Quiz

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Case report

Giant low-grade myofibroblastic sarcoma of the male breast: case report and literature review

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Low-grade myofibroblastic sarcoma is an uncommon malignancy that can be difficult to identify and for which there is no unified treatment protocol. We report herein a case of an 81-year-old male who presented with a giant irregular breast mass and was diagnosed with low-grade myofibroblastic sarcoma. In this study we summarise the clinicopathological features of 13 reported cases of myofibroblastic sarcoma arising in the breast, present the diagnostic process and treatment procedure of our case, and discuss the differential diagnosis from other similar diseases, to provide constructive information and promote deep understanding of myofibroblastic sarcoma in the future.

Key words: low-grade myofibroblastic sarcoma, male breast, diagnostic process, treatment procedure.

Introduction

Low-grade myofibroblastic sarcoma (LGMFS) is a malignant tumour that is mainly composed of atypical myofibroblasts [1–3]. Most tumours composed of myofibroblasts are benign, and some have low-grade malignant potential [4]. A definite diagnosis of myofibroblastic sarcoma (MFS) requires summation of morphological and ultrastructural features, corresponding to those first defined in proliferating myofibroblasts in granulation tissue. LGMFS has a propensity to recur locally, but rarely with distant metastases [5].

This tumour mostly occurred in the head or neck region with a slight male predominance [6]. The myofibroblastic sarcoma (MFS) of breast was rarely reported previously. We reviewed the current literature and found 13 cases of MFS diagnosed in the breast [1–4, 6–13]. Diagnosis of MFS mainly relies on pathological examination because non-specific clinical manifestations make clinical diagnosis difficult. Therefore, we present the diagnosis and treatment procedure of our case to provide further information about this tumour, and we investigated the histological and immunohistochemical criteria of 14 cases of mammary MFS to help further understand this tumour in the future.

Material and methods

The tissue specimen was fixed in 10% neutral buffered formalin solution. Slides were prepared from paraffin blocks and stained with haematoxylin and eosin stain. All sections for immunocytochemistry were stained on a Dako automated platform. Immunohistochemical stains for pancytokeratin (PCK), smooth muscle actin (SMA), desmin, myogenin, myoD1, CD34, ALK1*, STAT6, S-100, and Ki67 protein were performed. The 13 patients with breast MFS have been previously reported in references [1–4, 6–13].

Results

Case presentation

An 81-year-old man with diabetes and hypertension developed a non-tender mass in his left breast. He first palpated with a 2.5-cm mass in 2018 without constitutional symptoms and did not have treatment. Over the course of 2 years, the mass slowly expanded. Two years after the appearance of the primary lesion, the tumour recurred locally and grew rapidly. In April 2021, he came to our hospital for treatment, and we found that the size of mass was nearly 30 cm, extending into the armpit with no axillary lymph node enlargement (Fig. 1A). The patient had a lateral curvature of the thoracic vertebra because of the tumour's weight. Enhanced computed tomography (CT) (Fig. 1B) and magnetic resonance imaging (MRI) revealed that the tumour had uneven enhancement, with no enhanced necrotic area in the patchy interior, and the boundary between the tumour and the left pectoralis major, serratus anterior, and latissimus dorsi muscle was not clear. The sonography showed that the tumour was a cystic solid mass (sarcoma could not be ruled out), and he underwent an ultrasound-core needle biopsy from 4 different tissues, but the pathological results of puncture biopsy showed that abnormal spindle cells were found in the tissues, not excluding malignant, and a complete resection of the tumour was recommended, so the patient was treated with left breast lumpectomy.

After the surgery, the patient did not receive chemotherapy or radiotherapy. However, 2 months after the surgery, a 3.5-cm tumour near the armpit reappeared. The enhanced CT showed that the tumour was located near the left armpit and was indistinguishable from the axillary vein. After the MDT (multi-disciplinary team) discussion, we decided to perform a palliative lumpectomy. During the surgery, we found that the latissimus dorsi muscle mutated around the axillary vein, and the tumour originated in the mutated muscle near the axillary vein, so we removed the tumour again and some of the mutated muscle, the remaining mutated muscle was too difficult to detach from the axillary vein, so after surgery, we gave PGTV 68.12Gy/26F, PTV-high 2.94Gy/26F, PTV 55.76ZGy/26F radiotherapy to the patient; the target sites of radiotherapy were left chest wall, primary tumour bed, and new tumour site.

After 24 months of follow-up, the patient was still alive, with no evidence of recurrence.

Morphological findings

During the operation, a 30-cm, firm, greyish-white, deeply located muscle mass was resected. Haemorrhages and cyst changes were found at the site. Microscopically, the tumour was predominantly composed of spindle cells and displayed diffusely infiltrative growth in the subcutaneous tissues. Tumour stroma was predominantly collagenous containing thin-walled blood vessels, while focal myxoid areas were occasionally observed. The feathery or stellate tumour cells exhibited pale eosinophilic cytoplasm with frequent intracytoplasmic vacuoles, and a wavy nucleus tapering towards one end, or oval shaped nucleus with small nucleoli. In the hypercellular areas, mode-

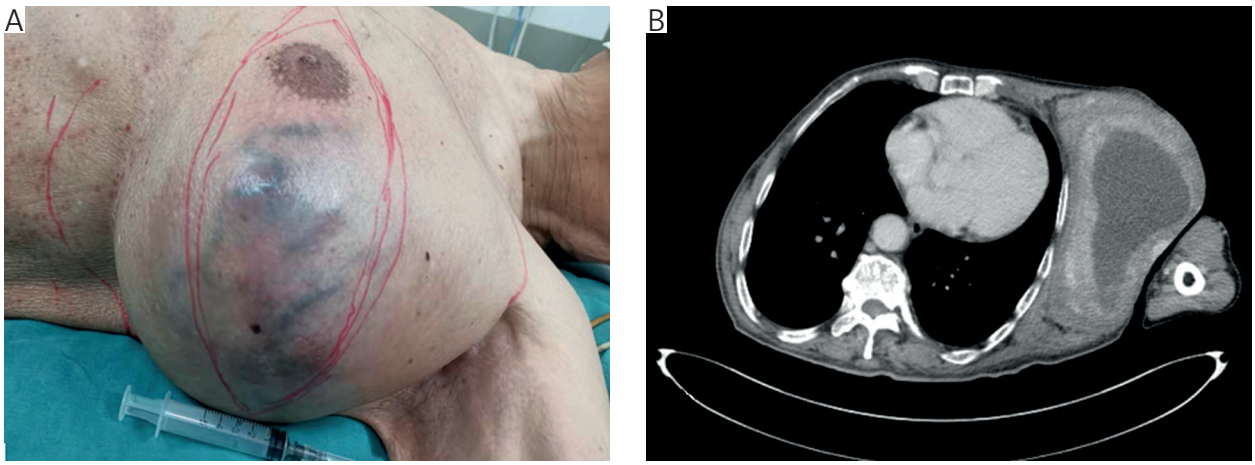

Fig. 1. A) Side view of the giant tumor. **B**) The computed tomography image of cross-sectional about tumor's relationship with muscle

rate cellular atypia was observed as well as occasional mitoses. The mitotic arranged from 1 to 3/10 HPF. Multinucleate cells and the cytoplasm-rich rhabdoid cells with deviated nuclei were not rare in these areas (Fig. 2A–D). Furthermore, necrosis can be observed.

Immunohistochemistry

Immunohistochemically, tumour cells showed diffuse expression of SMA and spotted expression of desmin (Fig. 2E, F), while no staining was obtained with CD34, S-100, MyoD1, myogenin, ALK1, Sox-10,

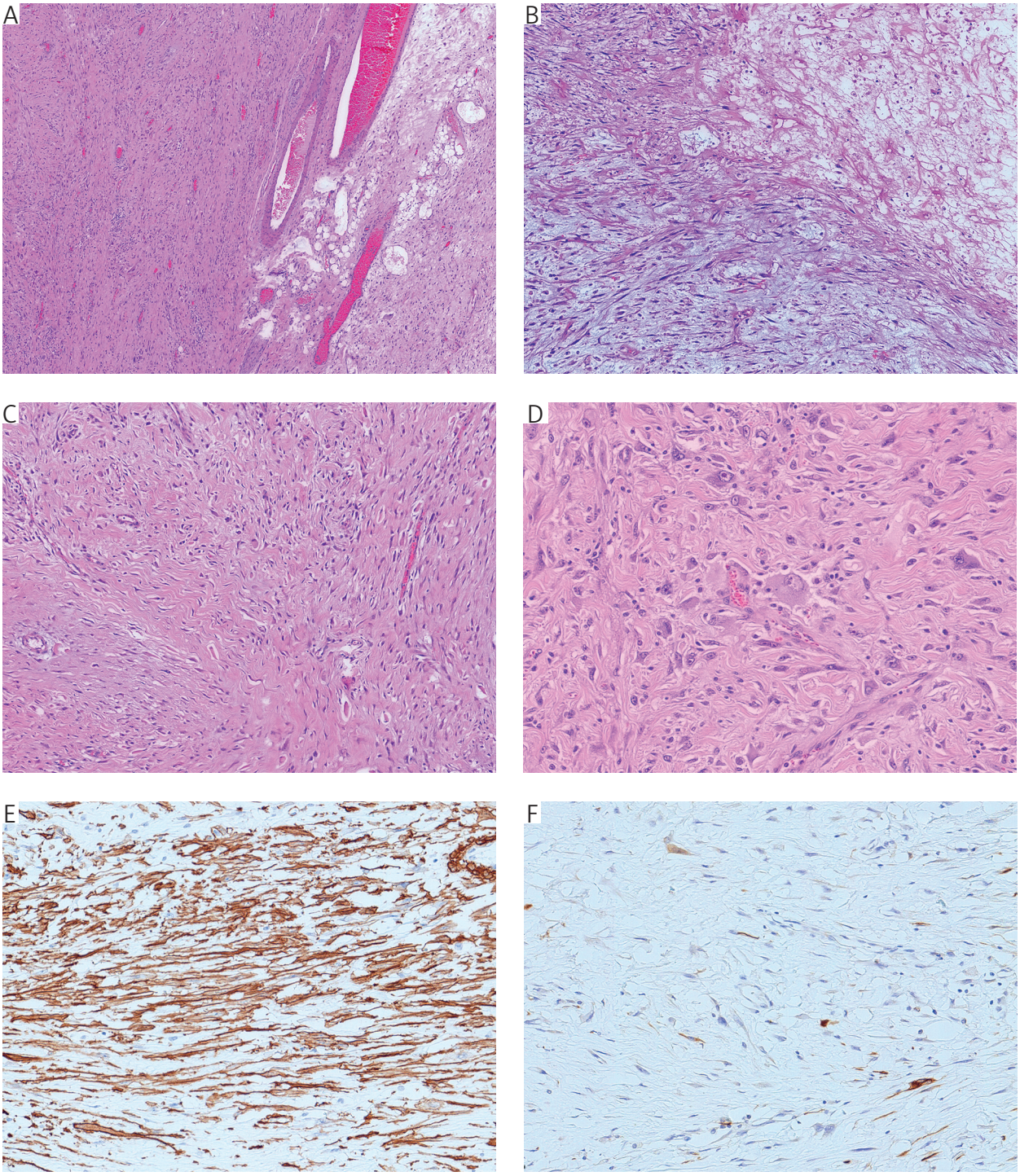

Fig. 2. A) Tumor infiltrated the surrounding adipose tissue, HE, 40×. **B**) Tumor stroma was predominantly collagenous, while focal myxoid areas were observed, HE, 100×. **C**) The intersecting cellular fascicles composed of spindle cells, HE, 100×. **D**) The feathery or stellate tumor cells with deviated nuclei, HE, 200×. **E**) The membranous tram-track like staining pattern of SMA. The reaction is accentuated in the periphery of the cytoplasm, IHC, 200×. **F**) Focal positivity of Desmin, IHC, 200×

Table I. Clinicopathological features of 14 cases with myofibroblastic sarcoma of the breast

Case No. [reference number]	Sex/ Age(years)	Size(cm)	Necrosis	Mitoses/10HPFs	Immunohistochemical Findings	Therapy	Follow-up (months)
1 [7]	F/46	2.2 × 2.1 × 1.6	NA	NA	VIM, SMA+/COL IV–	Lx, Mast	Alive (12 m)
2 [12]	F/49	2.8 × 1.5 × 1.2	No	16	SMA, CNN1, FN, CD99+	Lx, RTx	Alive (2 m)
3 [4]	F/51	22 × 20 × 15	Yes	8–35	VIM, SMA+/DES, h-caldesmon–	Radical Mast, Chemotherapy and RTx	Alive (24 m)
4 [1]	F/55	> 8	Yes	10–45	VIM, SMA, FN+/DES, LMN, COL IV–	Radical Mast	Died with pleuropulmonary Met (11 m)
5 [9]	F/57	NA	Yes	NA	SMA+/h-caldesmon, DES, S-100, CD34–	NA	Met (pulmonary and brain), Died (12 m)
6 [2]	F/59	2.3	No	6–15	VIM, SMA, FN+/LMN, DES, CD34, PCK–	Mast and lymphadenectomy, RTx	Alive (20 m)
7 [11]	F/61	5 × 3 × 3	Yes	5–16	SMA, Calponin, FN, CNN1+/ h-caldesmon, COL IV, DES, LMN, S-100, CD34–	Lx	Alive (18 m)
8 [13]	F/62	2	No	15	VIM, SMA+/AE1/AE3, CAM5.2, CD34, DES, S-100–	Lx, total Mast	Rec (24 m), Alive (42 m)
9 [6]	F/72	3.4	Yes	2	SMA+, DES focal+	Mast	Rec (5 m), Met (lung, 12 m)
10 [8]	F/81	4.2 × 3.5 × 2.5	NA	Numerous	VIM, SMA, Bcl-2+/DES, S-100, C-kit, CD34–	Mast, RTx	Met (lung, 14 m); Alive (16 m)
11 [9]	F/82	NA	Yes	NA	SMA, CNN1+, DES focal+/ h-caldesmon, S-100, CD34–	NA	Died (15 m)
12 [10]	M/40	4	No	2	VIM, SMA, FN+/h-caldesmon, COL IV, DES, LMN–	NA	Alive (27 m)
13 [3]	M/60	2.5	Yes	10	VIM, SMA+/DES, LMN, S-100, CD34–	Mast and lymphadenectomy	Alive with five local relapses (120 m)
14	M/81	30	Yes	3	SMA+, DES spotted +/PCK, CD34, S-100, MyoD1, MYOG, ALK1*, CD68, STAT6–	Lx, RTx	Rec (3 m), Alive (24 m)

1–13 – the presented case in the literature {1–3, 6–14}, 14 – the present report, CNN1 – calponin, DES – desmin, F – female, FN – fibronectin, HPF – high-power field, LMN – laminin, Lx – lumpectomy, M – male, MA – alpha smooth muscle actin, Met – metastases, MYOG – myogenin, mast-mastectomy, NA – not available, PCK – pancytokeratin, Rec – recurrence, RTx – radiotherapy, SCOL IV – type IV collagen, VIM – vimentin

CD68, STAT6, CK8/18, and PCK. Ki67 stain showed a proliferative index of 10% of neoplastic cells. Based on the above-mentioned morphological and immunohistochemical features, the diagnosis of low-grade myofibroblastic sarcoma was made.

Clinical characteristics

In this study, the age of the patients with MFS of the breast ranges from 40 years to 82 years (mean, 60 years), with a 3 : 11 male-female ratio. The size of lesions ranged from 2 to 30 cm. Mitotic activity averaged 2–45 per 10 high-power fields (HPFs). Histologically, all tumours had an infiltrative growth pattern. The tumours showed areas of necrosis in 8 of 14 cases. The immunohistochemical study of all cases revealed diffuse cell reactivity for SMA, and negative or focal positivity for desmin. Apart from SMA, 5 reported cases had an available IHC stain for fibronectin. The percentage of recurrences, metastasis, and death due to the tumour was 28.57%, 28.57%, and 21.43%, respectively (Table I).

Discussion

In the fifth edition of the World Health Organisation (WHO) classification of soft tissue and bone tumours, LGMFS was classified as a type of the fibroblastic and myofibroblastic tumour category, which has fibromatosis-like features.

The LGMFS is predominant in the head and neck region of adults, with a slight male predilection. LGMFS of the breast in older men is rare. The diagnosis of MFS depends on microscopic examination, immunohistochemistry and electron microscopy. Until recently, the diagnostic criteria of MFS was still controversial; some argued that electron microscopy is not the key point of diagnosis [7, 14]. Apart from SMA, 5 reported cases have revealed a currently available IHC stain for fibronectin to detect the presence of fibronexus junctions and fibronectin fibrils, instead of electron microscope to demonstrate specialised ultrastructural organelles. We found that those 5 cases all express fibronectin. Fibronectin may help doctors in hospitals without electron microscopy to make accurate diagnoses.

The main differential diagnoses of LGMFS in the breast include leiomyosarcoma, inflammatory myofibroblastic tumour, solitary fibrous tumour, and malignant phyllodes tumour, which are malignant spindle-cell tumours that resemble LGMFS histologically and should be distinguished.

Myofibroblasts are thought to arise from fibroblasts, and present common characteristics with both smooth muscle cells and fibroblasts [15]. For this reason, it may be confused with smooth muscle cell tumours, such as leiomyosarcoma. LGMFS can present immunopositivity for SMA and focal positivity/negative for desmin [4]. Electron micrograph of myofibroblastic cells shows myofilaments with focal densities arranged in bundles and frequently under the plasma membrane. These filaments originate from the cell membrane [17]. The immunohistochemical staining pattern of SMA in myofibroblastic cells is described as accentuated in the periphery of the cytoplasm (tram-track pattern), which is generally more diffuse and cytoplasmic in smooth muscle cells [16]. The different staining patterns of SMA can be used to support the diagnosis of myofibroblastic differentiation.

Morphologically, it is not difficult to distinguish LGMFS from leiomyosarcoma. Myofibroblastic tumour cells have abundant cytoplasm and more prominent nucleoli, with feathery or stellate features, arranged in fascicles or a storiform growth pattern in collagenous stroma. Leiomyosarcoma shows fascicles of spindle cells with hyperchromatic nuclei with abundant eosinophilic cytoplasm. The highly differentiated cells present cigar-shaped, blunt-ended nuclei with more brightly eosinophilic cytoplasm.

LGMFS has overlapping histological and immunohistochemical features with IMT. IMT is prevalent in children and adolescents, about half of whom show rearrangements of the ALK gene [17, 18]. The spindle cells of IMT show a variable myxoid stroma background and impressive infiltration of inflammatory cells, including lymphocytes, plasma cells, and eosinophils. Differences in clinicopathological and cytogenetic characteristics can be helpful in distinguishing IMT from low-grade myofibroblastic sarcoma.

Fibrosarcoma is composed of malignant spindle cells showing fibroblastic differentiation, which is different from myofibroblasts due to having no immunohistochemical staining with SMA or (and) desmin [11]. An MFS of the breast could develop by sarcomatous transformation of vascular pericytes or medial muscle cells in a long-standing fibroadenoma.

Phyllodes tumours usually have a similar histopathological appearance to fibroadenoma [11]. In malignant phyllodes tumour with sarcomatous stroma the sarcomatous component resembles a fibrosarcoma or a malignant fibrous histiocytoma [19]. Thus, malignant phyllodes tumour should be considered in differential diagnosis of MFS in the breast. In this case, there was no presence of an epithelial component in the resected specimen.

Furthermore, negative staining for STAT6 and CD34 of our case failed to diagnosis solitary fibrous tumour (SFT). LGMFS was diagnosed based on microscopic histopathology and immunohistochemical analysis.

In this study, the clinicopathological data showed that MFS of the breast had a clear difference in the incidence of gender, which tends to arise in older females. MFS were demonstrated to have a relatively

indolent course with the same percentage of recurrence and metastasis. Owing to the diverse diagnostic criteria of MFS, it is difficult to diagnose MFS with biopsy. Extensive resection was performed in all cases. A few cases had received radiotherapy and (or) chemotherapy treatments.

Disclosures

1. The study received approval from the the Research Ethics Committee of the Hubei Cancer Hospital (approval number: LLHBCH2025YN-004).
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3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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