Case report

Fibroma of the breast: a rare tumour in the spectrum of the benign spindle cell tumours of the mammary stroma

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Benign spindle cell tumours of the mammary stroma comprises different lesions that show a variable degree of fibroblastic/myofibroblastic differentiation. We herein report a previously under-recognised hypocellular fibrocollagenous tumour of the breast, for which the term “fibroma” is proposed. The tumour was composed of CD34-positive bland-looking spindle cells embedded in an abundant hyalinised stroma. Fluorescence in situ hybridisation (FISH) showed 13q14 deletion in most neoplastic cells, a chromosomal alteration typically found in mammary myofibroblastoma. Based on morphological, immunohistochemical, and cytogenetic features, we suggest that fibroma belongs to the group of the benign spindle cell tumours of the mammary stroma.

Key words: breast, mammary stroma, fibroma, benign spindle cell tumour, 13q14 deletion.

Introduction

Benign spindle cell tumours of the mammary stroma are an uncommon group of lesions, which share several morphological and immunohistochemical features [1, 2, 3]. Although myofibroblastoma is the most known and well-defined lesion [4, 5], the boundaries of the tumours with fibroblastic differentiation are poorly delineated. This is the main reason why different names, such as “benign spindle cell tumour” [1, 6, 7, 8, 9], “fibroma” [9], “spindle cell lipoma” [10, 11], “myogenic stromal tumour” [12], “solitary fibrous tumour” [13, 14, 15], and myofibroblastoma” [13, 14] have been used, often interchangeably, for the same tumour. There is increasing evidence that the group of “benign spindle cell tumours of the mammary stroma” comprise a wide spectrum of CD34-positive lesions ranging from tumours with fibroblastic differentiation (“benign fibroblastic spindle cell tumour”; “benign fibroblastic spindle cell tumour with fatty component”; spindle cell lipoma) to tumours with clear-cut myofibroblastic differentiation (classic-type myofibroblastoma and its morphological variants) [1, 3]. Solitary fibrous tumour, originally included in this group [2, 3], shows a different molecular profile [16, 17, 18, 19] and it is actually better classified as a soft tissue...
tumour occurring in the breast rather than a tumour specific to mammary stroma [1].

We herein report a previously unrecognised, hypocellular, benign mesenchymal spindle cell tumour of the breast with hyalised collagenous stroma, closely reminiscent of tendon sheath fibroma, for which the descriptive term "fibroma of the breast" is proposed. Because this tumour shares the 13q14 deletion with myofibrolastoma of the breast, we speculate that it belongs to the group of the benign spindle cell tumours of the mammary stroma.

Material and methods

A 58-year-old female presented a painless, well-circumscribed supra-areolar nodule at her right breast. Physical examination revealed a firm, mobile mass, measuring 2 cm in its greatest dimension. There was no associated skin retraction, and axillary lymph nodes were not appreciable on palpation. Ultrasoundography revealed a hypoechoic, well-circumscribed tumour without microcalcifications, and thus a fibroadenoma was suspected. The patient underwent fine-needle core aspiration biopsy (FNACB), but the material was not diagnostic. A lumpectomy was performed, accordingly.

Surgical specimen was submitted for histological examination in neutral-buffered 10% formalin, dehydrated using standard techniques, and embedded in paraffin. Five-micrometre sections were cut and stained with haematoxylin and eosin (HE). Immunohistochemical studies were performed with the labelled streptavidin-biotin peroxidase detection system using a Ventana automated immunostaining system (Ventana Medical Systems, Tucson, AZ). The following antibodies were applied: vimentin, CD34, α-smooth muscle actin, desmin, h-caldesmon, wide spectrum cytokeratins (CKMNF116), epithelial membrane antigen (EMA), S-100, myogenin, and oestrogen and progesterone receptors (all from DakoCytomation, Glostrup, Denmark). Polyclonal rabbit antibody (s20-S621, Santa Cruz Biotechnologies, Santa Cruz, CA, USA) against the STAT6 C-terminal was used at a dilution of 1:200, after antigen retrieval (96°C EDTA for 30 min).

FISH analysis for the detection of FOX1 (previously FKHR), located on 13q14.11, was performed on 4- to 6-μm paraffin-embedded tissue sections, deparaffinised with xylene and subsequently enzymatically digested with a commercial kit (Paraffin Pretreatment Reagent Kit; Vysis-Abbott Molecular, Downers Grove, IL). Sample DNA was denatured at 75°C for five minutes. The Locus-Specific Identifier FOX1 Break Apart Probe (Vysis-Abbott), which hybridises to band 13q14, was used. The Locus-Specific Identifier FOX1 consists of a mixture of 2 DNA probes: the first (720 kilobase) is labelled with Spectrum Orange that extends distally from the FOX1 gene and the second one (650 kilobase) is labelled with Spectrum Green and lies proximal to the FOX1 gene. The probe mix (10 μl), previously denatured for five minutes at 75°C, was applied on each slide. The slides, covered with a glass cover slip, were incubated for 5 minutes at 79°C for codenaturation and placed in a humidified chamber at 37°C overnight to allow hybridisation to occur. After post-hybridisation washes, carried out according to the manufacturer's protocols, tissue sections were counterstained with DAPI I (Vysis-Abbott) and examined with a fluorescence microscope (Olympus, Tokyo, Japan).

Results

Grossly tumour presented as an unencapsulated, well-circumscribed, 2-cm nodule surrounded by a peripheral rim of normal-apparing breast tissue. The cut surface revealed a homogeneous, nodular mass, whitish in colour and firm in consistency. No areas of haemorrhage or necrosis were seen. Histological examination revealed an unencapsulated, hypocellular tumour with pushing margins (Fig. 1A, B). It was predominantly composed of bland-looking spindle cells with a minority of rounded cells, set in an abundant fibrocollagenous stroma containing only rarely capillary-like blood vessels (Fig. 2A, B). Some tumour areas were relatively more cellular and the spindle cells exhibited wavy nuclei (Fig. 3A). Mitoses, nuclear atypia, haemorrhage, and necrosis were absent. Only a few mammary ducts/lobules were entrapped within the tumour (Fig. 1B, 2B). Immunohistochemically neoplastic cells were diffusely stained with vimentin and CD34 (Fig. 3B). No immunostaining was obtained with all the other antibodies tested. Notably, FISH analyses revealed monoallelic deletion of the FOX1 gene in 67.3% of the cell population (Fig. 3C). Based on the morphological, immunohistochemical, and cytogenetic features, the term "fibroma of the breast" was coined for such an uncommon lesion.
Fig. 1. A) Low-magnification showing a fibrocollagenous tumour with pushing borders. B) Higher magnification showing a hypocellular fibrotic tumour with interspersed mammary ducts.

Fig. 2. Tumour is composed of bland-looking spindle cells set in an abundant hyalinised stroma (A) containing mammary ducts and rare capillary-like blood vessels (B).
Benign mesenchymal spindle cell tumours of the breast are relatively rare, and myofibroblastoma is the most known tumour of this group [1, 2, 3]. Other tumours that belong to this group are the benign fibroblastic spindle cell tumour and spindle cell lipoma [1]. Although several studies have emphasised that myofibroblastoma and spindle cell lipoma share morphological, immunohistochemical, and cytogenetic features [2, 3, 5], there is increasing evidence that solitary fibrous tumour, originally included in this group [2, 3], is actually viewed as a distinct entity with different immunohistochemical and molecular profiles [16, 17, 18, 19].

The present paper contributes to widening the morphologic spectrum of the benign spindle cell tumours (BSCT) of the mammary stroma, adding to myofibroblastoma, benign fibroblastic spindle cell tumour, and spindle cell lipoma a previously unrecognised, hypocellular tumour with abundant fibrocollagenous stroma, for which the term “fibroma” is proposed. Immunohistochemistry, showing the expression of vimentin and CD34, revealed the fibroblastic nature of the tumour. Given the vague morphological resemblance to tendon sheath fibroma, the term “fibroma of the breast” is proposed. Although the term “fibroma” has already been used for two spindle cell tumours of the breast, based on the illustrations provided by the authors, one case should be best regard-

**Fig. 3.** A) In this tumour area the spindle cells exhibit wavy nuclei. B) The spindle cells are stained with CD34. C) FISH analysis showing monoallelic loss of FOXO1/13q14 loci as indicated by the presence of one fusion red/green signal in most tumour cells.
ed as recurrent phyllodes tumour [20] and the other case as a benign fibroblastic spindle cell tumour [9]. Our case could be confused with fibrous masses of the breast that have been reported in the literature under different names including “fibrous tumour”, “fibrous disease”, “fibrosis of the breast”, “focal fibrous disease”, and “fibrous mastopathy” [21]. These uncommon lesions present as discrete breast mass composed of acellular collagenised stroma with admixed atrophic mammary ducts and lobules. As previously suggested [21], some of these lesions could be better classified as examples of pseudoangiomatous stromal hyperplasia (fascicular variant), the diagnosis can be challenging [1]. Unlike our case, however, the fascicular variant of pseudoangiomatous stromal hyperplasia, which imparts to the tumour mass a “fibroma-like” appearance.

The histological diagnosis of fibroma of the breast is usually straightforward due to its typical morphological features (hypocellular, spindle cell tumour with extensive fibrocollagenous stroma), but this tumour needs to be distinguished from other potential mimics. Differential diagnosis mainly includes pseudoangiomatous stromal hyperplasia (cellular variant), fibroadenoma with fibrotic stroma, nodular fasciitis, fibromatosis, myofiromablastoma (collagenised variant), benign fibroblastic spindle cell tumour, solitary fibrous tumour, and neurofibroma. The diagnosis of pseudoangiomatous stromal hyperplasia is straightforward if anastomosing, slit-like pseudovascular spaces are present. When these features are absent, the diagnosis of pseudoangiomatous stromal hyperplasia needs to be distinguished from other potential mimics. The fascicular variant of pseudoangiomatous stromal hyperplasia shows a proliferation of spindle cells arranged in distinct fascicles with interspersed keloid-like collagen fibres, resulting in a myofiromablastoma-like appearance [1].

Although rare ducts/lobules were entrapped throughout the tumour, the classic biphasic pattern of fibroadenoma, namely spindle cell proliferation around tubular/ductal structures, was lacking in our case. Desmoid-type fibromatosis of the breast is a potentially locally-recurrent tumour composed of spindle cells set in a fibrous stroma [22, 23]. Unlike fibroma, desmoid-type fibromatosis exhibits infiltrative margins, arrangement of neoplastic cells into long fascicles and immunohistochemical expression of both α-smooth muscle actin and β-catenin [1]. Nodular fasciitis is a spindle cell proliferation that can be composed predominantly of collagenous stroma. However, unlike fibroma, nodular fasciitis has, at least focally, infiltrative margins, short and not well-formed fascicles, a tissue culture-like appearance, and immunoreactivity for α-smooth muscle actin [1]. The collagenised variant of myofiromablastoma can be confused with fibroma due to its well-circumscribed margins [1]. However, the spindle cells of this myofiromablastoma variant are myofiromablastic in nature, with the expression, apart from CD34, of myogenic markers (desmin; α-smooth muscle actin) [1].

Although fibroma and benign fibroblastic spindle cell tumour share vimentin and CD34 expression, the latter is more cellular and is composed of fibroblast-like cells arranged haphazardly or into short fascicles, closely intermingling with thick collagen fibres [1]. However, the possibility that the present case may reflect the collagenised variant of the benign fibroblastic spindle cell tumour cannot be completely ruled out. Solitary fibrous tumour may show extensive fibrocollagenous stroma, posing differential diagnostic problems with fibroma. However, the diagnosis of solitary fibrous tumour is usually based on the presence of medium-sized blood vessels with hyalinised walls and branching configuration and the diffuse nuclear staining for STAT6 [19, 24]. In addition, our case showed the 13q14 deletion, a cytogenetic alteration that is lacking in solitary fibrous tumours [25]. Although in our case there were focal areas with spindle cell exhibiting wavy nuclei, neurofibroma was excluded on the basis of the absence of S-100 expression.

Notably, our case exhibited the 13q14 deletion by means of FISH. This finding is very intriguing in that the same chromosomal abnormality is shared with mammary myofiromablastoma [26, 27], suggesting that these tumours are histogenetically-related. Accordingly, we speculate that the fibroma described herein belongs to the spectrum of the benign spindle cell tumours of the mammary stroma, which comprises myofiromablastoma, benign fibroblastic spindle cell tumour, and spindle cell lipoma. As previously suggested, it is likely that these tumours represent subtle variations of the same entity, probably arising from the uncommitted vimentin+/CD34+ fibroblasts of the mammmary stroma, capable of both fibroblastic and myofiromablastic differentiation [1].

The authors declare no conflict of interest.

References