Case Report

Primary intraosseous solitary fibrous tumor: an extremely rare case report and brief review of the literature

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Summary

Solitary fibrous tumor (SFT), a rare mesenchymal neoplasm of fibroblastic origin, was initially discovered in the mediastinal pleura and then described in many extra-pleural sites. The reports of primary solitary fibrous tumor of bone are extremely rare and only a few cases have been previously mentioned in the literature, most of which in flat and short bones.

Here we present the case of a 53-year-old female, who was referred to the emergency department of a peripheral hospital after an accidental fall. Imaging studies revealed an intertrochanteric fracture with an underlying intramedullary lytic lesion. A biopsy was performed and a diagnosis of Ewing sarcoma was initially suggested. She arrived at our hospital where we reevaluated the case. The biopsy was reviewed and a diagnosis of intraosseous SFT was proposed. She underwent en-block resection of the proximal right femur.

Primary SFTs of the bone are, like in our case, easily misdiagnosed due to the low specificity of the imaging studies and the extreme rarity of the localization. An accurate diagnosis and early resection are very important and with careful long-term follow-up is essential, particularly in those who with malignant behavior, for the early detection of possible recurrence or metastasis.

Key words: solitary fibrous tumor, primary bone neoplasm, bone tumor, pathological fracture, STAT-6

Introduction

Solitary fibrous tumor (SFT), an uncommon mesenchymal neoplasm of fibroblastic origin, was firstly described by Klemperer and Rabin  in 1931 as localized fibrous mesothelioma arising in pleura and following a generally benign clinical course. SFT was previously labeled “hemangiopericytoma”, a now-abandoned term that has erroneously been used to encompass a wide variety of unrelated lesions, both benign and malignant, sharing the presence of thin-walled blood vessels often exhibiting a “staghorn” configuration 2. Thanks to immunohistochemistry (IHC) and molecular biology this entity has been better studied and characterized. Extra-thoracic SFTs occur, more frequently, in the deep soft tissues of the proximal limbs, pelvic fossa, retroperitoneum and the head and neck 3. Primary SFTs arising in bone are extremely rare and only a few cases have been previously reported in the literature 4-8, most involving flat and short bones.
Herein, we present the first case of SFT arising in the femur, without evidence of other organ involvement, that was initially interpreted as a possible Ewing sarcoma, due to uneven cytoplasmatic immunopositivity for CD99 in neoplastic cells. We also provide a review of the published literature on this lesion.

Case presentation

A 53-year-old woman went to the emergency department of a peripheral hospital after an accidental fall complaining of pain and loss of function of the right leg. Imaging studies were performed and radiographs revealed an intertrochanteric fracture in the right femur with an well-defined underlying intramedullary lytic lesion measuring 6.4 cm in maximum size. Total-body CT scan was performed to exclude metastatic disease and a biopsy was taken to understand the nature of the lytic lesion that was initially interpreted as a Ewing sarcoma, due to uneven cytoplasmatic immunopositivity for CD99 in neoplastic cells. After that first diagnosis, the patient was referred to our Institute for a second opinion and to assess the proper treatment. We performed further imaging studies and radiographs confirmed both the fracture and the osteolytic lesion, previously described. Magnetic resonance imaging (Fig. 1) displayed an intramedullary lesion measuring 6.4 cm in maximum size that was hypointense on T1-weighted images and unevenly hyperintense on T2-weighted images. The mass showed intense and homogeneous enhancement. The lesion presented some areas of cortical disruption with extensive periosteal reaction and soft tissue edema.

FDG PET/TC was also performed and showed an os-

![Figure 1](image1.png)

**Figure 1.** Axial (A), sagittal (B) and coronal (C) MRI sequences at the same level showing intense and homogeneous post-contrast enhancement of the bone lesion associated with perifocal oedema of the femoral neck spongiosa and of the muscular compartment associated to areas of cortical disruption.

![Figure 2](image2.png)

**Figure 2.** FDG PET/CT axial (A), sagittal (B) and coronal (C) fused view of a solitary fibrous tumour of the right proximal femur, appearing as an osteolytic bone lesion characterized by a faint [18F] fluorodeoxyglucose uptake.
teolytic bone lesion characterized by a faint \(^{18}\text{F}\) fluoro-deoxyglucose uptake (Fig. 2). The pathological re-examination of the biopsy specimen (Fig. 3) showed an intraosseous neoplastic proliferation composed of spindle/round cells arranged haphazardly with monomorphic, small nuclei and indistinct, pale eosinophilic cytoplasm. Those cells were admixed with occasional branching and hyalinized staghorn-shaped blood vessels. There was no evidence of mitosis or necrosis. The immunohistochemical analysis revealed diffuse positive staining in the neoplastic cells for STAT6 and uneven positive cytoplasmatic staining for CD99 while CD34, S100, CD56, FLI1, EMA and CKAE1/AE3 were all negative. Reverse transcription-polymerase chain reaction (RT-PCR) detected NAB2 exon6-STAT6 exon16 fusion gene and NAB2 exon7-STAT6 intron15 fusion gene. These clinical, radiological, morphological, immunophenotypic and molecular findings were consistent with the diagnosis of a primary intraosseous solitary fibrous tumor of the femur.

The patient underwent surgical en-block resection of the proximal region of the right femur (Fig. 4). The post-operative course was uneventful. The patient was asymptomatic without any evidence of local recurrence or distant metastasis at 12 months after surgery.

**Figure 3.** (A) Microscopic evaluation showed spindle/round cells arranged haphazardly with small nuclei and indistinct, pale eosinophilic cytoplasm (hematoxylin & eosin-stained, x20 magnification). (B) Those cells were admixed with hyalinized staghorn-shaped blood vessels (hematoxylin & eosin-stained, x20 magnification). (C) Neoplastic cells showed strong and intense nuclear immunopositivity for STAT-6 (x20 magnification). (D) Neoplastic cells showed intense, dishomogeneous, cytoplasmatic immunopositivity for CD99 (x20 magnification).

**Figure 4.** Surgical en-block resection of the proximal right proximal right femur.
Discussion

SFTs are rare mesenchymal neoplasms of fibroblastic origin that account for less than 2% of all soft tissue tumors and have an incidence of 0.2/100,000 people-year. It typically has a peak age incidence in the adult life, with the mean age presentation during the 50-60 years and affects both sexes equally. Although formerly believed to be restricted to the pleura, these tumors can be found all over the body. Extra thoracic SFTs occur more frequently in the deep soft tissues of the proximal limbs, pelvic fossa, retroperitoneum and the head and neck. While several cases of SFT involving the soft tissue are reported in the literature, only a few cases of intraosseous SFT have been described, two involved the metaphysis of the humerus. From 1991 until now, only five cases of intraosseous SFT have been reported, two involved the metaphysis of the humerus, one the vertebral arch of the L1 vertebra, one the occipital skull and one the right ileum. All patients arrived at the hospital referring local pain or with pathological fractures and the imaging studied revealed an osteolytic lesion without any specific diagnostic features. Three developed lung metastases during long-term follow-up. One patient died with multiple metastases six months after the initial diagnosis. To the best of our knowledge, the current case is the first case of SFT arising in the femur. When arising in bone, diagnosis of SFT can be challenging, due to the extreme rarity of localization, the low specificity of the imaging studies, and the overlapping histological features with other soft tissue tumors that can lead to misdiagnosis. Integration of clinical, histomorphological, immunohistochemical and molecular features is necessary to establish the correct diagnosis. Among the differential diagnoses we must consider round cell tumors and tumors with hemangiopericytoma-like vasculature. The round cell tumors category includes a group of non-mesenchymal neoplasms (such as lymphoma and leukemia, neuroendocrine tumors, malignant melanoma, and neuroblastoma) and mesenchymal neoplasms (especially Ewing sarcoma, mesenchymal chondrosarcoma and round cell synovial sarcoma, but also alveolar rhabdomyosarcoma, desmoplastic small round cell tumor, round cell liposarcoma, CIC-rearranged sarcoma, Sarcoma with BCOR genetic alterations and Round cell sarcoma with EWS-non-ETS fusion). The main tumors with hemangiopericytoma-like vasculature to include in the differential diagnoses are Ewing sarcoma, poorly differentiated synovial sarcoma, mesenchymal chondrosarcoma, low-grade fibromyxoid sarcoma, deep-seated fibrous histiocytoma and phosphaturic mesenchymal tumor. Hypercellular SFTs can mimic small round cell sarcomas such as Ewing sarcoma (ES). Both ES and SFT express CD99 but, in ES, positivity for NFX2.2 and negativity for CD34 and STAT6 help with the correct diagnosis.

Synovial sarcoma mimic SFTs owing to spindle to ovoid cell morphology, hemangiopericytoma-like vascular pattern and CD99 and BCL-2 expression. Strong nuclear expression of TLE1 favors the diagnosis of synovial sarcoma, which is also characterized genetically by a specific t(X;18) translocation. Mesenchymal chondrosarcoma is characterized by a biphasic pattern, composed of neoplastic cells associated with areas of mature cartilage with branching, thin-walled vascular spaces featuring a hemangiopericytoma-like pattern. The differential diagnosis is particularly challenging when the amount of differentiated cartilaginous areas is limited. Positive nuclear staining for SOX-9 and a HEY1-NCOA2 fusion gene confirm the diagnosis.

Low-grade fibromyxoid sarcoma may exhibit some morphologic overlaps with SFT, particularly when dealing with core biopsies, wherein the distinctive HPC-like blood vessels can be easily overlooked. Diffuse positivity for MUC4 and EMA and negativity for STAT6/CD34 represent an important diagnostic clue. Deep-seated fibrous histiocytoma and SFT are related not only to the presence of a hemangiopericytic morphology but also to the expression of CD34. Tumor cells may show positive expression for CD34 and ASMA but STAT6 is negative.

The phosphaturic mesenchymal tumor, like SFT, presented prominent HPC-like vascular pattern; however, the presence of the distinctive calcified matrix, the absence of nuclear expression of STAT6 and the FN1-FGFR1 fusion genes allow distinction.

In our case the clinical presentation was a pathological fracture. Imaging studies revealed an intertrochanteric fracture of the right femur with an underlying well-defined intramedullary lytic lesion measuring 6.4 cm in maximum dimension. The pathological re-examination of the first surgical specimen showed an intraosseous neoplastic proliferation made by spindle/round cells arranged haphazardly with monomorphic, small nuclei and indistinct, pale eosinophilic cytoplasm. Those cells were admixed with few and rare branching and hyalinized staghorn-shaped blood vessels. The immunohistochemical analysis revealed diffuse positive staining in the neoplastic cells for STAT6 and un-even positive staining for CD99. Reverse transcription-polymerase chain reaction (RT-PCR) detected NAB2 exon6-STAT6 exon16 fusion gene and NAB2 exon7-STAT6 intron15 fusion gene. These morpho-
logical, immunophenotypic and molecular findings led us to confirm the diagnosis of solitary fibrous tumor involving the femur. Metastatic SFT to the bone is more common than primary bone SFT so it is important to rule out this possibility with a total body CT scan. Although most SFTs are generally considered as a low-grade neoplasm, a small proportion may display an aggressive behavior. Unfortunately, the clinicopathological criteria of malignancy devised for SFT of soft tissues failed to predict outcomes in primary SFT of the bone. A recent paper by Bianchi et al. showed that no correlation emerged between Demiecco’s risk assessment criteria and clinical behavior as instead evidenced for the SFT of soft tissue. Further validation on wider and more homogeneous samples is necessary to validate some molecular differences between primitive SFT of the bone with respect to that of soft tissues and to evaluate the eventual prognostic implications. Due to this unpredictable biological behavior and the rarity of primary SFT in the bone, long-term follow-up through total body CT scan should be recommended.

**Conclusion**

Due to the particularity of this localization, we observed a challenging case of SFT. Primary SFTs of the bone are, like in our case, easily misdiagnosed due to low specificity of the imaging studies, the unusual site and the overlapping of some histologic features with other soft tissue tumors. An accurate diagnosis and early resection are very important. Careful long-term follow-up is essential considering that some SFT may display aggressive behavior and that the clinicopathological criteria of malignancy devised for SFT of soft tissues fails to predict outcomes in primary SFT of the bone. In fact, no correlation emerged between Demiecco’s risk assessment criteria and clinical behavior as instead evidenced for the SFT of soft tissue. Due to this unpredictable biological behavior and the rarity of primary SFT in the bone, long-term follow-up is strongly suggested.

**Acknowledgements**

We would like to thank Claudia Bonomo for her technical support.

**Conflict of Interest**

The authors declare no conflicts of interest.

**Funding**

The authors declare that they have not received funding.

**Ethical Consideration**

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

**Author Contributions**

CG wrote the manuscript; ZC and BJ participated in the surgery; AA: made and commented the instrumental evaluation; MV and DT: shot and commented the images; CR: analyzed the pathologic specimen and wrote and supervised the writing of the manuscript.

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