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CASE REPORT

Challenges in treating pleomorphic bone sarcoma in elderly patients: a case report

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Abstract
Pleomorphic sarcomas or spindle cell sarcomas of the bone are rare malignant tumors that affect the adult. Fracture in the affected bone is the most frequent first symptom. Multimodal treatment is similar to the one for osteosarcoma, but the benefit is less evidence-based, due to the rarity of this sarcoma subtype. The present paper is a case report of a 73-year-old patient, who presented with a comminuted fracture of the distal third of the femur after a fall on ice. Differential diagnosis of bone metastasis was made. After the histopathological confirmation, the surgical team decided to amputate, with prior patient consent. The tumor was staged pT1NxMx, R0. Immunohistochemical studies confirmed the histopathological diagnosis. A lytic lesion in the stump bone appeared on post-operative MRI and was interpreted as skip metastasis. No other metastatic sites were detected. The multidisciplinary team decided for adjuvant chemotherapy (3 courses) and then radiotherapy. He was unable to receive the total planned dose of radiotherapy due to local toxicity. Even so, he is free of recurrence on long-term follow-up.
Keywords: bone sarcoma, multimodal treatment, skip metastasis

Introduction

Spindle cell or pleomorphic sarcomas of the bone are malignant, undifferentiated mesenchymal tumors, which arise in the adult life, usually between 30 and 60 years of age. They represent 2 to 5% of the total bone malignant tumors and usually affect men. A frequent first sign of the disease is a fracture of the affected bone. On imaging studies, they present as a lytic lesion and usually differential diagnosis with bone metastases is imperative. The surgical and medical therapeutic conduct is similar to the one for osteosarcoma, although further studies have to be conducted to accurately establish the rate of response to chemo and radiotherapy [1].

Case report

We present the case of a male patient, 73 years old, who was admitted in the Orthopedics Department of "Elias" University Emergency Hospital, Bucharest in January 2016 for pain

and loss of function in the right lower limb after a fall on ice. He also suffered from arterial fibrillation (permanently anticoagulated with acenocoumarol), had arterial hypertension and gout. On clinical examination, he was tachycardic, had high blood pressure, swelling and bruising of the right thigh was observed, he had significant pain (VAS 9/ 10). Laboratory results showed mild anaemia (Hgb=9.8 g/ dl), INR=3, high levels of LDH and alkaline phosphatase. On the X-ray exam, a comminuted fracture of the distal third of the femur could be observed together with a lytic region of the whole affected area, poorly defined, with punctate calcifications and no periosteal reaction. An underlying bone tumor was suspected. Rapid differential diagnosis of bone metastasis vs. primary tumor was made. PSA levels were normal and chest X-ray was not specific for primary lung cancer. The team decided to operate. The possibility of amputation was discussed with the patient, for which he consented. On extemporaneous exam, the extracted fragment of bone was highly suspicious for sarcoma and the surgical team completed the amputation of the right lower limb.

Pathology report described a tumor of less than 8 cm diameter, with margins free of a tumor (malignant cells present up to 2.2 cm away from the edge, suggestive for undifferentiated sarcoma) (pleomorphic cells surrounded by coagulative necrosis) - pT1NxMx (Fig. 1). Immunohistochemistry of the specimen proved positive for vimentin, desmin, CD34, EMA, and was negative for S100, ki67 being 60%. This confirmed the histopathological diagnosis. The patient recovered one month after surgery and was ambulant using a cane. He had an ECOG score of 1.

Post-operative MRI, at one month after surgery, in both T1 and T2 sequences, in all three planes, revealed a skip metastasis on the stump bone (a lytic lesion of 0.5 cm) at 4 cm away from the amputation edge. CT of the thorax, abdomen, and pelvis was non-specific for other metastases. The patient was carefully assessed in the multidisciplinary team. The treating oncologist consulted with his cardiologist who established he was compensated (LVEF=50%), so he was considered fit for doublet chemotherapy including anthracyclines. Re-operating for the skip metastasis was not considered feasible. The radiotherapist considered he would have benefited from radiotherapy, but after completing 3 courses of chemotherapy. The patient underwent 2 courses of cisplatin 100 mg/ m2 on day 1 and doxorubicin 25 mg/ m2 on days 1 to 3, every three weeks, with careful cardiology monitoring. After the second course, we had grade 4 neutropenia so the dose was reduced to 75% for the third course. Although the planned total radiotherapy dose was 60-65 Gy, he was unable to finish the local treatment because of skin ulceration on the surgical suture site and infected exfoliative dermatitis. The total dose received was 45 Gy with a boost of 5 Gy on the skip metastasis site. After a 4-week treatment break, the patient continued with another 3 courses of carboplatin AUC=6 and doxorubicin 25mg/ m2.

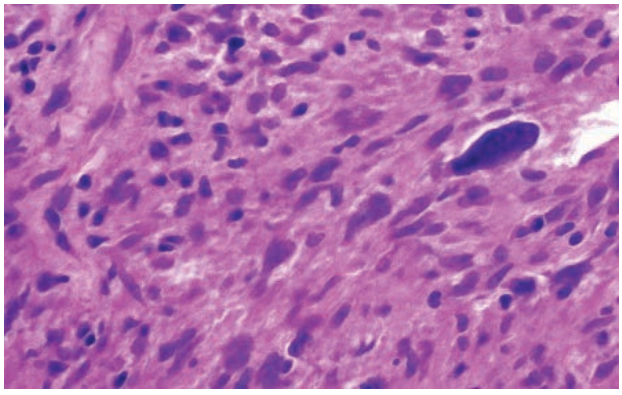

Fig. 1 H&E Image (high) of undifferentiated pleomorphic sarcoma

On MRI follow-up he had a complete clinical response. Up to date, after 2 years from diagnosis, he is free of disease.

Discussion

Considering that the disease presented

as a pathological fracture, the surgery's first approach was a must in the present case. Neoadjuvant treatment was not an option. However, the benefit of neoadjuvant therapy in this histologic subtype was demonstrated [2]. Pleomorphic, undifferentiated sarcoma is a chemosensitive tumor. Brauwell et al. proved in their trial that neoadjuvant chemotherapy induces important pathological response (42% of the studied patients had more that 90% necrosis in the resected specimen). Progression-free survival and overall survival were also superior in the neoadjuvant treated arm. The chemotherapy regimen studied in this trial was doxorubicin 25 mg/ m2, day 1-3 and cisplatin 100mg/ m2 day 1, repeated every 3 weeks [3]. The same regimen was used for adjuvant treatment in our patient.

Considering the patients' age and comorbidities, it was considered that a three-agent regimen was unfit. However, the strongest evidence for efficacy in this histologic subtype is for doxorubicin/ cisplatin [4]. Changing cisplatin with carboplatin was because the patient developed incipient renal failure, with GFR of under 50 ml/ min/ 1.73 m2. Although the carboplatin regimen is not listed in the most popular chemotherapy protocols, there are case reports advocating for its efficacy in pleomorphic sarcoma [5].

The most suitable moment for radiotherapy is always a challenge in sarcoma cases. Radiotherapy is usually indicated as adjuvant treatment in positive margin resected tumors. In our case, the presence of the skip metastasis led to this decision. The concomitant chemo-radiotherapy option exists but should be reserved for the cases in which definitive treatment is intended. This treatment doubles the risk for severe thrombocytopenia and is associated with higher incidence of local complications [6].

To conclude, patients with undifferentiated pleomorphic sarcoma are always a therapeutical challenge, which is best to manage in the multidisciplinary team. Treatment in a highly specialized centre is advised. Therapy sequence should be established for each patient individually considering the age, comorbidities, presentation and last, but not least, the patients' wishes. Better prognostic tools, prospective, randomized trials of more chemotherapy regimens and better predictive biomarkers are needed to improve outcomes in these rare tumors.

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