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Case Report

Epihtelioid Sclerosing Fibrosarcoma of the Chest Wall: A Case Report and Review of the Literature

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Abstract

Background: SEF is a rare variant of fibrosarcoma, mostly occurring in extraosseous sites. It is a clinically challenging entity as no standardized treatment regimens are available. SEF's literature is limited, due to its rarity and recent recognition. The current study reports the case of a patient with SEF arising from the anterior chest wall.

Case Presentation: A 26-year-old man presented with a 6 years history of a left superior chest mass. Imaging revealed an invasive tumor of the right pectoral region, without metastases. The patient undergone surgical resection of the tumor. Histology and immunohistochemistry confirmed the diagnosis and revealed a hypocellular tumor with large areas of hyalinized fibrous stroma. The patient was referred to the oncology department to undergo postoperative treatment (radiotherapy/chemotherapy).

Keywords: SEF; Fibrosarcoma; Extraosseous; Hypocellular tumor; Fibrous stroma

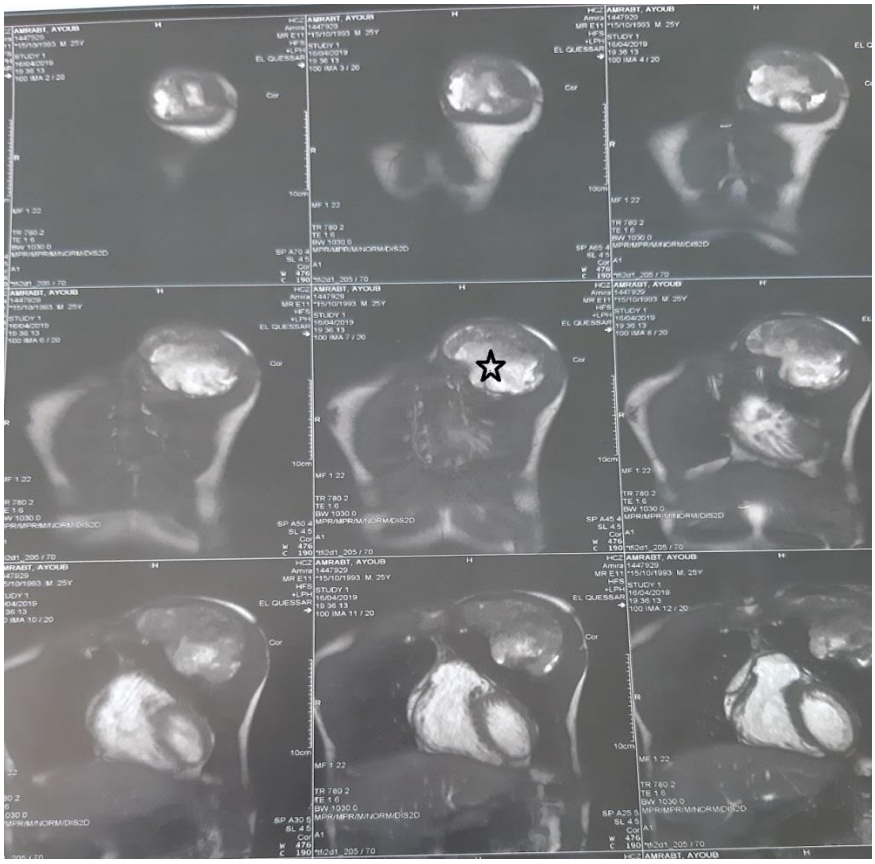
1. Introduction

Sclerosing epithelioid fibrosarcoma (SEF) has been originally described in 1995 by Meis–Kindblom [1] and lately been recognized as a distinct clinical entity. It is a rare variant of fibrosarcoma [2] showing predominantly epithelioid cells embedded in a fibrotic and hyalinized stroma [1]. Together with low-grade fibromyxoid sarcoma and hyalinizing spindle cell tumour with giant rosettes, SEF is classified as fibrosing fibrosarcomas [3]. SEFs mainly present as tumors of the lower extremities (39%) followed by the trunk (21%) and upper extremities [4] and sometimes involve the head and neck [1]. High frequencies of local tumor relapse and distant metastases have been reported (30%–40%) [4]. Due to its scarcity and relatively recent recognition as a distinct diagnostic entity, SEF has not been intensively investigated. Thus, SEF's literature information is limited. The aim of the current study is to report on a patient with SEF arising from the anterior chest wall.

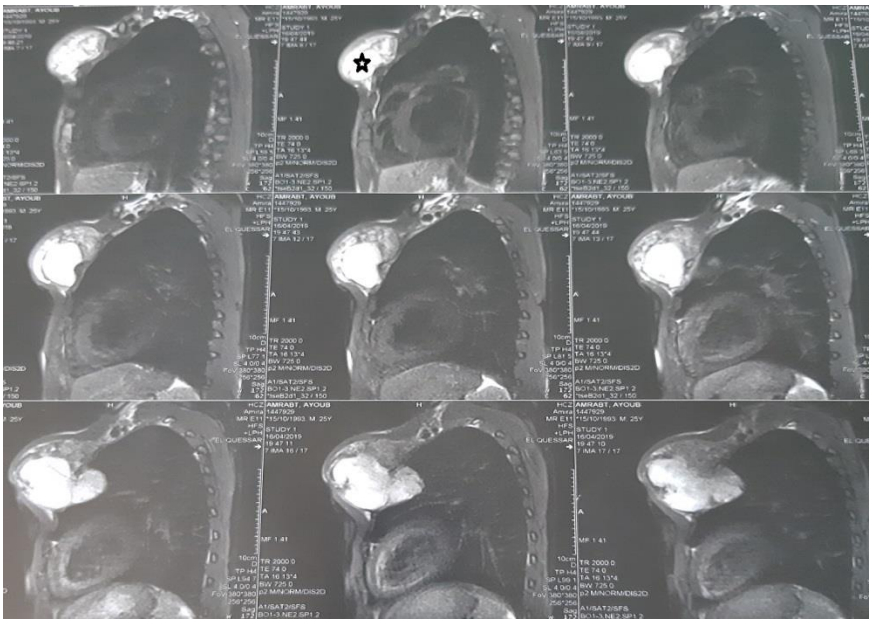
2. Case Presentation

A 26-year-old man presented with a 6 years history of a left superior chest mass. Except his smoking history, he had no major medical troubles. According to the patient, the mass had progressively increased in size during this time, and dramatically especially during the last 6 months. On examination, he was a healthy male with stable vital signs. The chest examination showed a firm, non-tender, and adherent to deeper structures mass; measuring 12 cm × 10 cm with a normal overlying skin. Rest of the examination was unremarkable. The patient's blood cell counts, serum electrolyte levels, renal and liver functions were within normal range. Conventional thoracic radiographs showed a soft tissue mass on the left side of the chest with normal lung fields.

Chest magnetic resonance imaging (MRI) revealed an invasive tumor of the right pectoral region measuring 12.25 × 9.5 × 9 cm, which was hypointense on T1-weighted images and heterogeneously hyperintense on T2-weighted images (Figure 1). There were no intra pulmonary's invasion signs. The primary site of involvement could not be identified; the tumor might have arised in the soft parts or the superior ribs. The radiological findings were suggestive for an osteosarcoma. The routine staging was negative for metastases. The patient undergone surgical resection of the tumor. The diagnosis was confirmed by the histological study of the resected tumor. On gross, the mass measured 12 × 9.5 × 9 cm, it was well circumscribed, lobulated, firm and gray-white. It shows a myxoid pattern and calcifications. Hematoxylin-eosin stained sections revealed a hypocellular tumor with large areas of hyalinized fibrous stroma. It consists of nests and cords of small to medium sized, round, relatively uniform epithelioid cells (Figure 2). Nuclei were vesicular with finely stipple chromatin and small nucleoli. Mitoses were inconspicuous (3 MF / 10 HPF). *The resection's margins were negative (*RO *resection)*. On immunohistochemistry, the neoplastic cells were nagative for MUC4, cytokeratin (AE1/AE3), EMA, CD34, SMA, H caldesmon, desmin and beta catenin (Figure 3). The detection of translocation t(X;18)(p11.2;q11.2) by fluorescence in situ hybridization was negative. The patient was referred to oncology department to undergo postoperative treatment (radiotherapy/chemotherapy).

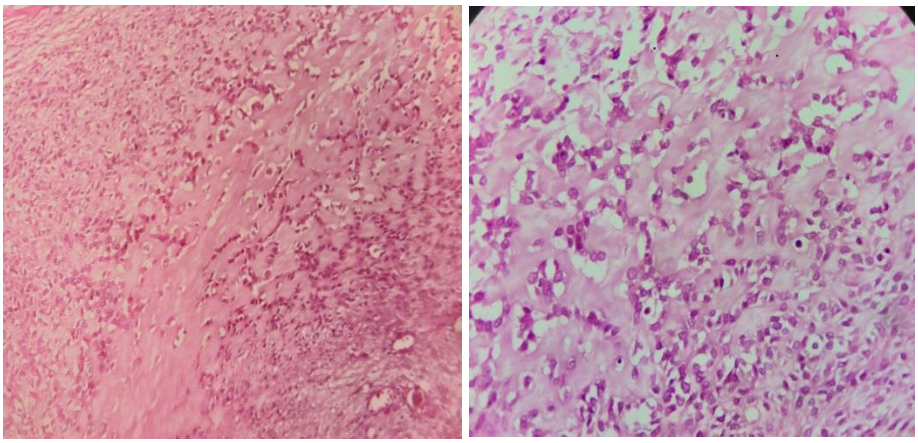


A : Sagittal sections



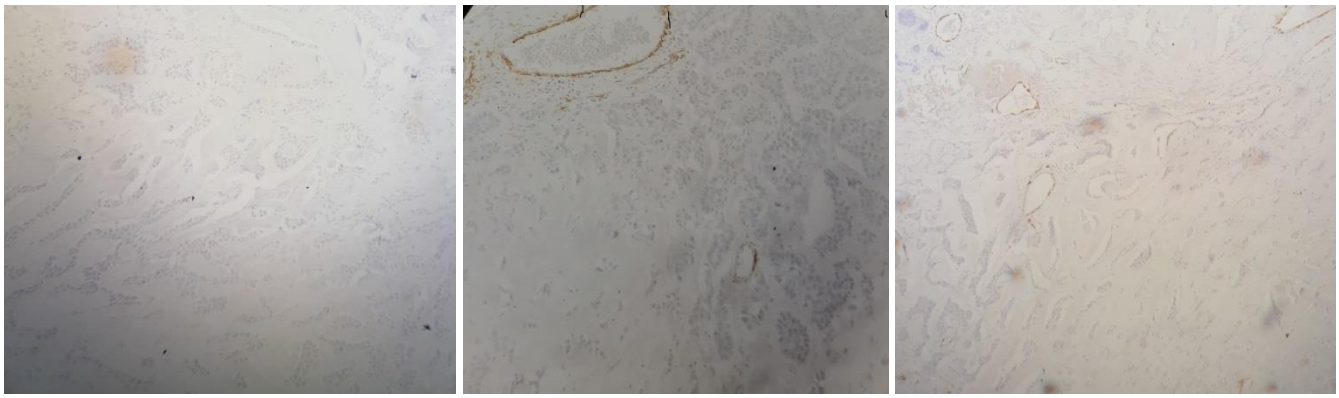
B: Coronal sections

Figure 1: Chest magnetic resonance imaging (MRI) showing an invasive tumor of the right pectoral region measuring (black asterisk) 12.25 × 9.5 × 9 cm, which is heterogeneously hyperintense on T2-weighted images



A: Hematoxylin and eosin, X 200 **B**: Hematoxylin and eosin, X 400

Figure 2: Sclerosing epithelioid fibrosarcoma, showing epithelioid cells, arranged in cords within a sclerotic matrix.



A **B** **C**

Figure 3: The neoplastic cells are MUC4 negative (A), SMA (B) negative and CD34 negative (C). (Immunohistochemical stain, X 200).

3. Discussion

SEF is a very rare distinctive variant of fibrosarcoma with a metastatic potential. It is characterized by the World Health Organization (WHO) as a malignancy of deep soft tissue [5]. Although the majority of the reported cases arise in the extremities, limb girdle, and trunk, SEF can also affect unusual sites including the kidney; the ovary, the ceacum, the liver, the lung and the pancreas [6]. It mainly affects patients of middle age (our case: 26 years old) with equal gender predisposition. SEF presents as a very slow growing mass, in most cases, taking around 33 months from the onset of symptoms to the diagnosis. It had an extremely high potential to metastasize and a high rate of local recurrence because of its locally and systemically infiltrative phenotype **[7]**. Due to its rare occurrence and confusing imaging characteristics, SEF preoperative imaging diagnosis remains challenging. In fact, it can mimic other common soft tissue tumor [8].

To the best of our knowledge, radiological aspects of SEF were not described in the three largest series of SEF in the litterature (Antonescu CR et al. [9], Meis-Kindblom JM et al. [10] and Chew W et al. [11]. In fact, radiological findings were distinctive in only few case reports such as the study of Xu, Jingjing et al; where MRI revealed a focal mass, with hypo- and iso-signal intensity on T1-weighted imaging and mixed-signal intensity on T2-weighted imaging. In our case, the mass showed the same radiological features on MRI, but no evidence of primary tumor's site could be found (rib or soft part). The fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) findings have been reported in 4 studies [8], revealing that the FDG uptake of SEF is closely associated with its histopathologic features regarding differentiation and aggressiveness. In fact the high-grade SEF is probably FDG-avid, and the low-grade one is likely to show less FDG uptake [8]. Histologically, the tumor's classical morphology is nests and cords of mildly atypical cells within a dense collagenous matrix [12]. Malignant epithelioid cells are round to ovoid with sparse and sometimes clear cytoplasm, embedded in hyaline sclerosis. The tumor may exhibit other changes such as areas of conventional fibrosarcoma, myxoid zones, and sometimes foci of hyaline cartilage, calcification, or metaplastic bone formation. In addition, SEF sometimes shares features with low-grade fibromyxoid sarcoma (LGFMS) and hyalinizing spindle cell tumor with giant rosettes [13]. In some cases, more or less extensive areas reminiscent LGFMS can be seen, either in synchronous or metachronous combination with SEF areas; such tumors are known as hybrid SEF/LGFMS [14]. The SEF may not show the typical morphologic features of sarcomas including infiltrative growth pattern, pronounced pleomorphy, mitotic activity and necrosis [2].

Immunohistochemistry and molecular studies may be of substantial utility in supporting a diagnosis of SEF. The immunohistochemistry profile includes positive MUC4 (sensitive and specific in up to 70% of cases), focal or weak positivity of EMA (epithelial membrane antigen), S100 and cytokeratins and negativity for CD34, leukocyte markers, HMB45, CD68, desmin, H-caldesmon and SMA (smooth muscular actin). Transducin-like enhancer of split 1 (TLE1) positive staining have been reported in one case [15]. In our case, the neoplastic cells were negative for MUC4, cytokeratin (AE1/AE3), EMA, CD34, H caldesmon, desmin and beta catenin. SEF's genomic alterations are complex [14]. The majority of the cases exhibited a reciprocal chromosomal translocation t(11;22)(p11;q12) resulting in generation of EWSR1-CREB3L1 fusion gene [6] which leads to higher expression of the *CD24* gene [14]. Genomic profiling by clinical-grade next generation sequencing (NGS) revealed a fusion gene between intron11 of EWSR1 (22q12.2) and intron5 of CREB3L1 (11p11.2) [16]. Other complex genomic rearrangements have been reported, including recurrent intragenic deletions of the *DMD* gene encoding dystrophin. Thus DMD and CD24 represent promising treatment targets [14]. The shared and distinct genetic features could perhaps explain the intriguing clinical and morphologic overlaps and differences between SEF and LGFMS. LGFMS is by far the more extensively analyzed subtype of the two [14]**.** The differential diagnosis of SEF may be broad especially in small biopsies; because of its epithelioid morphology. It includes other soft tissue tumors such as epithelioid hemangioendothelioma, clear cell sarcoma, ossifying fibromyxoid tumors as well as carcinoma and melanoma. Immunostains are predominantly useful for excluding other neoplasms in the differential diagnosis. Some cases show indistinguishable from LGFMS, areas. In addition, the immunophenotype of SEF might be similar to that of LGFMS [17]. In fact, the shared and distinct genetic features could perhaps explain the intriguing morphologic

and clinical overlaps and differences between SEF and LGFMS. Around 95% of the cases show a *FUS-CREB3L2* fusion gene, typically on the basis of a balanced translocationt (7;16) (q33;p11) [14].

The prognosis of SEF is generally poor. According to the literature, local relapse have been reported in 30 to 50 % of SEF patients; between two to five years after initial diagnosis [18]. Due to the rarity of the condition, no standard treatment protocols have been reported [7]. To the best of our knowledge, the only study recording the outcome of a consecutive series of patients (13 cases) with SEF treated at a single referral center; has been conducted by Chew. W et al. [11]**.** 11 patients underwent radical resection for localized disease with microscopically involved resection margins R1. All of patients experienced tumor relapse. In only 1 case where R0 resection was achieved, no evidence of relapse has been reported (follow-up of 105 months). Palliative chemotherapy was established in 7 cases among the 10 with metastatic disease. The median progression-free survival post 1st line chemotherapy was 2.7 months. Thus**, s**ensitivity to chemotherapy regimens widely used for soft tissue sarcomas (doxorubicin, Ifosfamide, gemcitabine, docetaxel) appears to be limited [11]. Moreover, preoperative or postoperative radiation as used in other soft tissue sarcomas also should be considered in cases which cannot be excised with clear margins **[7].**

4. Conclusion

In summary, we have reported the clinical and histopathologic features of a case of SEF as SEF is an extremely rare cancer. Up to present, no standard efficient treatment regimens have been clearly identified. There is a need for a further understanding of SEF's biology to improve its poor prognosis and collecting a sizable patient cohort remains essential to review treatment outcomes.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors read and approved the final manuscript.

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