Rare disease

Osteoblastic and fibroblastic multicentric osteosarcoma

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Summary

Bone sarcomas are uncommon tumours, of which osteosarcoma is the least rare, as well as the third most common malignant tumour in childhood, appearing usually between the 10 and 20 years of age. The case the authors present in this work is of a patient suffering from a long-standing condition encompassing skin and soft tissue lesions. After multiple medical treatments, the patient was diagnosed with squamous osteosarcoma, which required aggressive surgical management and chemotherapy.

BACKGROUND

Bone sarcoma is an uncommon tumour of mesenchymal origin, of which there is approximately 2500 cases per year in the United States. Osteogenic sarcoma is the least rare bone tumour and the third most common malignant tumour in childhood. The body regions on which most frequently occurs are the distal femur, proximal tibia and proximal humerus; although it can present itself in any bone.¹

The most common cases occur in patients between 10 and 20 years of age; which often show lasting pain that increases with time. This is often associated with tumour penetration of the cortical bone, irritation of the periosteum or with pathological fractures. Night pain is common, often making it difficult for the patient to fall asleep. Physical examination may reveal localised pain, decreased mobility and muscle atrophy; masses or tissue deformities can often be confirmed.^{1 2}

Recommended radiological studies:

- ▶ X-rays are suggested in cases where lithic and sclerotic lesions can be observed; the latter are the result of the tumour's osteoid production and are typically observed as small and irregular bone densities. Many osteosarcomas cause cortical bone destruction and mass formations in soft tissues, where calcification can be observed. This method can also identify pathological fractures.^{1 3}
- ▶ MRI can be very useful in helping to determine the intra or extra bone extent of the tumour; it can also help determine if the tumour is associated with blood vessels and/or nervous tissue.¹⁻³
- ▶ X-ray CT is useful in determining the extent of the tumour when there is extensive necrosis and oedema. It is also very useful for detecting metastatic lesions in lung tissue.³

Even with the efficiency of the aforementioned methods, a biopsy is still the best and most reliable diagnostic tool.

For classification purposes, osteosarcomas are histologically divided into high and low-degree sarcomas,

depending on cellularity, pleomorphism, anaplasia and mitosis number.¹⁻⁵

CASE PRESENTATION

A 34-year-old farmer was presented. He showed no medical history relevant to his condition, which started one and a half years before his admission to our institution. His medical condition consisted of an injury on his left arm caused by a fall from his own height. Two weeks later after this event a nodular lesion appeared on his

Figure 1 Ulcerative lesions and fetid hematic scabs in left forearm and wrist.

Figure 2 Radiography of the left arm and forearm.

Figure 3 Left arm after amputation.

left wrist and elbow crease, which later began to drain purulent material. The patient received an unspecified treatment for his injury, which yielded a poor outcome; there was an increase in injury volume and more nodular lesions appeared. The patient subsequently suffered further trauma in the affected area, which caused some of the injuries to drain purulent material. He went through multiple unspecified treatments without success, and eventually he was referred to our institution.

The patient's physical examination revealed oedema and swelling of the left forearm; ulcerative lesions (3×3 cm and 5×4 cm) and fetid hematic scabs covered up to one third of the limb, and no vascular or nerve damage was evident. At an axillary level, three adenomegalies showing a solid consistency were identified (figure 1).

The arm and forearm radiographs showed radiolucencies compromising 70% of the soft tissue of the left

forearm; also sequestration in the proximal third of the radius, bone destruction of the wrist joint and periostitis in the proximal phalanges, carpus and metacarpus were evident (figure 2). A bone gammagram showed osteoblastic lesions indistinguishable from those provoked by an infectious process.

A microbiological culture prepared from the ulcer secretions made evident the presence of *Staphylococcus epidermidis*; the patient was then treated with intravenous dicloxacillin. Facing the possibility of mycosis, an sporotrichin intradermal test was performed, which proved negative. A bone tissue biopsy, as well as sporotrichosis and mycetoma cultures were also negative.

After 2 weeks of antibiotic treatment, the lesions showed no more purulent discharge, although a bloody and invasive lesion in the anterior left wrist was still evident. This injury presented necrotic tissue and fibrosis, which limited mobility of the flexor muscle. Oedema and other injuries in the forearm and anterior face of the upper arm were also evident. Clinical, microbiological and mycological studies ruled out chronic osteomyelitis, mycetoma and sporotrichosis.

A biopsy of a 2 cm lesion in the anterior portion of the arm was performed and the dermatopathologic study of the biopsy reported epithelioid sarcoma. After analysing the case, it was decided to provide surgical treatment for the patient in the form of interscapulothoracic disarticulation; to which he agreed.

During the pathological study of the specimen, an osteolytic lesion involving the radius and ulna was observed. The injury was grayish white in color and showed destruction of the entire medullar and cortical bone, infiltrating the soft tissues (figure 3). During microscopic analysis, a multifocal tumour in the bones of the arm, forearm and hand was observed; this tumour was composed of fusiform and pleomorphic neoplastic cells, showing atypia and abnormal mitotic activity among the calcified osteoid material. The

Figure 4 Pathology of the left arm showing a fibroblastic pattern.

tumour destroyed the bone trabeculae, extending to the deep and superficial soft tissues and all the way to the skin, presenting fistulization to the exterior. The predominant growth pattern was fibroblastic, and in lesser proportion osteoblastic (figures 4 and 5); reason why the patient was diagnosed with osteoblastic and fibroblastic peripheral osteogenic sarcoma in the radius and ulna, showing soft tissue and skin invasion. After surgery, the patient was treated with cisplatin and adriamycin; he recovered and rejoined his family showing promising emotional development. He died 15 months after surgery at his home, after 2 weeks of health complications due to the unsatisfactory progress of his cancer.

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis
- Sporothricosis
- Soft tissue infection.

DISCUSSION

Of the originally proposed diagnoses, sporotrichosis was considered because it is a chronic fungal infection caused by *Sporothrix schenckii*, which affects the skin and develops painless deforming lesions with distal and proximal ulcers, which may remain for years.⁶ Another possibility was that of mycetoma caused by either actinobacteria or true fungi; since it produces deformation and chronic enlargement of the affected region, plus fistulae. This infection is frequently associated with bone destruction, such as the one presented by the patient.^{7 8}

Bacterial osteomyelitis was relevant to this study because it is a bone infection that can occur in chronic form.^{9 10} In this kind of pathology long bones are more likely to be affected; showing inflammation, suppuration and bone necrosis; also, soft tissues can be compromised.⁸ All these symptoms were present in the patient. In fact, cultures prepared from the drainage obtained from these lesions made evident the presence of *Staphylococcus epidermidis*. Imaging studies also showed signs of osteomyelitis.

Radiographic alterations such as the ones shown by the patient may mimic bone lesions like Langerhans cell histiocytosis (eosinophilic granuloma), Ewing sarcoma and

Figure 5 Pathology of the left arm showing a fibroblastic and osteoblastic growth pattern.

osteosarcoma.^{9 10} Possible complications can occur in the form of joint shrinkage, pathological fracture, amyloidosis and skin squamous cell carcinoma, which may present a persistent infection for years.

Epithelioid sarcoma is included among soft tissue sarcomas, which are neoplastic malignancies of mesenchymal and neuroectodermal origin. Depending on the type, soft tissue sarcomas can be low-grade malignancy sarcomas (small risk of distant metastasis) and high-grade malignancy sarcomas, which are locally aggressive and metastasize more frequently.¹¹

Proximal epithelioid sarcoma is a variant that is characterised by being more aggressive and capable of showing metastasis; but unlike conventional epithelioid sarcoma it can affect limbs. During histological diagnosis, sarcomas can be confused with several kind of tumours: undifferentiated carcinomas, melanomas, epithelioid or rhabdoid sarcomas (such as epithelioid sarcoma of the peripheral nerve sheath), epithelioid angiosarcoma, epithelioid leiomyosarcoma, epithelioid rhabdomyosarcoma and epithelioid synovial sarcoma. For accurate diagnosis, immunohistochemistry and electronic microscopy studies are necessary.¹²

Between 1% and 3% of osteosarcoma patients show tumours at multiple sites at the time of diagnosis, and between 15 and 20% show macro metastasis in the lung, bones, pleura, pericardium, kidney, adrenal glands and brain.¹³

Multifocal osteosarcomas constitute a subset of rare intramedullary osteosarcomas. They are classified into two types: synchronous and asynchronous; synchronous tumours appear simultaneously within the next 6 months from each other. The hypothesis of multiple primary tumours has been proposed, as they occur simultaneously and are often symmetrical.¹⁴ The tumours that occur during childhood and adolescence exhibit histological characteristics that are predominantly osteoblastic; at the time of initial diagnosis the lesions are not normally extra-osseous; however, the lesions can evolve and be highly aggressive, showing pulmonary metastasis.¹⁵

The diagnostic difficulties in this case were related to sampling conditions of the neoplasm and its atypical clinical behaviour; as such, the condition was initially diagnosed

as epithelioid sarcoma due to the absence of osteoid material in the tumour. The surgical specimen produced from the amputation showed osteoblastic and fibroblastic multicentric osteosarcoma.

There are several conclusions that need to be considered in this case. First, we need to keep in mind that there are many chronic diseases, and that a high percentage of them can show an infectious aetiology. However, in the case of limb injuries there are diseases with can result from different causes, so in order to avoid delay during diagnosis and reduce complications, a diagnostic pathway that considers both infectious and neoplastic aetiologies must be followed. In this case, the most common diseases: fungal and bacterial infections, were dismissed. When the diagnosis failed, other pathologies were considered and osteoblastic and fibroblastic multicentric sarcoma was eventually diagnosed; so a more adequate treatment was possible.

Our conclusion obtained from this case is that clinical manifestations can lead us to probable diagnoses, but it is necessary to follow a step by step diagnostic guide until causal demonstration of the studied pathology is obtained. We present this case in order to showcase a diagnostic problem we faced and we believe that our experience can be useful for those working in clinical diagnosis.

Learning points

- ▶ So many different clinic manifestations could make us to think about so many different diagnosis.
- ▶ It is really necessary to follow a diagnostic guide, one step ahead, until the demonstration of the pathology in study.
- ▶ We reported this case with the objective to show a diagnostic problem we faced of, and we believe that our experience could be useful to another physicians who could have cases like this.

Competing interests None.

Patient consent Obtained.

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