Lipomatous (Fat-Forming) Solitary Fibrous Tumor of the Breast: A Case Report of an Uncommon Variant of a Rare Clinical Entity

Najla Saleh Ben Ghashira
Nahed Ahmed Balalaab
Warda Anamb
Rawia Mubarak Mohameda

aPathology Department, Sheikh Shakhbout Medical City, Abu Dhabi, UAE; bGeneral Surgery Department, Sheikh Shakhbout Medical City, Abu Dhabi, UAE

Keywords
Breast · Lipomatous · Solitary fibrous tumor

Abstract
Solitary fibrous tumor (SFT) is an uncommon tumor of mesenchymal origin, which can arise at any anatomic location and can exhibit versatile histological features and a clinical course ranging from benign to frankly malignant. Lipomatous (fat-forming) SFT is a morphological variant of SFT characterized by an adipose tissue component. Breast SFT is an extremely rare clinical entity, and the literature review yielded only 28 previously reported cases. However, lipomatous (fat-forming) SFT is much less common than conventional tumors and, to our knowledge, it has never been reported in the breast. We describe a case of a 54-year-old postmenopausal woman who presented with a palpable mass on her right breast. No other associated features such as nipple discharge, skin changes, or axillary lymphadenopathy were present. The clinical differential diagnosis included fibroadenoma, phyllodes tumor, and mammary hamartoma. A ultrasound scan examination demonstrated a large, oval, well-circumscribed lesion with indeterminate features, but suspicious of malignancy. However, a needle core biopsy was performed and histological examination with ancillary immunohistochemical staining confirmed the diagnosis of SFT, a lipomatous variant. The lesion was excised with clear margins and histological examination confirmed SFT with low-risk features and follow-up was planned. Careful histological evaluation with diffuse and strong nuclear expression of STAT6 helped to distinguish lipomatous SFTs from other mimics. Here, we describe the first case of a lipomatous variant of a SFT involving the breast.

© 2022 The Author(s). Published by S. Karger AG, Basel

Correspondence to:
Najla Saleh Ben Ghashir, nsghashir@ssmc.ae
Introduction

Solitary fibrous tumor (SFT) is a relatively uncommon spindle cell fibroblastic tumor that was first described in the pleura [1]. However, SFT in extrapleural locations is more common, and 10–15% of these occur in the trunk. However, breast involvement by SFT remains rare. SFT presents incidentally or as a painless enlarging mass with or without mass effect. Paraneoplastic syndromes such as hypoglycemia can also be a rare presentation. SFTs are mostly benign, although 12% of cases may present with metastasis or locally recurrent tumors [2]. The appearance of the tumor is usually that of a well-circumscribed mass of spindle cells arranged in a hemangiopericytomatous pattern. A conventional SFT inherently has a wide spectrum of histological features, a distinct variant of which is the lipomatous SFT. Given the morphological diversity and the possible involvement of almost any anatomic location, SFTs can mimic other soft tissue neoplasms of different lineages or even mimic organ-specific lesions depending on the site of involvement. STAT6 is a highly sensitive and specific immunohistochemical (IHC) marker for SFT and can be helpful in distinguishing this tumor type from histological mimics [3]. To our knowledge, only 28 cases of breast SFT have been described in the English literature, and our case is the first case of breast SFT reported in Gulf countries [4]. Furthermore, this is the first case to describe the lipomatous variant of SFT that arises in the breast. We present our case of lipomatous solitary fibrous tumor of the breast, with a discussion and review of the literature on its clinical presentation, histopathological features, and treatment.

Case Presentation

A 54-year-old postmenopausal woman came to the breast clinic complaining of a palpable, painless lump on her right breast, which she had noticed for a year. On physical examination, there was a soft, deep-seated mass in the upper inner quadrant of the right breast, measuring 4.5 × 4.0 cm. The mass was located at the 1 o’clock position, 7 cm from the nipple. There were no skin changes, nipple discharge, or axillary lymphadenopathy. Clinically, the differential diagnosis included a fibroepithelial lesion, such as a fibroadenoma or phyllodes tumor, and mammary hamartoma. However, malignancy remained a concern in a patient of this age. No history of trauma or previous abnormalities in the breast was known. She had no known family history of breast malignancy. She is diabetic controlled on medication and a known case of nonobstructive coronary heart disease and status after pacemaker insertion in 2019; therefore, she was seen and assessed in the pacemaker clinic.

A mammogram and ultrasound examinations of the right breast were performed, which revealed a well-marginated oval lesion, measuring 4.1 × 2.9 × 2.7 cm, located in the upper inner quadrant, 6.8 cm posterior to the nipple. The lesion had an inhomogeneous isoechoic-hyperechoic signal with a small hypoechoic halo and minimal peripheral vascularity. The diagnosis was indeterminate, but there was a suspicion of malignancy, and therefore the lesion was radiologically classified under the BIRADS4 category (Fig. 1a, b).

The patient had a diagnostic needle core biopsy. Histological examination showed a cellular spindle cell lesion consisting of short fascicles of bland, fusiform, ovoid cells disposed in a patternless architecture around branching vascular spaces within a fibrous stroma with wispy collagen and scattered mast cells. The lesional stroma contained mature adipose tissue without atypia or lipoblasts. No ductal epithelial component was observed, unlike in hamartoma or fibroepithelial lesions (Fig. 2). Ancillary IHC studies showed that tumor cells were negative for a wide range of pancytokeratins, CKA1/AE3, CK 5/6, 34 betaE12, MNF116, CAM5.2, CK7, and CK19, and also negative for EMA and p63, which importantly exclude a low grade metaplastic carcinoma. Tumor cells were strongly and diffusely immunopositive with vimentin,
CD34, STAT-6, and negative with SMA, desmin, and S100-P, an IHC profile that favors the diagnosis of a solitary fibrous tumor, lipomatous variant (Fig. 2a–d).

The patient underwent a wide local excision of the right breast mass. Upon surgical resection, a soft, well-defined lesion was excised in total, using blunt and sharp dissection to separate the encapsulated mass from the breast tissue. During surgery, the patient was strictly monitored to ensure that the pacemaker functioned; moreover, the use of bipolar electrocautery intraoperatively was taken into account as a safety precaution tool to minimize
electromagnetic interference in the presence of a pacemaker. The postoperative course was uneventful and the patient was discharged home safely.

The resection specimen appeared grossly as a well-circumscribed grayish-yellow nodule measuring 4 × 3 × 2.7 cm with a firm fibrotic cut surface showing fatty streaks. Microscopic examination confirmed the biopsy diagnosis of a lipomatous solitary fibrous tumor of the right breast. No frank atypia or tumor necrosis was observed and mitotic activity was inconspicuous. Therefore, the tumor was stratified in the low-risk category, predictive of a favorable course. The tumor appeared completely excised. Despite the lack of aggressive histologic features, the patient underwent a staging CT scan due to the intermediate nature of the tumor. No distant disease was observed. Follow-up was planned and no recurrent disease was observed 5 months postoperatively.

Discussion

SFT comprises a histological spectrum of fibroblastic mesenchymal neoplasms that include tumors previously classified as hemangiopericytoma and were first described in the pleura [5, 6]. The first series of extrapleural SFTs was published in 1991 [7]. Subsequently, SFT and hemangiopericytoma were considered to represent two ends of the histomorphological spectrum given their clinicopathological similarities. A single SFT entity was accepted in the 4th edition of the World Health Organization (WHO) Classification of Soft Tissue and Bone Tumors. In the current version of the latter classification, SFT is considered a fibroblastic neoplasm with intermediate (rarely metastasizing) behavior. The genetic hallmark of SFT is the recurrent gene fusion NAB2-STAT6, located in the chromosomal region 12q13, and involving several different exons in each gene. However, a novel gene fusion, NFIX-STAT6, was identified [8].

SFTs can occur in patients of any age group with a peak incidence in adults between 40 and 70 years of age. The tumor usually presents as a slow-growing, painless soft tissue mass. SFTs can occur at almost any anatomical location. Frequent extrapleural locations are the meninges, abdominal cavity, trunk, extremities, and head and neck. Other reported locations include the upper respiratory tract, mediastinum, central nervous system, kidney, and breast [6]. Breast SFT is rare and, to our knowledge, only 28 cases have been described in the English literature [4]. In addition, this is the first case to describe the lipomatous variant of SFT arising in the breast. Fat-forming (lipomatous) SFTs contain a component of mature adipose tissue and constitute a rare distinct variant of SFTs. However, lipomatous SFT shares the clinical, pathological, IHC, and ultrastructural characteristics of conventional SFT [9]. The lipomatous variant usually involves deep soft tissues but has been reported in the orbit, neck, parotid gland, mediastinum, stomach, retroperitoneum, paratesticular soft tissue, and thigh [9]. Breast involvement, as in our case, has not been previously described.

Despite the histomorphologic diversity of SFT, staghorn-type branching of vessels and bland cell morphology with a pattern-less arrangement of fusiform cells are characteristic. Traditionally, a combination of CD34, CD99, and BCL-2 has been widely used to diagnose SFT. However, these IHC markers are sensitive but not sufficiently specific to distinguish SFT from other spindle cell lesions, particularly on a small preoperative biopsy. Furthermore, CD34 can be absent in 5–10% of histologically characteristic SFTs [1]. BCL-2 is a more sensitive marker, while CD99 is less specific. Nuclear immunostaining of STAT6 (signal transducer and transcription activator6) and/or identification of the fusion of the NAB2-STAT6 gene are confirmatory of SFT. STAT6 IHC staining has emerged as a useful surrogate marker of the fusion of the NAB-2-STAT6 gene with excellent sensitivity and specificity [1, 3]. In this index case, the tumor was diffusely stained for STAT6 in more than 90% of the tumor cells in both the biopsy and surgically removed specimens. However, it should be noted that the STAT6 IHC marker can
also be expressed in some other soft tissue neoplasms, including, but not limited to, liposarcoma and desmoid tumor, both of which can create diagnostic confusion with lipomatous SFT, particularly on a small core biopsy. However, combining the histomorphologic characteristics with the result of the appropriate IHC can produce the correct diagnosis.

Similarly to conventional SFT, lipomatous SFT enters the differential diagnosis of other soft tissue lesions; specifically, fat-containing lesions including benign tumors such as spindle cell lipoma and malignant lipomatous tumors such as well-differentiated or dedifferentiated liposarcoma. When in the breast, mammary hamartoma and phyllodes tumor with heterologous fatty component are among the differential diagnoses of lipomatous SFT. On a small biopsy, the differential diagnosis may extend to include metaplastic carcinoma of the breast, desmoid tumor, and some other mesenchymal lesions. Differentiating SFT from malignant tumors is important, and so is the case for a desmoid tumor, which is a benign but locally aggressive lesion with a higher incidence of local recurrence [7]. Vigilant histologic evaluation along with the use of appropriate additional studies and clinical correlation are all important steps to make the correct diagnosis and plan the correct surgical treatment.

SFTs with a high mitotic count with or without increased cellularity, atypia, necrosis, and infiltrative growth have traditionally been termed malignant. However, to date, not a single histologic feature determines the biological potential of the tumor. By combining histological and clinical parameters, several risk stratification models were designed with the aim of achieving a more accurate prediction of the prognosis. The most widely used model for metastatic risk by Demicco et al. incorporates mitotic count (= >2 mitoses/mm²), patient age (= >55 years), tumor size stratified by 5 cm tiers, and necrosis [10]. Based on this model, SFTs can be classified into low-, intermediate-, and high-risk groups. In the case of our patient, the tumor did not show nuclear pleomorphism, increased mitoses or necrosis, and had a low proliferative index, which added up to a low-risk score predictive of benign biology.

The current World Health Organization Classification of Soft Tissue and Bone Tumors classifies SFT as a fibroblastic neoplasm with intermediate (rarely metastasizing) behavior. Recurrence, local or metastatic, occurs in 10–15% of SFT. Although most SFTs are benign, there is an indication for follow-up to assess recurrence or relapse in cases with unfavorable histological features [4]. There is also a view that clinical follow-up may be warranted for tumors lacking malignant features in primary resections because some of these may acquire malignant features at the time of local relapse or metastasis [11]. Moreover, despite surgical excision with clear margins, local recurrence and distant metastases can still occur in some cases [12]. Relapse of the disease can occur several years after treatment [13]. Therefore, long-term follow-up is often recommended for intermediate- to high-risk patients.

Extrapleural tumors, in particular, tumors located in the meninges, pelvis, retroperitoneum, and mediastinum, have been associated with a higher risk of recurrence [14]. However, there are no comparable data for mammary SFT. Similar to SFT in any other location, complete surgical resection is the optimum treatment. Close and long-term follow-up, to monitor local or distant relapses, should be considered in both benign and malignant cases [12, 13, 15].

**Conclusions**

SFT is a rare soft tissue tumor, and breast involvement is extremely rare. The lipomatous variant of SFT has not previously been reported in the breast. However, the lipomatous variant of SFT is considered clinically and biologically similar to conventional SFT. The presence of fat raises a wide range of differential diagnoses with other fat-containing lesions in the breast, both on radiologic and histological examination. We believe that the correct diagnostic interpretation is primarily dependent on the awareness that such a rare tumor can arise at this
unusual site. Careful pathologic evaluation and the use of appropriate additional studies is the key to diagnosis. Surgical resection with extended margins is the gold standard treatment. A multidisciplinary team approach is recommended for the treatment and management of these tumors.

**Statement of Ethics**

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

**Conflict of Interest Statement**

All the authors have no conflicts of interest to declare.

**Funding Sources**

No funding was received.

**Author Contributions**

Data collection and assembly: Nahed Balalaa and Warda Anam. Data interpretation: Najla Ben Ghashir and Rawia Mohamed. Manuscript writing: Najla Ben Ghashir and Warda Anam. Revising the work critically for intellectual content: Najla Ben Ghashir, Nahed Balalaa, and Rawia Mohamed. All the authors approved the final manuscript and agree to be accountable for all aspects of the work.

**Data Availability Statement**

Data that support the findings of this case report are not publicly available due to confidentiality issues but are available from the corresponding author, Dr. N. Ben Ghashir, upon reasonable request.

**References**

1. Fletcher CD, Gibbs A. Solitary fibrous tumour. In: Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC, editors. WHO classification of tumours of the lung, pleura, thymus and heart. Lyon: IARC Press; 2015. p. 142–3.
2. Yoshida A, Tsuta K, Ohno M, Yoshida M, Narita Y, Kawai A, et al. STAT6 immunohistochemistry is helpful in the diagnosis of solitary fibrous tumors. *Am J Surg Pathol.* 2014 Apr;38(4):552–9.
3. Doyle LA, Vivero M, Fletcher CD, Mertens F, Hornick JL. Nuclear expression of STAT6 distinguishes solitary fibrous tumor from histologic mimics. *Mod Pathol.* 2014;27:390–5.
4. Jung MJ, Alrahwan D, Dubrowsky E, Baek D, Ayala AG, Ro JY. Solitary fibrous tumor of breast with anaplastic areas (Malignant Solitary Fibrous Tumor): a case report with review of literature. *J Breast Cancer.* 2019 Jun; 22(2):326–35.
5. Gengler C, Guilhou L. Solitary fibrous tumour and haemangiopericytoma: evolution of a concept. *Histopathology.* 2006 Jan;48(1):63–74.
6 Tariq MU, Din NU, Abdul-Ghafar J, Park YK. The many faces of solitary fibrous tumor; diversity of histological features, differential diagnosis and role of molecular studies and surrogate markers in avoiding misdiagnosis and predicting the behavior. Diagn Pathol. 2021; 16(1):32.

7 Goodlad JR, Fletcher CD. Solitary fibrous tumour arising at unusual sites: analysis of a series. Histopathology. 1991 Dec; 19(6):515–22.

8 Moura DS, Diaz-Martin J, Bague S, Orellana-Fernandez R, Sebio A, Mondaza-Hernandez JL, et al. A novel NFIX-STAT6 gene fusion in solitary fibrous tumor: a case report. Int J Mol Sci. 2021 Jul 13; 22(14):7514.

9 Guillou L, Gebhard S, Coindre JM. Lipomatous hemangiopericytoma: a fat-containing variant of solitary fibrous tumor? Clinicopathologic, immunohistochemical, and ultrastructural analysis of a series in favour of a unifying concept. Hum Pathol. 2000 Sep; 31(9):1108–15.

10 Demicco EG, Wagner MJ, Maki RG, Gupta V, John I, Lazar AJ, et al. Risk assessment in solitary fibrous tumours: validation and refinement of a risk stratification model. Mod Pathol. 2017 Oct; 30(10):1433–42.

11 Saynak M, Veeramachaneni NK, Hubbs J, Okumus D, Marks L. Solitary fibrous tumor of chest: another look with oncologic perspective. Balkan Med J. 2017; 34:188–99.

12 McMaster MJ, Soule EH, Ivens JC. Hemangioendothelioma. A clinicopathologic study and long-term follow-up of 60 patients. Cancer. 1975 Dec; 36(6):2232–44.

13 Granshaw IM, Gkas PD, Fisher C, Thway K, Thomas JM, Hayes AJ, et al. Clinical outcomes of extra-thoracic solitary fibrous tumors. Euro J Oncol. 2009; 35(9):994–8.

14 Fletcher CD, Bridge JA, Lee JC. Extra-pleural solitary fibrous tumor. WHO classification of tumours of soft tissue and bone. 4th ed. Lyon, France: IARC Press; 2013. p. 80–2.

15 Barco I, González C, Vallejo E, Pessarrodona A, Gímenez N, García-Fernández A. Malignant solitary fibrous tumour of the breast mimicking a benign tumor. Clin Pathol. 2019; 12:2632010X19868462.