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CASE REPORT

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Sclerosing epithelioid fibrosarcoma of the foot: A case report

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Abstract

Sclerosing epithelioid fibrosarcoma (SEF) is a rare and distinctive variant of fibrosarcoma. To date, about 100 cases only have been documented. Histopathologically, it resembles a variety of benign, pseudosarcomatous and other malignancies. Early diagnosis and treatment are vital for improving the treatment outcomes.

KEYWORDS

case report, diagnosis, foot, sclerosing epithelioid fibrosarcoma, Tanzania

1 | INTRODUCTION

Sclerosing epithelioid fibrosarcoma (SEF) is a rare and challenging entity because no standardized treatment regimens are available. Histopathologically, SEF is composed of epithelioid cells embedded within a sclerotic collageous matrix. A 32-year-old man presented with a foot swelling. Pathology investigations confirmed it to be SEF. He underwent amputation and chemotherapy.

Sclerosing epithelioid fibrosarcoma (SEF) is a rare aggressive malignant subtype of fibrosarcoma, and it was first described recently in 1995.[1] Typically, SEF is a mesenchymal tumor with unique architectural features consisting of cords, nests, or sheets of monotonous epithelioid cells within a dense collagenous background.[1] It involves the extremities or the trunk, followed by abdominal viscera, and head-and-neck areas.[1,2] SEF mostly occurs in extraosseous sites. It represents a clinically challenging entity especially because there are no standardized treatment regimens that are available. Intraosseous localization is an additional challenge with respect to the therapeutical approach. Herein, we report a case of SEF of the foot in a young adult male and provide a brief review of the literature.

2 | CASE REPORT

A 32-years-old man was referred to our facility; Kilimanjaro Christian Medical Centre (KCMC), which is located in Kilimanjaro region, Northern Tanzania in 2022; with complaints of severe swollen left foot with bleeding and fungating wound on the interdigital region for 3 years. He reports the wound to have been excised at two different facilities with recurrence and biopsy previously done was suggestive of benign tumor. The patient reported that he

has been using local herbs without improvement. A day prior visiting our facility, he experienced generalized body weakness. The weakness started suddenly following profuse bleeding from the wound site. He denied history of fevers, cough, difficulty in breathing and history of trauma. His past medical history and systemic examination were essentially unremarkable.

On examination, he was alert and oriented, moderately pale, and mild scleral jaundice. There was no lower limb edema. His blood pressure was low (96/43 mmHg) possibly due to severe dehydration, anemia and sepsis. He had axillary temperature of 36.5°C and random blood glucose of 5.9 mmol/L. On local examination, a swollen left foot with an ulcer on the dorsal part of the left foot with dressing stained green was noted. It was nontender with limited movement at the ankle joint. His systemic examination was essentially unremarkable.

His laboratory investigations revealed hemoglobin of 6.5 g/dL. Chest x-ray was normal but x-ray of the left foot showed huge soft tissue mass associated with bone destruction (Figure 1A), while x-ray of left leg showed focal cortical thickening of left tibia (Figure 1B). Abdominal-pelvic USS was normal. Histopathology of an incisional biopsy from the lesion demonstrated a typical monotonous epithelioid clear cell morphology, embedded in a dense collagenous or fibrous stroma. The findings were pointing to SEF. The differential diagnoses of low-grade fibromyxoid sarcoma, solitary fibrous tumor, as well as other entities, were considered. He was transfused with 3 units of whole blood, 2 units of PRC because of anemia and was scheduled for transtibial (at the level of ankle (ankle disarticulation)) amputation after thorough counseling. The operation was performed by experienced specialized surgeons. The resected specimen (Figure 2A, B) was sent for histopathology analysis. The histopathology of the specimen revealed proliferation of uniform, small, round to ovoid epithelioid cells with sparse, often clear cytoplasm and round to oval nuclei with inconspicuous nucleoli. Individual cells were arranged in nests, cords, or sheets. Prominent hyalinized sclerotic collagenous stroma was associated (Figure 3A). The tumor cells were immunoreactive with Vimentin while negative for cytokeratin, SMA, and Desmin. The findings were consistent with SEF (Figure 3B).

Postoperatively, he was kept on antibiotics, physiotherapy and was discharged home on day 10 postoperative. He was later seen at orthopedic clinic; he was clinically stable, the wound was clean and dry. He was scheduled for postoperative chemotherapy for optimal local disease control and continued with wound dressing as well as attending rehabilitation unit. Six months postoperative, the patient was clinically stable ready to start using prosthesis.

3 | DISCUSSION

Sclerosing epithelioid fibrosarcoma (SEF) is a rare, malignant mesenchymal tumor with unique architectural features consisting of cords, nests, or sheets of monotonous epithelioid cells within a dense collagenous background.[1] A subset is related morphologically and molecularly to low-grade fibromyxoid sarcoma.[2] Importantly, SEF appears to be sporadic and of unknown etiology. It is aggressive fibroblastic neoplasm composed of cords, nests, or sheets of uniform epithelioid cells embedded in a dense collagenous stroma. SEF are primarily arise from soft tissue; however, a very few primary bone SEF have been reported. Some cases show morphologic and molecular overlap with low-grade fibromyxoid sarcoma.[3,4]

Epidemiologically, SEF is a very rare fibrosarcoma variant with a wide age spectrum (median age 45 years) and equal sex distribution.[5] As it was the case in our patient,

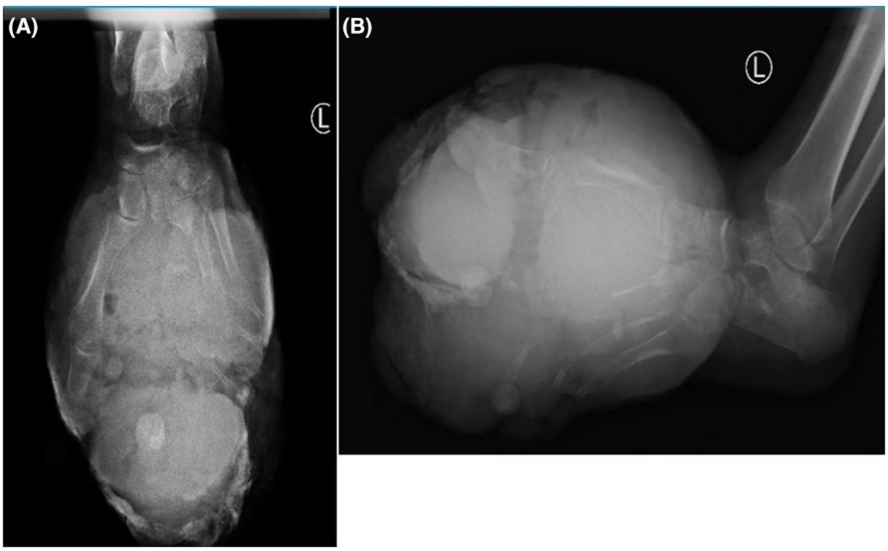

FIGURE 1 X-ray of the foot showing a soft tissue mass associated with bone destruction (A); x-ray of the affected leg highlighting focal cortical thickening left tibia (B); July 20, 2022.

FIGURE 2 Transtibial amputation demonstrating grossly circumscribed ulcerated mass of the foot measuring 15 × 13 cm (A); Cut section of the tumor highlighting a homogeneously white or white-tan, lobulated tumor and very firm surface (B); August 3, 2022.

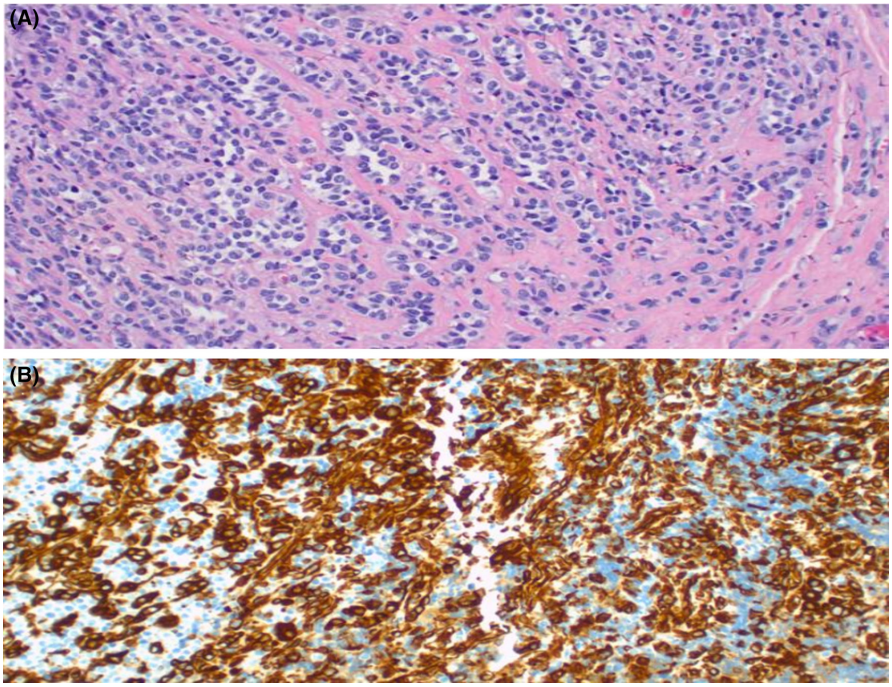

FIGURE 3 Photomicroscopy of SEF demonstrating densely sclerotic containing nests, strands and acini of small cells with scant clear cytoplasm; Hematoxylin and Eosin stained 200× original magnification (A); Aug 10, 2022. Immuno-expression of tumor cells with Vimentin antibody; IHC 200× original magnification (B); August 3, 2022.

most patients present with a mass of variable duration, with 33% reporting recent enlargement or pain.[6] In general, SEF are deep seated and arise most often in the lower extremities and limb girdles, followed by the trunk, upper limb girdles and the head and neck.[7] However, rarely the tumors arise in the kidneys, intestinal tract, mesentery, and bone.[4,7]

Sclerosing epithelioid fibrosarcoma is a clinically aggressive but histologically low-grade sarcoma with unsatisfactory treatment results. It typically takes 33 months from the first onset of symptoms to diagnosis. Sclerosing epithelioid fibrosarcoma can occur from adolescence to the older years and is localized mainly in soft tissues, but it also can arise as a primary tumor of bone, in the neural system, or in the ovary [40]. Sclerosing epithelioid fibrosarcoma has a predisposition for local recurrence with metastasis primarily to the lung. The role of systemic treatment remains unclear. Consequently, SEF may be treated preferably by resection, including re-excision after intralesional excision. Moreover, preoperative or postoperative radiation as used in other soft tissue sarcomas also should be considered.

Diagnosis of SEF can be very problematic especially in resources limited settings undoubtedly related to the

rarity of its presentation. It is a challenging problem to distinguish SEF from undifferentiated carcinoma, which might be impossible based purely on histology. Thus, immunohistochemistry testing is essential to make definitive diagnosis. Specific biomarker protein expression or genetic changes have not been well-described in SEF. As it was the case in our patient, the only immunostaining marker consistently reported positive is vimentin, which is a general marker for soft tissue sarcomas and, therefore, not specific for SEF.[7] In some cases, the deceptively low cellularity, mild cellular pleomorphism, and densely sclerotic hyaline matrix may suggest rather benign clinical behavior.[7] Cell morphology allows for the wide differential diagnoses benign and malignant neoplasia. The typical morphologic features of sarcomas such as pronounced pleomorphism, infiltrative growth pattern, necrosis, and mitotic activity may be inconspicuous or even absent. Histopathology with extensive tissue sampling is the gold standard for a definitive diagnosis. MUC4 expression and *EWSR1-CREB3L1* gene fusions have been also reported.[8,9]

Radical resection for localized disease is recommended treatment approach for SEF However, pre- or postoperative radiotherapy for optimal local disease control have been recommended.[10]SEF has limited responsiveness to conventional chemotherapy and recurrent genomic alterations (CD24 and DMD) constitute potential therapeutic targets.[11]

As it was in this case, SEF patients develop one or more local recurrences. Additionally, more than 40% have metastases at median intervals of 5 and 8 years.[6] Metastases are usually to lungs, pleura, and bone. After 11 years, half of the patients are either dead of disease or have persistent or recurrent tumor. Somewhat higher rates of metastases and tumor death have recently been reported and may well be due to larger average tumor size, intracranial location, and potential referral bias. Adverse prognostic factors include proximal tumor site, larger tumor size, male sex, local recurrences, and metastases.[6]

Potential caveat for our case is lack of access to molecular and a wider immunohistochemistry panel testing. Thus, molecular characterization, which is essential for excluding potential differential diagnoses was challenging to us. For instance, *Arbajian* et al. found recurrent EWSR1-CREB3L1 fusion transcripts by reverse transcription polymerase chain reaction in 3 out of 10 pure SEF cases and splits and deletions of the EWSR1 and/or CREB3L1 genes by FISH in 6 additional cases.[12] In addition, due to limited resources, the patient was unable to afford Locoregional MRI and general body scan extension investigations, which are critical in this case for a well-planned management of recurrent malignant tumor.

4 | CONCLUSION

SEF is an uncommon sarcoma whose diagnosis can be challenging as it resembles a variety of benign, pseudosarcomatous as well as other malignant entities. The tumor is a clinically aggressive but histologically may present with low-grade sarcoma morphology with unsatisfactory treatment results.

AUTHOR CONTRIBUTIONS

Alex Mremi: Conceptualization; data curation; investigation; methodology; validation; writing – original draft; writing – review and editing. **Adnan M Sadiq:** Data curation; writing – review and editing. **Gregory Goodluck:** Data curation; methodology; writing – review and editing. **Jay Lodhia:** Data curation; investigation; writing – review and editing.

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All authors have declared that no competing interests exist.

DATA AVAILABILITY STATEMENT

None.

ETHICAL CONSIDERATION

The patient provided written informed consent to allow for his deidentified medical information to be used in this publication. A waiver for ethical approval was obtained from the authors' institution review board committee.

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