Low-Grade Myofibroblastic Sarcoma Of The Bone

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Citation

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Abstract

Myofibroblastic tumours are soft tissue neoplasms arising in myofibroblasts, ubiquitous cells sharing ultrastructural features of muscular and fibroblastic cells. A malignant counterpart of the well-described myofibroblastic benign tumours was described by Vasudev and Harris in 1978, but was not fully characterized as a separate entity until recently. Most reported cases of this rare neoplasm have arisen in the head and neck area, although some cases affecting the soft tissues of the extremities have been reported. To our knowledge, there have only been 7 reports on primary myofibroblastic sarcoma/myofibrosarcoma of the bone, two of them affecting the jaws. We herein report a new case of this rare tumour affecting the right femur of a 24 year-old black African man and comment briefly on the confusing terminology regarding these lesions.

INTRODUCTION

Myofibroblasts are spindle mesenchymal cells sharing features of both muscular and fibroblastic cells.[1] They are important for wound healing and are considered the main cell originating some benign neoplasms, like myofibroblastoma [2] or angiomyofibroblastoma. Although in 1978 Vasudev and Harris described for the first time a sarcoma with ultrastructural features of myofibroblasts [3], the malignant neoplasm originating in these cells (myofibroblastic sarcoma) was not fully characterized until 1998,[4] when Mentzel et al. reported 18 cases arising in different locations and set forth criteria for diagnosis. Myofibroblastic sarcomas/myofibrosarcomas of the bone seem to be extremely rare and after a thorough Medline Search we have only 7 cases reported under these names in the world literature.[5,6]

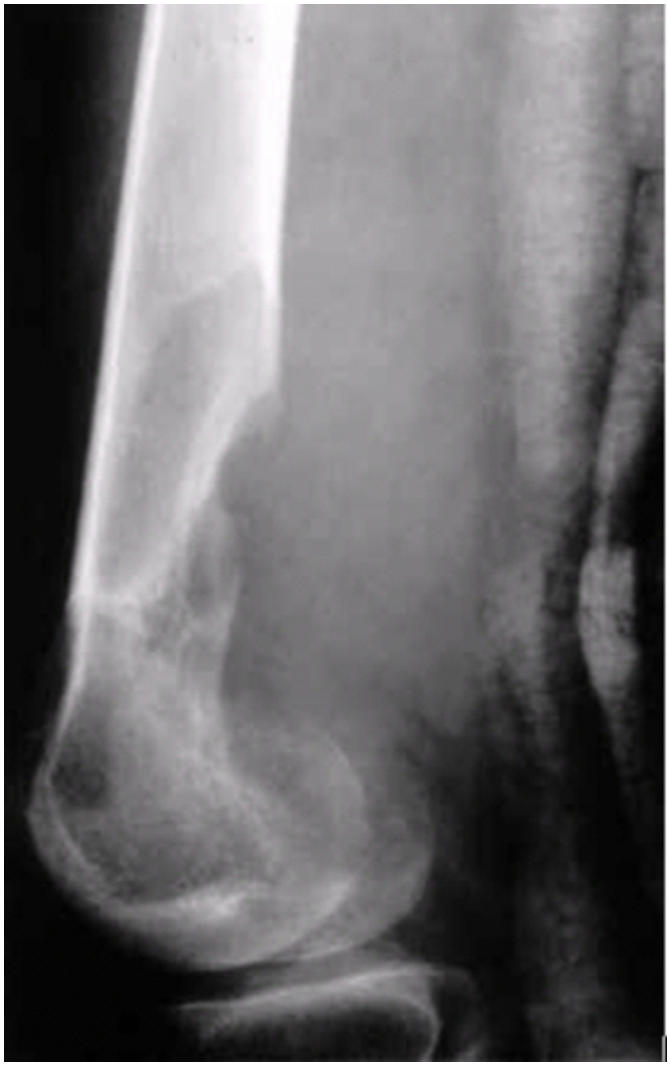
CASE REPORT

A 24-year-old black man born in Guinea consulted in March, 2001 on a huge mass in his right popliteal fossa. He had first noticed the mass three months before and he referred a rapid growth. He had no associated systemic symptoms and only referred pain and functional disability in the affected leg. His past medical history was irrelevant.

The plain radiograph of the right leg showed a lytic mass in the distal third of the femur with focal destruction of the cortical of bone and soft-tissue extension (Fig. 1).

Figure 1

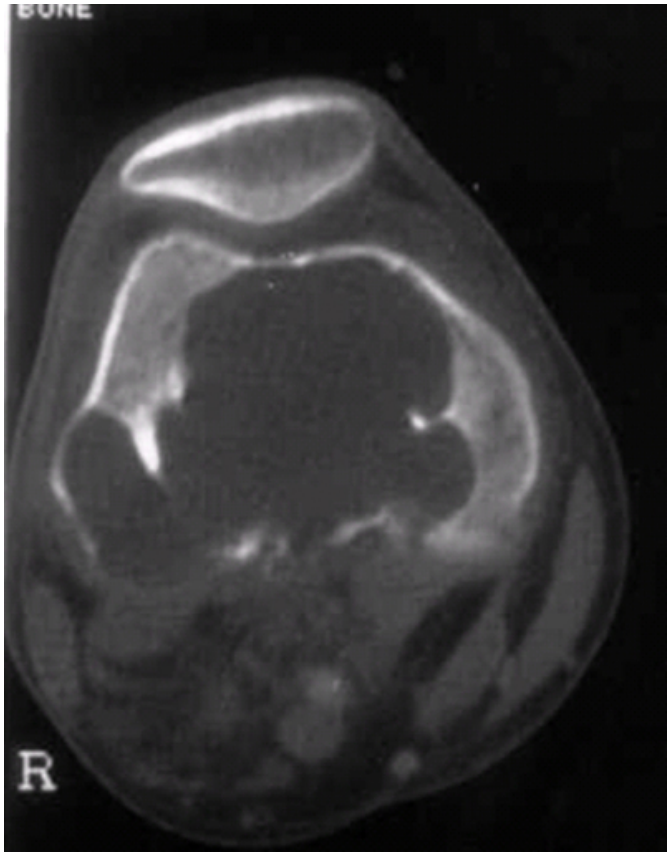
Figure 1: Plain radiograph of the distal femur showing a metaphysal lytic lesion.



Ultrasonography confirmed the cystic nature of the lesion and computed tomography scan revealed widespread destruction of the posterior cortical of the femur with a huge soft- tissue mass (Fig. 2).

Figure 2

Figure 2: Computed tomography scan of the right knee showing a metaphysal cystic mass with destruction of the posterior cortical of the femur and a huge soft-tissue mass



The radiological features suggested a primary bone origin for this tumour with secondary soft tissue extension. The radiological differential diagnosis included hydatid cyst of bone and aneurysmal bone cyst.

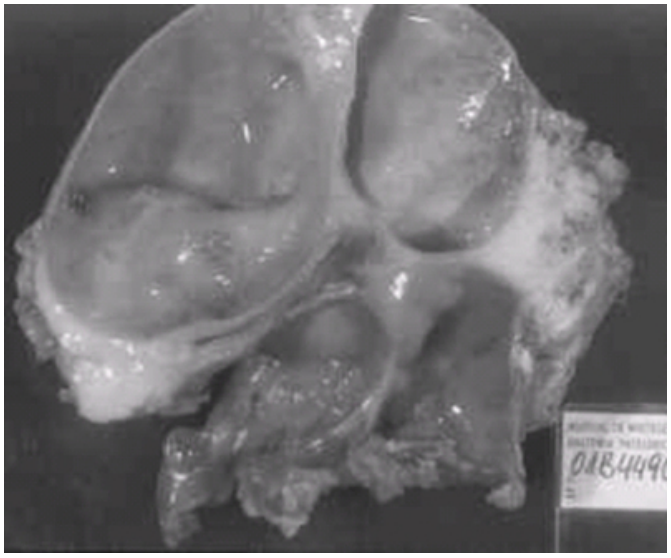
PATHOLOGICAL FINDINGS

With these presumptive diagnoses a biopsy of the mass was performed, but the material obtained from the cyst wall was not considered adequate for a definitive pathological diagnosis and resection of the whole mass was undertaken.

The resection specimen corresponded to a mass measuring 10 x 8 x 3 cm., that was sent unfixed to the pathology department. On cut section the mass was a trilocular cyst. One of the cystic spaces had been torn upon resection and was empty, but the two intact cysts were filled with a clear greenish fluid. There were no gross vesicles inside this fluid. The wall separating the cysts was predominantly thin, but in some areas there were thickened white tumour-looking areas (Fig. 3).

Figure 3

Figure 3: Gross picture of the trilocular cystic lesion, showing white thickened areas in the wall of the cysts.

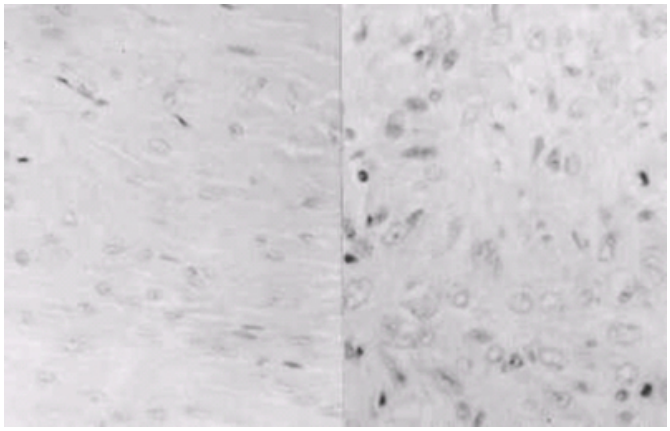


The frozen section of these areas showed a diffuse proliferation of spindle cells, lacking atypia or significant mitotic activity and diagnosis was delayed to paraffin.

The histological analysis of formaldehyde-fixed paraffin-embedded sections of the cyst walls showed a fusocellular proliferation. One striking feature was the mixture of cell-rich and hypocellular fibrous areas, resembling a keloid scar (Fig. 4a). The fusiform cells grew in the most cellular areas in a non-specific interlacing pattern. There were focal aggregates of inflammatory cells, including some eosinophils. At the periphery of the lesion we also found areas resembling a aneurysmal bone cyst and the tumour adopted an infiltrative pattern of growth, invading adjacent bone trabeculae. No osteoid deposition was noted either in these areas of bone invasion or in the cyst walls. At high power, the tumour cells had ill-defined eosinophilic cytoplasm and small vesicular nuclei with occasional small nucleoli (Fig. 4b). Mitotic activity was low (2 mitosis per 10 HPF) and only focal nuclear pleomorphism was seen.

Figure 4

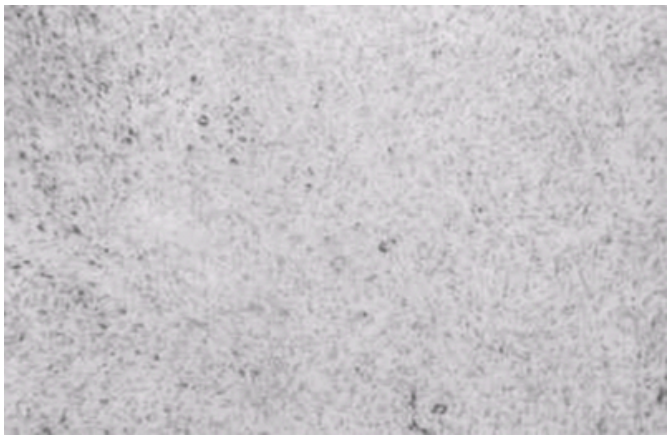
Figure 4: Different areas of the tumour. Paucicellular areas with dense collagenous tissue (4a). Moderately cellular areas composed of interlacing wavy fusocellular elements with vesicular nuclei, resembling myofibroblasts (4b). (hematoxylin-eosin, x



Immunohistochemistry showed intense positivity of the tumour cells for vimentin and muscle actin (HHF-35) (Fig. 5).

Figure 5

Figure 5: Intense positivity of the tumour cells with muscle-specific actin (HHF-35) (immunohistochemistry for HHF-35, x 40).



All other immunohistochemical markers performed, including keratins, desmin, S-100 and caldesmon, were negative.

The ultrastructural analysis could not be performed, for we had only paraffin-embedded material unsuitable for electron microscope analysis.

The final diagnosis was low-grade myofibroblastic sarcoma of the bone.

FURTHER TREATMENT

With this diagnosis a extension study was undertaken, that discarded regional and distant metastases and amputation of the right leg was decided. The patient initially denied this therapeutic option, but he finally accepted amputation, which was performed in October 2001 with good results and wide surgical margins. Although the first resection of the mass had been considered adequate and almost complete by the traumatologists, in the amputation specimen the tumour had regrown to fill the whole cavity of the previous resection and corresponded to a solid white mass. Histological analysis of the tumour showed a similar image and no higher-grade areas were found.

The oncologists decided no further treatment was needed. Today, almost three years after initial diagnosis the patient remains well and free of disease.

DISCUSSION

Myofibroblasts are mesenchymal cells sharing immunohistochemical and ultrastructural features of both fibroblastic and smooth muscle cells.[1,7] They have been shown to participate in many reactive processes, like wound healing, but are also the main cell proliferating in some benign tumours (e.g. myofibroblastoma of the breast).[8] Despite earlier descriptions of ultrastructural myofibroblastic differentiation in some sarcomas [3], it was only in 1998 when Mentzel et al.[4] reported for the first time a malignant lesion originating in this cell type, under the name of myofibroblastic sarcoma, and established the diagnostic criteria to delineate this entity from other low-grade fusocellular sarcomas. After this description, there have been some reports reclassifying lesions originally considered as inflammatory fibrosarcoma into this entity.[6,9] However, terminological confusion persists and recent reports have even introduced terms like myofibrosarcoma, considering this tumour to be different from the low-grade myofibroblastic sarcoma described by Mentzel,[6] and proposing criteria for differential diagnosis. Inflammatory fibrosarcoma probably represents a truly different entity, for it usually affects children and adolescents and arises in the retroperitoneum or the mesentery. We consider the term myofibroblastic sarcoma should be reserved for fusocellular low-grade tumours composed of cells with histological and immunohistochemical features of myofibroblasts, arising in extraabdominal sites and affecting middle-aged patients. It is not clear whether myofibrosarcoma represents a real different entity (as proposed by Watanabe et al.) or is only a part of the wide spectrum of myofibroblastic sarcoma. We think both terms are employed interchangeably in most reports.

As for the diagnosis of myofibroblastic sarcoma, some authors claim for the need of ultrastructural demonstration of fibronexus and other features of myofibroblasts,[10] while other authors base this diagnosis on the light microscope and immunohistochemical features of the lesion, following a more pragmatic approach. These authors consider diagnosis can be made on the presence of a proliferation of fusocellular wavy cells showing vesicular nuclei intermingled with paucicellular collagenous areas and immunohistochemical features of myofibroblasts (positivity for vimentin and specific muscle actin and/or desmin, but not for caldesmon).

Primary myofibroblastic sarcoma of the bone seems to be extremely rare and a Medline Search has only rendered 7 cases (Table 1).

Figure 6

Table 1: Summary of reported cases of myofibrosarcoma of bone

Case	Age	Sex	Site	Size	Therapy	Follow-up	References
1	60	M	distal femur	5 cm	WR + CHT	AWOD	5
2	63	F	distal femur	9 cm	C	AWOD	5
3	66	F	ilium	9,5 cm	WR + CHT	AWOD	5
4	71	F	ilium	7 cm	WR + CHT	DOD	5,6
5	65	M	tibia	6 cm	WR + AMP	AWOD	11
6	24	M	upper jaw	4 cm	WR	AWOD	10
7	49	M	upper jaw	8 cm	WR + RT	DOD	1
8	24	M	distal femur	10 cm	WR + AMP	AWOD	present case

F: female; M: male; WR: wide resection; CHT: chemotherapy; C: curettage; RT: radiotherapy; AMP: amputation; AWOD: alive without disease; DOD: death of disease

The most common location has been the distal femur, followed by the iliac bone. The age range has been wide (24-71 years) and there is a slight predilection for males (5:3). The surgical therapies employed in these patients have also been diverse, from simple curettage to amputation, and some patients have even received adjuvant therapy, mainly radiotherapy. The prognosis is not clear, but most cases (6 patients) have done well without local recurrences or metastasis after follow-up times ranging from 2 to 16 years. The two patients who died of disease were a 71-year-old woman with a tumour arising in the iliac bone (who died 5 years after diagnosis with widespread lung metastases) and a 49-year-old man with a tumour arising in his right upper jawbone (who died 3 years after diagnosis with local recurrence and lung metastasis, despite wide resection of the primary tumour and adjuvant radiotherapy). The two cases

with an aggressive behaviour shared a high mitotic count (6-8 mitosis/10 HPF) and areas of necrosis, but marked atypia was only present in the second one. Besides, some cases with high mitotic counts and atypia have behaved indolently. It seems that there are no definite pathological or immunohistochemical features that can help predict the biological behaviour of these tumours and all of them should be considered lesions with a low-malignant potential. This lack of prognostic indicators makes it difficult to select which cases should receive further adjuvant therapy. In our case we chose to amputate, as limb-sparing surgical techniques were not developed in our Hospital.

CONCLUSIONS

In summary, we report a new case of low-grade myofibrosarcoma of the bone, a rare tumour that poses difficulties for correct histopathological diagnosis and appropriate management.

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The patient has given written consent for the publication of this case. The authors acknowledge no interest conflict.

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