

## Case Report

# Primary sclerosing epithelioid fibrosarcoma of chest wall in a patient with breast cancer: a case report

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**Abstract:** Sclerosing epithelioid fibrosarcoma (SEF) is a rare neoplasm mostly arising in limbs and limb girdles, with a high rate of recurrence. Herein, we describe a rare case of primary SEF in the chest wall with concurrent breast cancer. A 41-year-old female was found to have an asymptomatic mass in the upper chest wall on magnetic resonance imaging that was performed for breast cancer. Histology of the resected tumor showed features of SEF, with epithelioid cells arranged in nests or a retiform pattern within a sclerosing stroma. By immunohistochemistry, the tumor cells showed staining for vimentin and epithelial membrane antigen, and were negative for cytokeratin. *EWSR1* rearrangement was found by fluorescence in situ hybridization. She is currently disease free at 29-month follow-up. We herein report a rare case of SEF with concurrent breast cancer. The top differential diagnosis was between SEF and metastatic breast cancer. The distinction is important for implications in tumor staging and clinical management.

**Keywords:** Sclerosing epithelioid fibrosarcoma, breast cancer, chest wall

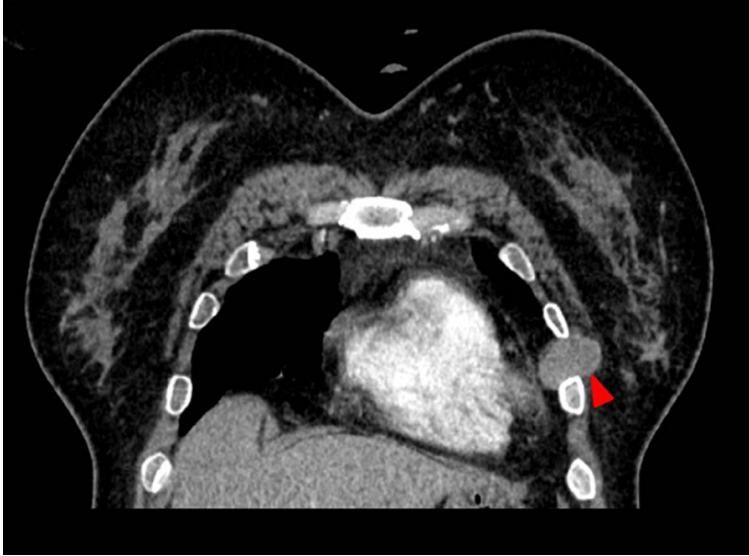
## Background

Sclerosing epithelioid fibrosarcoma (SEF) is a rare, distinct variant of fibrosarcoma. It was first described by Meis-Kindblom in 1995, microscopically characterized by epithelioid fibroblasts arranged in strands, cords, nests and sheets, embedded in a densely sclerotic and hyalinized stroma [1]. Subsequently, several series of SEF were published [2-4]. SEF occurs primary in middle-aged and elderly patients. It involves deep soft tissue, mainly affecting the lower extremity or limb girdles, followed by the upper extremity, shoulder region, trunk, head and neck areas. The most common presentation is a mass of variable duration, which in one third of patients is associated with recent enlargement and pain [5]. Grossly, SEF is typically well circumscribed with a white and firm cut surface. Microscopically, SEF shows a low-grade histology, composed of small to medium-sized epithelioid cells, with rare foci of necrosis and low mitotic rate. It has been reported to have relatively high incidence of

local recurrence (>50% of cases) and distant metastatic spread (40-80% of cases) [2-5]. By immunohistochemistry, SEF frequently shows vimentin staining, stains for MUC4 in up to 70% of cases, and variably for other markers including epithelial membrane antigen (EMA), S-100 protein and neuron-specific enolase (NSE) [5]. Therapy of choice is wide local resection, and the role of adjuvant radiation therapy or chemotherapy remains controversial [5]. Concurrent SEF in the chest wall and breast cancer has never been reported in the literature. Here we report a rare case of primary SEF found in a patient during the workup for her breast cancer.

## Case presentation

A 41-year old woman presented with a 2-month history of pain in the left breast. Magnetic resonance imaging disclosed a 1.7×1×0.7 cm mass in the left breast, as well as a 3.1×3.0×2.8 cm mass in the lateral left chest wall between the third and fourth rib, near the level of the inferior



**Figure 1.** Contrast-enhanced oblique coronal CT image showing tumor in the left chest wall (arrowhead).

edge of left breast. Contrast-enhanced oblique coronal computed tomography (CT) image confirmed the tumor in the left chest wall (**Figure 1**).

A core needle biopsy of the breast mass was performed. Due to the close proximity to the chest cavity, the chest wall mass was not biopsied. The pathologic diagnosis of the breast mass was invasive carcinoma of no special type, Nottingham histological grade 1 (total score 5). Almost all tumor cells were strongly positive for estrogen receptor (ER) and progesterone receptor (PgR) with a Ki-67 proliferation index of 10%. The tumor showed equivocal HER2 overexpression by immunohistochemistry, and negative HER2 gene amplification by fluorescence in situ hybridization (FISH). The features were consistent with a luminal A type invasive carcinoma of breast for molecular classification.

Following the consensus reached at a multidisciplinary clinical management meeting, the patient underwent a simple mastectomy and sentinel lymph node biopsy for the left breast tumor, and a wide local resection of the mass in the left chest wall. The pathologic diagnosis of the left breast tumor was invasive mammary carcinoma of no special type, measuring 1.0×0.7×0.7 cm microscopically (**Figure 2**). The tumor cells were diffusely and strongly positive for cytokeratin AE1/AE3, and negative for vimentin. One sentinel lymph node showed no evi-

dence of metastasis. The chest wall mass was resected with two segments of adjacent ribs. The specimen revealed a well-circumscribed, gray-white, firm mass, measuring 3.2×3.0×2.0 cm, involving the soft tissue between the two ribs, without bone destruction (**Figure 3**). Microscopically, cords and nests of small bland epithelioid tumor cells were embedded in a prominent hyalinized fibrous stroma, with variable cellularity (**Figure 4**). There were rare mitotic figures, about 0-1 per 10 high power fields. No obvious swirling pattern of bland spindle cells or necrosis was observed in the entire tumor.

By immunohistochemistry, the tumor was diffusely positive for vimentin and focally positive for EMA. Staining for cytokeratin AE1/AE3, CK7, ER, PgR, E-cadherin, SMA, desmin, MyoD1, CD34, S-100, CD99, and bcl-2 were all absent. The proliferation index as demonstrated by Ki-67 staining was approximately 3% (**Figure 5**). *EWSR1* rearrangement was found by FISH (**Figure 6**). A pathological diagnosis of primary SEF was rendered. In addition, some mutations were detected in her breast cancer tissue by next generation sequencing with a multiple genes panel (**Table 1**). However, we speculated they were somatic mutations based on the low frequency.

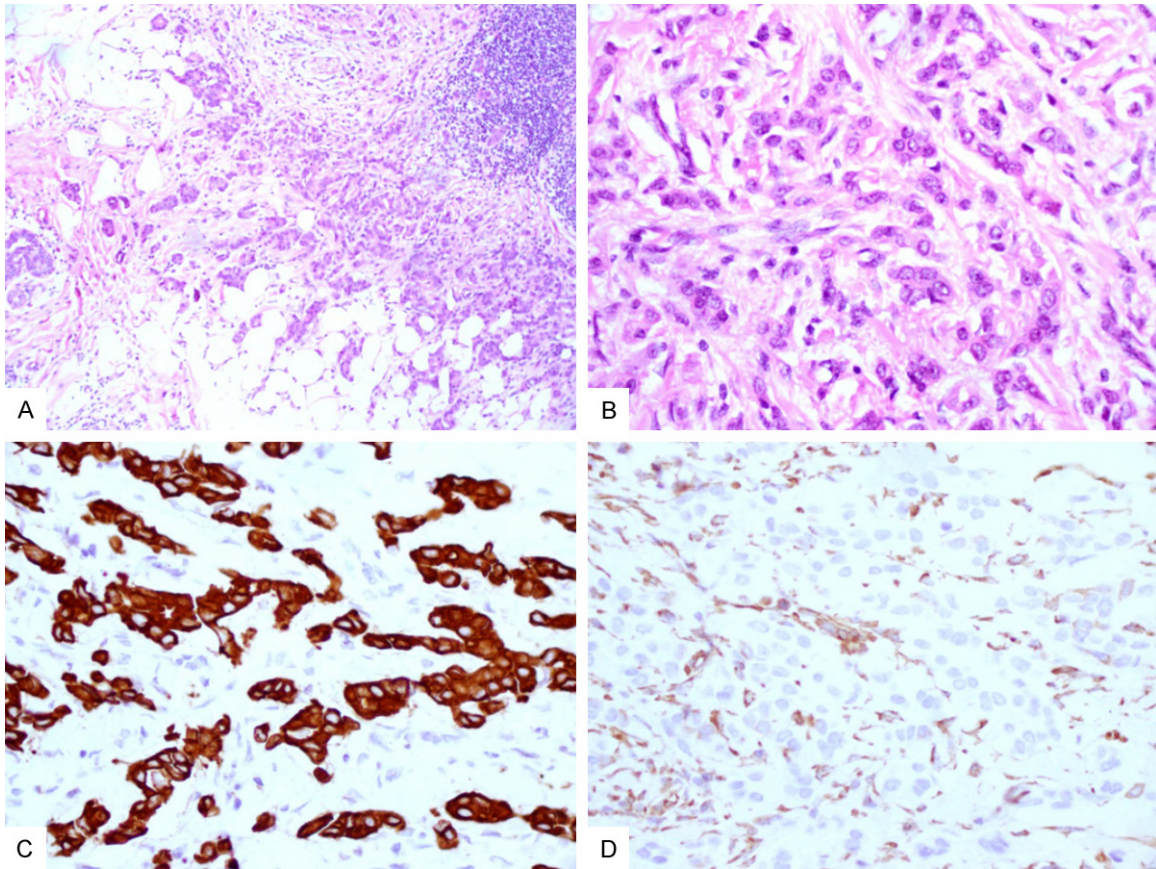
The patient received adjuvant endocrine therapy for the breast cancer and no other adjuvant therapy for SEF after wide local resection. To date, 29 months after the diagnosis of SEF, the patient is well with no evidence of disease.

### Discussion

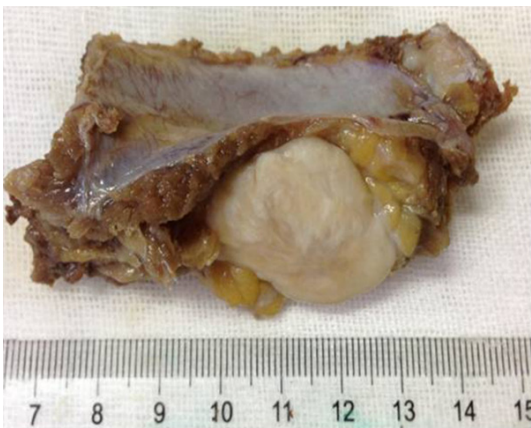
Although there have been several studies of SEF published in the literature since it was first described in 1995 [1-4, 6], SEF with concurrent breast carcinoma has not been reported. Our patient had a rare case of primary SEF in the chest wall and invasive carcinoma in the breast.

In our case, because of the epithelioid appearance of the tumor cells in SEF, the low grade nature of the tumor in the breast, and the close proximity of the chest wall mass to the breast

## Sclerosing epithelioid fibrosarcoma with breast cancer



**Figure 2.** Invasive carcinoma in the breast showing low grade tumor cells infiltrating in a desmoplastic stroma (hematoxylin and eosin, A, 100 $\times$ , B, 400 $\times$ ), with cyokeratin expression (C, 400 $\times$ ) and negative staining for vimentin (stromal cells as the internal control stained positive) (D, 400 $\times$ ).



**Figure 3.** Resected chest wall tumor showing homogeneous white firm cut surface.

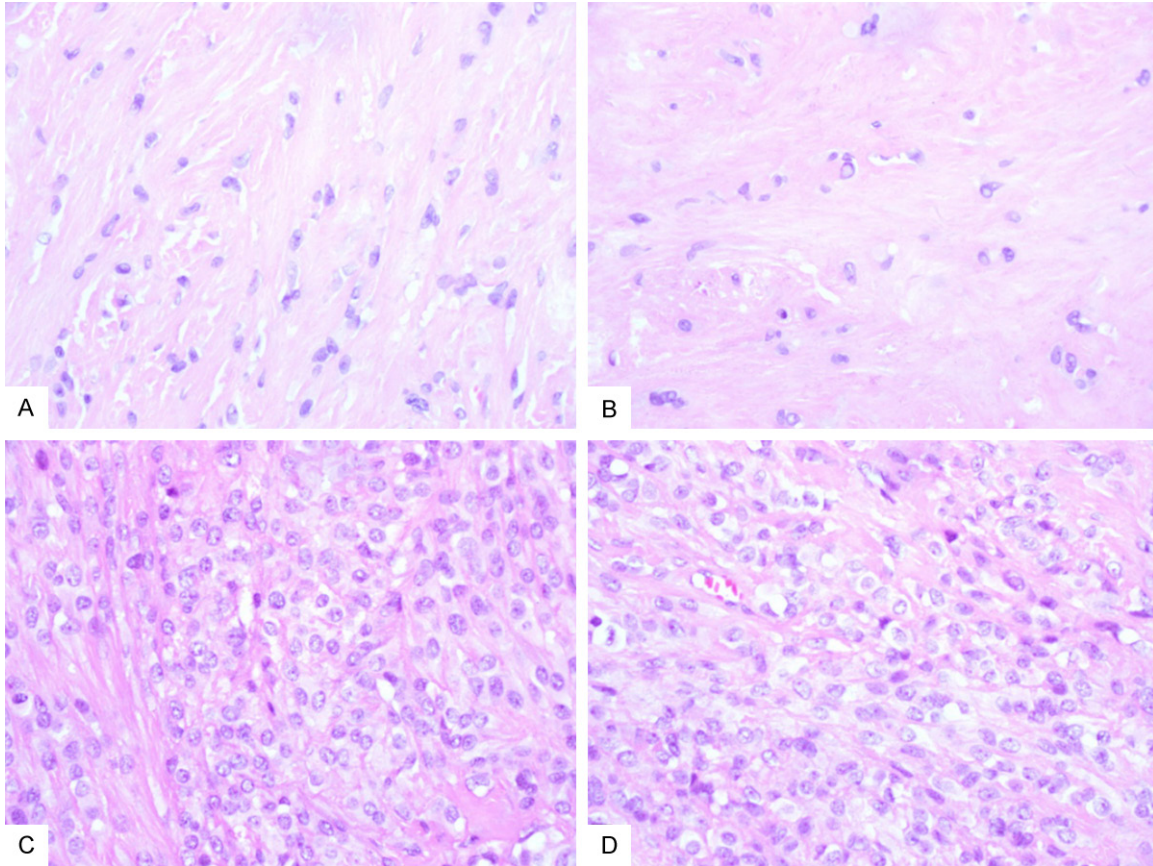
that harbored the carcinoma, the differential diagnosis for the chest wall tumor was between a primary soft tissue tumor and metastasis from the breast. The distinction was clinically important for tumor staging and management.

If it were metastasis to the chest wall soft tissue, the breast tumor staging would be stage IV, and the patient would need additional examinations such as FDG PET/CT, X-rays of symptomatic bones and long and weight-bearing bones, some of which could be quite costly. For premenopausal women with ER/PgR-positive, HER2-negative stage IV breast cancer, ovarian ablation or suppression may be needed for systemic treatment. In contrast, if the chest wall mass were a primary soft tissue tumor, the breast tumor staging would be stage IA, and the patient would only need adjuvant endocrine therapy. Based on the morphological features and immunohistochemical staining results including positive vimentin and negative cyokeratin staining, we established the diagnosis of SEF for the chest wall tumor and excluded metastatic breast cancer.

For primary soft tissue tumor with epithelioid tumor cells arranged within a sclerosing stroma, the most essential differentiation diagno-



## Sclerosing epithelioid fibrosarcoma with breast cancer



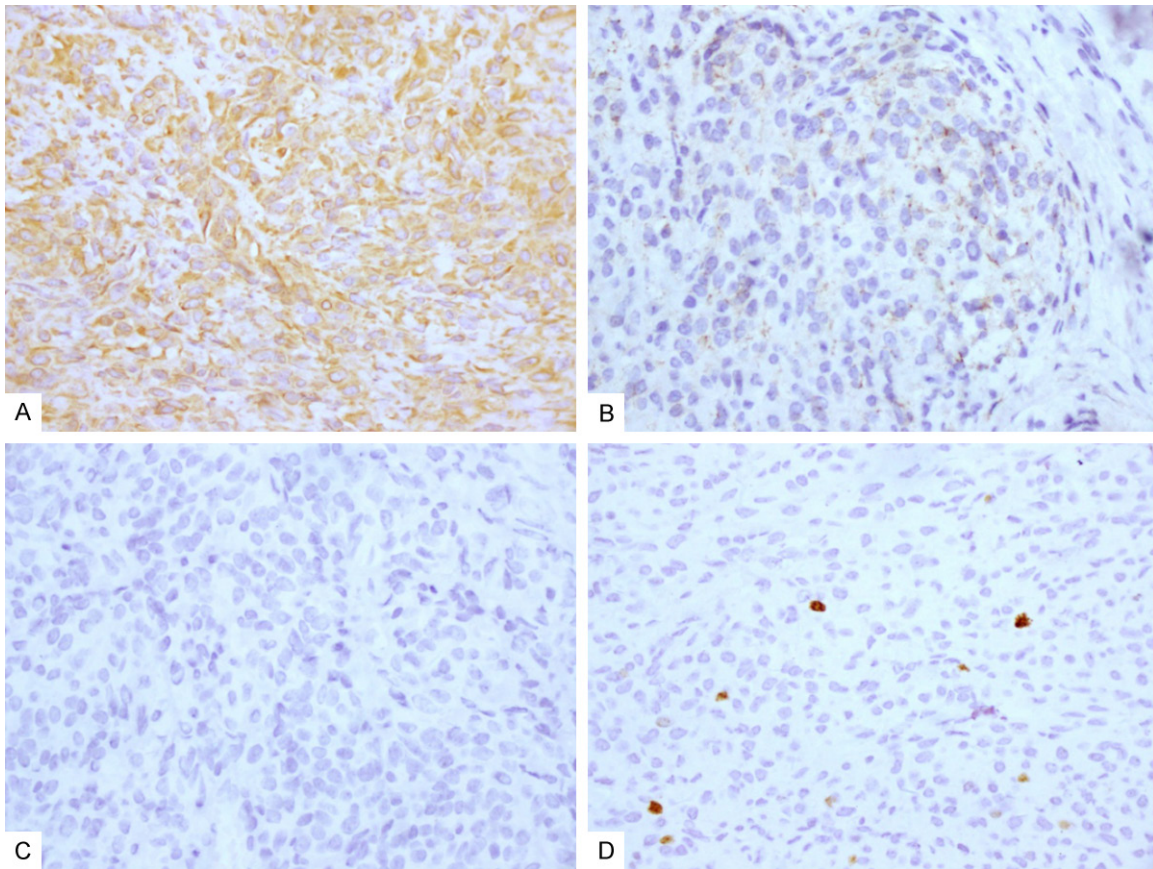
**Figure 4.** Sclerosing epithelioid sarcoma within hyalinized fibrous stroma (A and B) and cellular areas (C and D, hematoxylin and eosin, 400 $\times$ ).

sis is between SEF and low grade fibromyxoid sarcoma (LGFMS). SEF behaves clinically as higher-grade fibrosarcoma, with higher rates of recurrence and metastasis than LGFMS, and needs close follow-up [5]. A subset of SEF appears to be share similar features with LGFMS, both histomorphologically and by immunohistochemical and genetic studies, including the expression of MUC4 and *FUS-CREB3L2*, *FUS-CREB3L1* and *EWSR1-CREB3L1* gene fusion. The classic morphologic picture of LGFMS shows a bland spindle cell proliferation arranged in a swirling pattern in a myxoid and variably fibrotic background. Throughout all the sections of our case, there were no areas of extensive spindling with fascicular growth or significant nuclear pleomorphism. Therefore we excluded the diagnosis of LGFMS or SEF with LGFMS component.

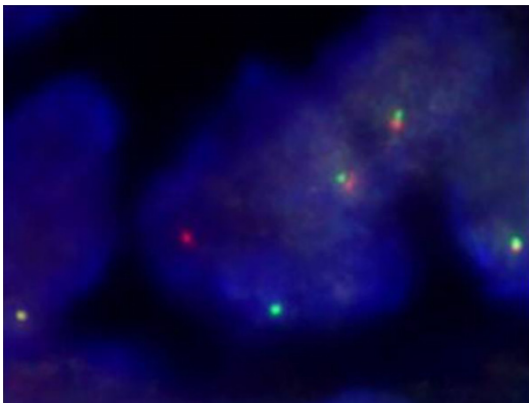
During review of the literature, we found a case of SEF of the lung in a patient with Lynch syndrome [7]. The patient developed three meta-

chronous tumors, which included SEF, colon carcinoma and basal cell carcinoma of skin. Interestingly, the SEF showed normal staining for proteins of all four mutated MMR genes, which made an association with the Lynch syndrome less likely. A possible link between the SEF of chest wall and breast cancer in our case is speculated in a setting of Li-Fraumeni syndrome (LFS) [8]. Associated with germline mutations in the TP53 gene [8], this syndrome is an autosomal dominant inheritable condition predisposing affected individuals to a broad spectrum of neoplasms. The common tumors in LFS are sarcomas of soft tissue and bone, breast cancer, brain tumors and adrenocortical carcinomas [8]. Our patient meets the criteria that a proband has multiple tumors, two of which belong to the narrow LFS tumor spectrum and the first of which occurs before the age of 46 years [9]. Based on the low frequency of these mutations in breast cancer tissue, there was few possibility of germline mutation.

## Sclerosing epithelioid fibrosarcoma with breast cancer



**Figure 5.** Sclerosing epithelioid fibrosarcoma showing expression of vimentin (A, 400×), focal expression of epithelial membrane antigen (B, 400×), negative cyokeratin AE1/AE3 (C, 400×), and a low proliferation index by Ki-67 (D, 400×).



**Figure 6.** *EWSR1* testing by fluorescence in situ hybridization. The break-apart red signals indicated rearrangement of the *EWSR1* gene.

In addition, considering she was without a family history of cancer, peripheral blood was not further detected to confirm germline mutation.

### Conclusion

We reported a rare case of primary SEF in the chest wall with concurrent breast cancer. The diagnosis is supported by histomorphologic features and immunohistochemical and gene rearrangement studies. For the particular location and morphology, the most clinically important differential diagnosis was metastasis from the breast. Another relevant differentiation diagnosis was LGMFS, as SEF has higher rates of recurrence and metastasis.

### Acknowledgements

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### Disclosure of conflict of interest

None.

## Sclerosing epithelioid fibrosarcoma with breast cancer

**Table 1.** Next generation sequencing with a multiple gene panel in breast cancer tissue

Gene Symbol	Position	Ref	Variant	Frequency	Locus Name	cDNA Change	Codon Change	Mutation Type	Somatic Status	PMID
PIK3CA	chr3: 178916929	G	C	0.053	COSM86046	c.316G>C	p.G106R	SNC	Confirmed somatic variant	23797736
PIK3CA	chr3: 178952085	A	G	0.24	COSM775	c.3140A>G	p.H1047R	SNC	Confirmed somatic variant	Not_found
TP53	chr17: 7577126	T	C	0.064	COSM43879	c.812A>G	p.E271G	SNC	Variant of unknown origin	16151725
ALK	chr2: 29432715	G	T	0.093	COSM5277656	c.3773C>A	p.T1258N	SNC	Confirmed somatic variant	Not_found
ALK	chr2: 29443666	C	T	0.132	COSM1570337	c.3551G>A	p.G1184E	SNC	Variant of unknown origin	23639785

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