The hundredth case of Sclerosing Epithelioid Fibrosarcoma (SEF)

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Sclerosing Epithelioid Fibrosarcoma (SEF) is a rare and distinct variant of low grade fibrosarcoma, found mainly in deep soft tissue of adult extremities.
We report a case of Sclerosing Epithelioid Fibrosarcoma of soft tissue, which developed in a 69-year-old woman who presented a tumor involving the fourth finger of her right foot and which has not progressed much in size during the three months prior the surgical excision.
Our patient is the hundredth case of Sclerosing Epithelioid Fibrosarcoma reported in literature since 1995, thus confirming the rarity of the tumor.
Our experience showed that it is important to make an early diagnosis, in consideration of the clinical aggressiveness of this cancer. Another important aspect concerns the postoperative follow-up. The monitoring of PET-CT technique , although not standardized, could become part of proceedings of therapy and follow-up of tumor, thus allowing oncological radicality and avoid large amputations.
To date, 24 months after diagnosis of SEF, our patient feels well, attends our outpatient clinic regularly and shows no evidence of relapse and/or metastasis.

KEY WORDS: Fibrosarcoma, PET-CT, Sclerosing Epithelioid Fibrosarcoma, SEF

Introduction

Sclerosing Epithelioid Fibrosarcoma (SEF) is a rare and distinct variant of low grade fibrosarcoma, found mainly in deep soft tissue of adult extremities [1-2].

Low-grade fibrosarcoma are mesenchymal tumors that mainly affect the extremities and trunk of adults of either sex [3-4]. Among these, low-grade fibromyxoid sarcoma (FMS), hyalinizing spindle cell tumor with giant collagen resettes (HST) and sclerosing epithelioid fibrosarcoma (SEF) are well-established entities [2].
SEF was originally described in 1995 by Meis-Kindblom et al. as an uncommon low grade variant of fibrosarcoma carcinoma. Meis-Kindblom et al. also reported that there was a high rate of recurrence and metastasis: local recurrence occurred in 53% patients and metastasis occurred in 43% patients [5-7].
We report a case of Sclerosing Epithelioid Fibrosarcoma of soft tissue, which developed in a 69-year-old woman who presented a tumor involving the fourth finger of her right foot and which has not progressed much in size during the three months prior the surgical excision.

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Case report

A 69-year-old woman with a 3-month history of minor swelling at her fourth finger of the right foot. Lesion size was about 1 cm, unchanged in size and shape over time.
In December 2009 the patient was admitted to our Plastic and Reconstructive Department and underwent an excisional biopsy, leaving behind a scar (about 1 cm in length) localized at the level of metatarso-phalangeal articulation on the plantar surface of the fourth finger of her right foot.
Histological examination of the specimen highlighted that "the lesion was composed of a proliferation of monomorphic neoplastic, round, small and medium size cells arranged in nests or cord, and had small nucleoli and clear cytoplasm. The index of cell proliferation, rated by Ki-67, was about 5%. Immunohistochemical staining and the neoplastic cells tested highly positive for vimentin, but negative for CD68, melan-A, smooth muscle actin, desmin, cytokeratin MNF116, cytokeratin AE1/AE3, factor XIIIa, CD45, S100 protein, CD31, CD34". These morphological and immunohistochemical findings were compatible with the diagnosis of Sclerosing Epithelioid Fibrosarcoma (Fig. 1). The lesion was incompletely excised in depth.
First the patient underwent a Total Body CT and a CT of the right leg to determine the stage of tumor. The Total Body CT showed no significant pathological findings; while the CT of the right leg showed an osteosclerotic area of nonspecific nature at the right talus.
Therefore, in February 2010 the patient underwent a second surgery, which consisted of the matatarso-phalangeal disarticulation with the amputation on the fourth finger of the right foot (Fig. 2).

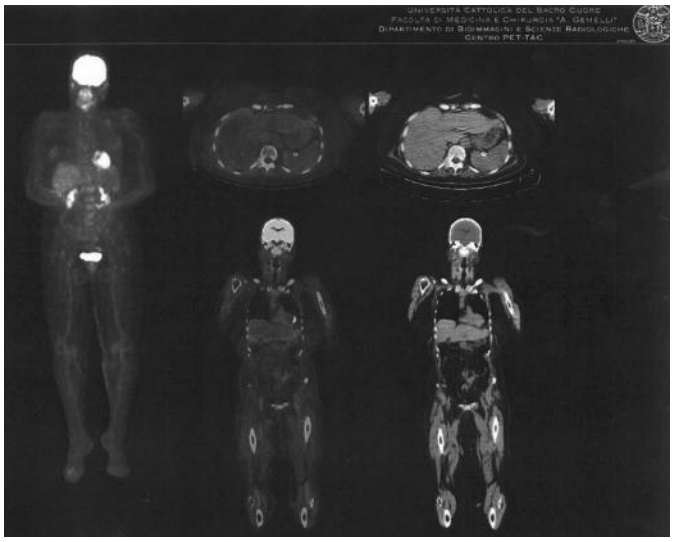

Fig. 1: Matatarso-phalangeal disarticulation with amputation on the fourth finger of the right foot.

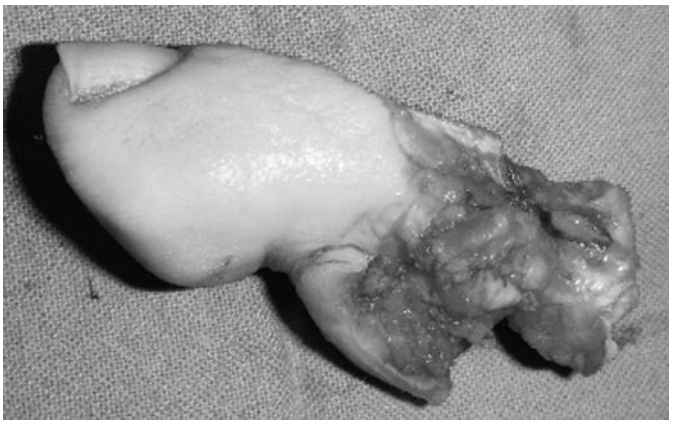

Fig. 2: Histological examination.

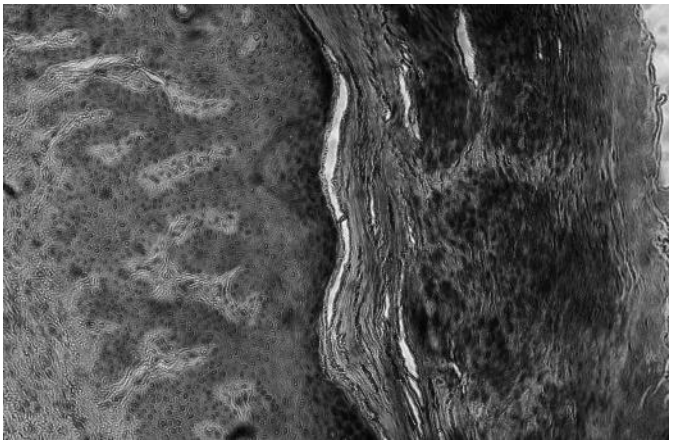

Fig. 3: Total body PET-CT.

The histological examination of the specimen, highlighted morphological and immunohistochemical features similar to those of the previous surgery specimen, being consistent with SEF. The tumor infiltrated the superficial and deep dermis, and the hypodermis and muscle, but without infiltrating the underlying bone. The diagnosis of Sclerosing Epithelioid Fibrosarcoma was confirmed and the lesion was resulted completely excised.
To complete the staging an MRI of the right foot was also performed: the imaging study showed no recurrence of disease.
No adjuvant radiotherapy or systemic treatment was given. Subsequently, the patient was placed in a program of post-operative follow-up. For this reason, during the following months she underwent several diagnostic investigations including both the normal procedural control algorithm based on Total Body CT and liver MRI, and an innovative imaging method, the Total Body ^{18} F-FDG *PET-CT*. All examinations showed no pathological changes attributable to neoplastic disease.
The use of PET-CT examination, which we indicated in the fibrosarcoma postoperative follow-up, is entirely new for this type of neoplastic disease. The reason for our

choice is based on the fact that it allows for much earlier detection of residual and/or recurrent tumor of infinitesimal size compared to other currently used methods such as CT and MRI. The Positron Emission Tomography (PET) is a nuclear medicine technique that provides (unlike CT and MRI which give morphological information on the anatomical region examined) body images and functional information. It is therefore possible, by using the PET scan, to obtain maps of cellular functional processes.

In our clinical case the PET acquisition was carried out in 3D mode, after about 60 minutes, upon intravenous injection of radiopharmaceuticals; CT acquisition was performed with multislice spiral low-dose technique. The total body PET-CT was carried out three times (every six months) in the first year and a half, post-amputation, and showed no images of increased metabolic activity due to neoplastic disease (Fig. 3).

One year and a half, postoperatively, imaging studies, including PET-CT, confirmed no local tumor and no evidence of systemic disease.

Discussion

Our patient is the hundredth case of Sclerosing Epithelioid Fibrosarcoma reported in literature since 1995, thus confirming the rarity of the tumor. Based on our literature review, the clinical behavior of SEF was generally aggressive with recurrence after resection in 31out of 100 patients (31%) at the various times of reported follow-ups. Tumor size at diagnosis averaged 7.9 cm (range, 1–25 cm). The most frequent tumor sites were the lower extremities/limb girdle (n = 41 [41%]; average tumor size, 9.15 cm) and trunk (n = 20 [20%]; average tumor size, 7.55 cm). Overall, 79 out of 100 patients (79%) were reported to have distant disease at a mean of 36 months after diagnosis. The most frequent site of distant tumor manifestation was the lung (n = 26 [63%]) followed by osseous lesions to multiple bones (n = 17 [42%]) and to the pleura/ chest wall (n = 6 [15%]). One out of 100 patients received preoperative radiation therapy (50 Gy). Twenty-two out of 100 patients (22%) received postoperative radiation therapy (50.4–70.2 Gy). Fourteen out of 100 patients (14%) received chemotherapy, and four patients underwent combined radiation therapy and chemotherapy. Thirty out of 100 patients (30%) experienced local recurrence after a mean of 36 months (range, 2–132 months) after diagnosis and treatment. With respect to location, patients with SEF of the head and neck had the worse prognosis with six out of 13 patients (46%) DOD followed by SEF of the upper extremities (five of 13 [38%]) and the trunk (five of 20 [25%]). The influence of local treatment could not be assessed adequately because of incompletely reported data regarding surgical procedures, resection status, follow-up, and missing criteria for radiotherapy.

In general, SEF appears to be a slowly growing tumor often present for several months or years before diagnosis. In most cases of SEF, it took 33 months from the first onset of symptoms to correct diagnosis [3].

The delayed diagnosis (3 months) in our patient once again emphasizes the difficulty arising from the inconclusive clinical, radiological, and histopathological presentation of this tumor. Although the tumor macroscopically has a circumscribed appearance, it routinely infiltrates soft tissues, including periosteum, and can even invade bone [3,7-12]. Although histomorphology of SEF suggests that it is low-grade, it clinically appears as a high-grade tumor [3-4].

SEF belongs to the family of fibrosing fibrosarcomas and appears to be the most malignant variant of this family of low-grade fibrosarcomas [3]. 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 reexcision after intralesional excision. Moreover, preoperative or postoperative radiation as used in other soft tissue sarcomas also should be considered.

However, the high mortality rate observed in patients with SEF may also be due to the lack of experience of most of physicians in how to treat patients with SEF potentially leading to inadequate therapy and unfavorable outcome [3].

Due to the rareness of this tumor, there are no established treatment regimens. So far, patients have been treated with amputation, wide excision, radio- and chemotherapy, or various combinations thereof. The role of systemic therapy, however, still remains unclear.

Our experience showed that it is important to make an early diagnosis, in consideration of the clinical aggressiveness of this cancer, even in the case of small innocuous-looking lesions; furthermore, surgical resections should regard preferably wide margins, in order to ensure a complete excision of the lesions.

Another important aspect concerns the postoperative follow-up: a careful monitoring should be performed when the current techniques, such as CT and IMR, are used but a proper monitoring is also required with the use of PET-CT. The monitoring of PET-CT technique, although not standardized, could become part of proceedings of therapy and follow-up of tumor, thus allowing oncological radicality and avoid large amputations.

Currently, the rate of large amputations in those patients with sarcoma is reduced to 6% (6 out of 100 analyzed patients, in our series, underwent amputation of a compartment).

This approach has enabled the survival of our patient and the sparing of her leg.

To date, 24 months after diagnosis of SEF, our patient feels well, attends our outpatient clinic regularly and shows no evidence of relapse and/or metastasis.

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Riassunto

Il fibrosarcoma epitelioide sclerosante (SEF) è una variante rara e distinta di fibrosarcoma di basso grado di malignità, presente soprattutto nei tessuti molli profondi delle estremità nei soggetti adulti. Riportiamo un caso di fibrosarcoma epitelioide sclerosante dei tessuti molli, sviluppatosi in una donna 69 anni che presentava un tumore che aveva coinvolto il quarto dito del piede destro e che non era progredito di molto in dimensioni durante i tre mesi precedenti l'escissione chirurgica. Il nostro paziente è il centesimo caso di fibrosarcoma epitelioide sclerosante riportato in letteratura dal 1995, confermando così la rarità del tumore. La nostra esperienza ha dimostrato che è importante effettuare una diagnosi precoce, in considerazione della aggressività clinica di questo cancro. Un altro aspetto importante riguarda il follow-up postoperatorio. Il monitoraggio mediante esame PET-CT, anche se non standardizzato, potrebbe diventare parte di un procedimento di terapia e follow-up del tumore, permettendo così sia una radicalità oncologica che di evitare amputazioni di grandi dimensioni. Ad oggi, 24 mesi dopo la diagnosi della SEF, il nostro paziente si sente bene, frequenta regolarmente il nostro ambulatorio e non mostra segni di recidive e/o metastasi.

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