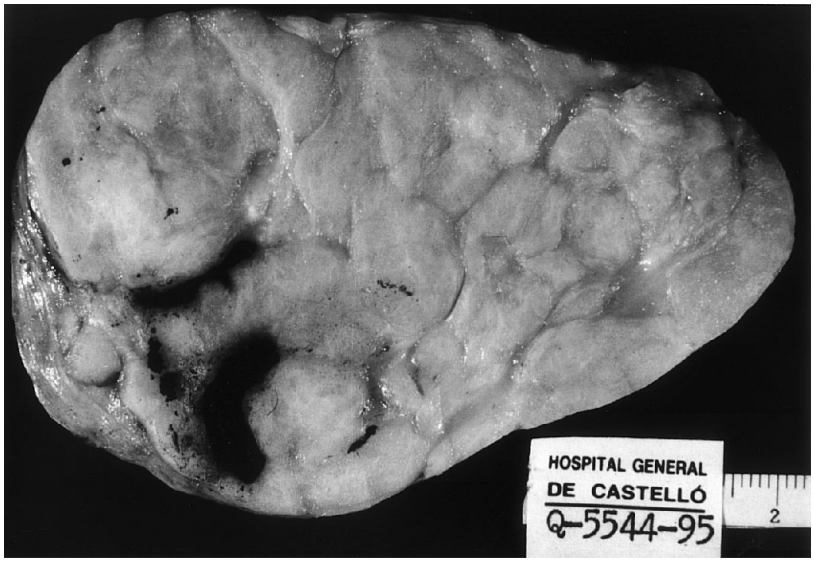

Fig. 1 Gross section of case 1. This 9×5 cm myofibroblastoma is well circumscribed, whitish with yellowish areas, and rubbery

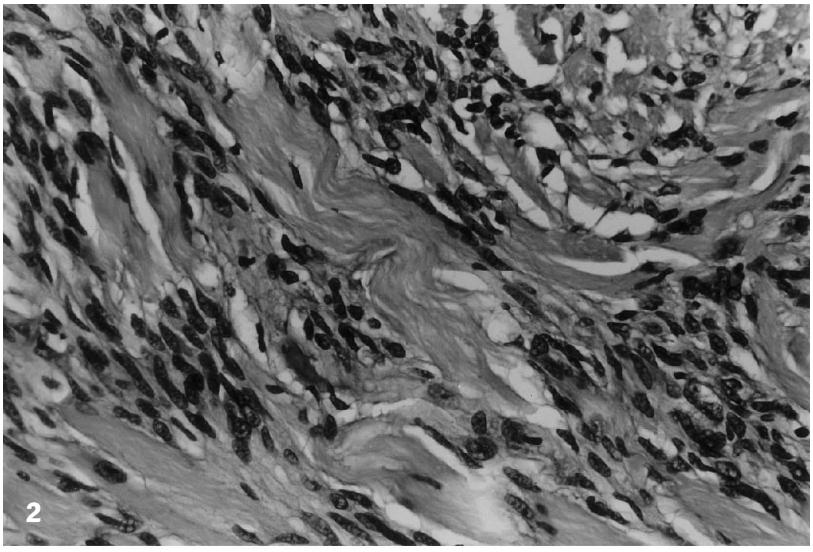

Fig. 2 Case 1: monomorphic spindle cells are arranged in bundles and intermingled with thick collagen fibres. H&E, ×400

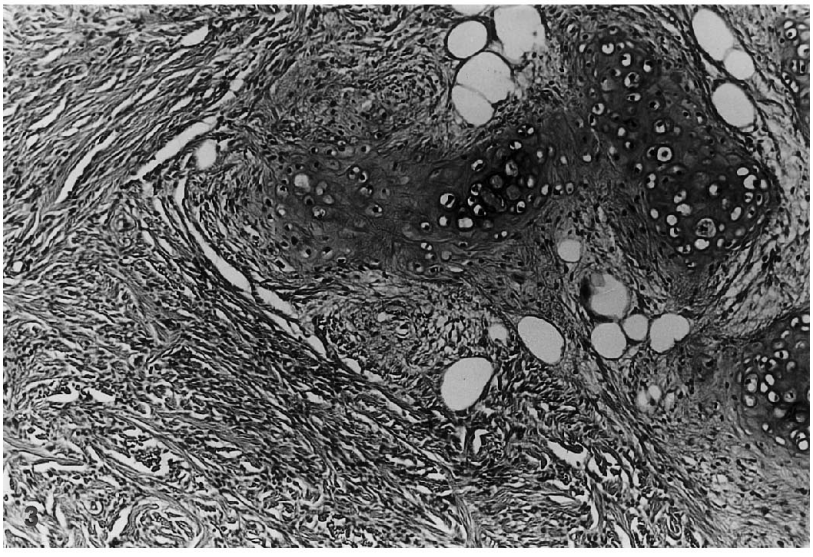

Fig. 3 Case 1: islands of myxoid tissue with central differentiation to mature cartilage, and also adipocytes, can be seen within the tumour. H&E, ×100

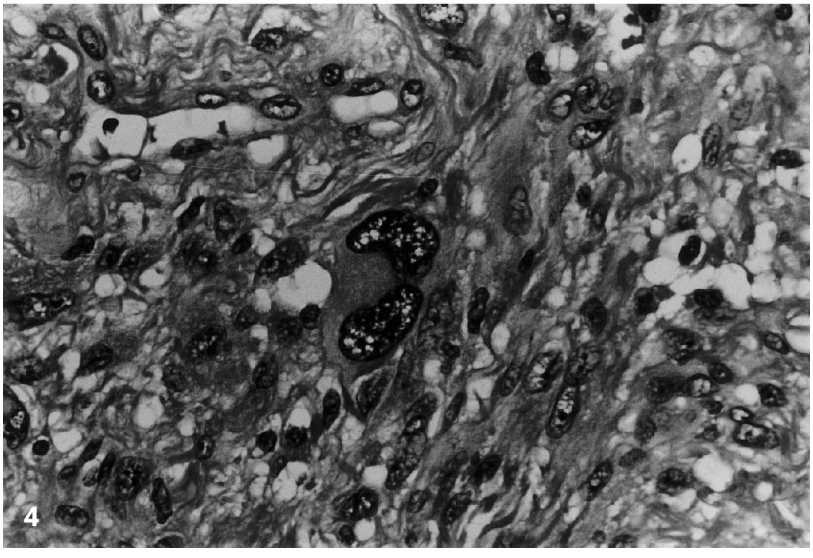

Fig. 4 Case 2: the tumour shows hypercellularity and wide variability in nuclear size. There are abundant pleomorphic cells with bizarre and hyperchromatic nuclei. H&E, ×400

bundles. Diagnosis is difficult, both because this lesion is so rare and because there is frequently diverse differentiation.

Most breast tumours containing cartilage are malignant, most of them being metaplastic carcinomas and (in lower proportions of cases) true sarcomas and phyllodes tumours [14].

Wargotz et al. [18] reported a case of myofibroblastoma containing cartilage islands intermingled with spindle cells typical of this tumour and with fat tissue. Our first case is similar, with foci of cartilage throught the tumour. Most cartilage islands are surrounded by myxoid tissue, with undifferentiated stellate cells, from which chondrocytes are derived. Immunohistochemically mature chondrocytes are positive for S-100 protein, as is normal cartilage, whereas the surrounding stellate cells are positive for vimentin and CD 34, which suggests lack of differentiation.

The differential diagnosis includes other benign tumours that can contain cartilage. Benign chondrolipomatous tumour [6] is a variety of hamartoma in which foci of cartilage are intermingled with fat, fibrous tissue, and epithelial elements. Pleomorphic adenomas [10] are very rare and are similar to those arising in salivary glands. Exceptional cases of cartilaginous metaplasia within fibroadenomas have been reported [8]. A lesion termed choristoma [9] combines mature cartilage, fat tissue, smooth muscle, fibrosis and epithelial elements, and should be grouped with the hamartomas. Epithelial breast elements are present within all these tumours, in contrast to myofibroblastoma, which is an exclusively mesenchymal tumour.

Only two previously reported cases of myofibroblastoma [7, 18], and case 1 of the present report, contained foci of cartilage. Other authors [15] have termed a similar case ”mesenchymoma”. Two other tumours, diagnosed as mesenchymoma [2] and fibroma with cartilaginous metaplasia [8], had features similar to those of myofibroblastoma, but the illustrations are not conclusive.

Our case 2 contains a large number of pleomorphic cells throughout the tumour, with evident nuclear atypia and ample eosinophilic cytoplasm, suggesting malignancy. The presence of isolated multinucleated giant cells, mostly in small numbers and devoid of pleomorphism, is not rare in myofibroblastomas of the breast [18]. The histiocytic appearance of these cells is not confirmed on immunohistochemistry, showing that they are intrinsic tumour cells and positive for CD 34 and desmin like the rest of the tumour cells. Fukunaga et al. [4] reported a similar case, even though pleomorphic cells were not present throughout the tumour but formed a small nodule 1 mm in diameter. Such cells were interpreted as reflecting myogenic differentiation similar to that observed in atypical or bizarre uterine leiomyomas, since they stained positively for muscle markers. Indeed, we observed strong positivity for desmin in pleomorphic cells, and some cells had subplasmalemmal filaments with dense bodies on electron microscopy. However, the occurrence of benign pleomorphic cells is not peculiar to smooth muscle tumours. The presence of these features in the so-called ancient schwannomas is well known, and in addition, similar cells have also been described previously in tumours showing fibroblastic-myofibroblastic differentiation [13], like the present cases.

Given the intense cytological atypia and the cytological differences from classic myofibroblastoma [11], the possibility that this lesion could be a malignant tumour was considered. However, the absence of mitosis and necrosis, the good demarcation and the absence of relapses or metastases at 3 years’ follow-up support a benign prognosis for this tumour, in contrast to myofibrosarcoma [16].

Myofibroblasts, fibroblasts, adipocytes, smooth muscle cells, chondrocytes and undifferentiated cells have all been described within myofibroblastomas, suggesting that they are derived from pluripotential undifferentiated mesenchymal cells [4]. The ultrastructural features of our cases, with very different amounts of each cell component in case 1 and case 2, and the predominant immature mesenchymal cell component in case 2 support this hypothesis.

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