

Osteosarcoma with Pulmonary Metastasis and Pulmonary Tuberculosis Coinfection in a Young Patient: Case Report

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Osteossarcoma com Metástase Pulmonar e Coinfecção por Tuberculose Pulmonar em Paciente Jovem: Relato de Caso
Osteosarcoma con Metástasis Pulmonar y Coinfección por Tuberculosis Pulmonar en una Paciente Joven: Informe de Caso

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ABSTRACT

Introduction: Osteosarcoma is a primary malignant bone tumor characterized by the presence of malignant mesenchymal cells producing osteoid. Although it can occur at any age, it is more common in children, adolescents, and young adults. Early recognition of the disease is essential for a favorable prognosis. **Case report:** Female patient L.S.M., 19 years old, sought medical care complaining of right knee pain after trauma. A bone biopsy confirmed the presence of osteosarcoma. The patient underwent neoadjuvant chemotherapy, completing two cycles before surgery for tumor resection and endoprosthesis implantation. Three months after surgery, a chest CT scan revealed bilateral pulmonary nodular metastases, as well as findings compatible with a tuberculous cavity and pulmonary parenchymal lesions. **Conclusion:** Although osteosarcoma is a rare neoplasm, it should be considered as a diagnostic hypothesis in young patients with persistent bone pain, even in cases associated with trauma. Early diagnosis is crucial to enable effective treatment in the localized phase of the disease, increasing the chances of cure. In the reported case, despite the relatively late diagnosis and progression to pulmonary metastases, the treatment provided clinical improvement for the patient.

Key words: Osteosarcoma/diagnosis; Neoplasm Metastasis/diagnosis; Prostheses and Implants; Case Report.

RESUMO

Introdução: O osteossarcoma é um tumor ósseo maligno primário caracterizado pela presença de células mesenquimais malignas produtoras de osteoides. Apesar de ocorrer em qualquer faixa etária, é mais comum em crianças, adolescentes e adultos jovens. O reconhecimento precoce da doença é essencial para um prognóstico favorável. **Relato do caso:** Paciente L.S.M., sexo feminino, 19 anos, procurou atendimento médico com queixa de dor no joelho direito após um trauma. A biópsia óssea confirmou a presença de osteossarcoma. A paciente iniciou quimioterapia neoadjuvante, realizando-se dois ciclos antes da cirurgia para ressecção do tumor e implante de endoprótese. Três meses após a cirurgia, a tomografia de tórax revelou metástases nodulares pulmonares bilaterais, além de sinais compatíveis com caverna tuberculosa e lesões no parênquima pulmonar. **Conclusão:** O osteossarcoma, apesar de ser uma neoplasia rara, deve ser considerado como hipótese diagnóstica em pacientes jovens com dor óssea persistente, mesmo em casos associados a trauma. O diagnóstico precoce é essencial para possibilitar um tratamento efetivo na fase localizada da doença, aumentando as chances de cura. No caso relatado, apesar do diagnóstico relativamente tardio e da evolução com metástases pulmonares, o tratamento instituído proporcionou melhora clínica da paciente.

Palavras-chave: Osteosarcoma/diagnóstico; Metástase Neoplásica/diagnóstico; Próteses e Implantes; Relatos de Casos.

RESUMEN

Introducción: El osteosarcoma es un tumor óseo maligno primario caracterizado por la presencia de células mesenquimales malignas productoras de osteoides. Aunque puede ocurrir a cualquier edad, es más común en niños, adolescentes y adultos jóvenes. El reconocimiento temprano de la enfermedad es esencial para un pronóstico favorable. **Informe del caso:** Paciente L.S.M., femenino, 19 años, buscó atención médica con queja de dolor en la rodilla derecha después de un trauma. La biopsia ósea confirmó la presencia de osteosarcoma. La paciente inició quimioterapia neoadyuvante, realizando dos ciclos antes de la cirugía para la resección del tumor e implantación de endoprótesis. Tres meses después de la cirugía, la tomografía de tórax reveló metástasis nodulares pulmonares bilaterales, además de hallazgos compatibles con una cavidad tuberculosa y lesiones en el parénquima pulmonar. **Conclusión:** Aunque el osteosarcoma es una neoplasia rara, debe considerarse como una hipótesis diagnóstica en pacientes jóvenes con dolor óseo persistente, incluso en casos asociados con trauma. El diagnóstico temprano es crucial para permitir un tratamiento efectivo en la fase localizada de la enfermedad, aumentando las posibilidades de cura. En el caso informado, a pesar del diagnóstico relativamente tardío y la evolución con metástasis pulmonares, el tratamiento instituido proporcionó una mejoría clínica en la paciente.

Palabras clave: Osteosarcoma/diagnóstico; Metástasis Neoplásica/diagnóstico; Prótesis e Implantes; Informes de Casos.

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INTRODUCTION

Osteosarcoma is a malignant neoplasm that develops from immature mesenchymal cells that are able to produce osteoid or immature bone. It is the most common primary malignant bone tumor with high incidence in children, adolescents and young adults, although may affect individuals of any age-range^{1,2}. Predominant anatomic locations are metaphysis of long bones, especially distal femur, tibia and proximal humerus².

The initial clinical setting is usually unspecific with progressive bone pain, night pain, fatigue and later, edema and functional restraint. At advanced stages, respiratory symptoms in case of pulmonary metastases may appear³. The etiology of osteosarcomas is currently unknown, although genetic syndromes and hereditary factors are associated with increased risk^{3,4}.

Therapeutic management includes neoadjuvant chemotherapy followed by surgery – amputation or preservation of the limb with tumor resection and implantation of endoprosthesis – and adjuvant chemotherapy. Preoperative chemotherapy aims to reduce the tumor volume and allow least mutilating surgeries, in addition to facilitating local control of the disease^{5,6}.

The objective of the present study is to report a singular clinical case of a young patient diagnosed with lower limb osteosarcoma whose evolution was marked by infectious complications and pulmonary metastatic progression and eventually leading to concomitant diagnosis of lung tuberculosis. This report stands out for its rarity and complexity of the clinical conditions, adding value to the literature while approaching challenging diagnoses and therapies in the course of the disease.

It is a descriptive, observational study based on retrospective analysis of clinical and radiological data obtained directly from the electronic charts of *Hospital Ophir Loyola (HOL)* where the patient was assisted.

The institution's Ethics Committee approved the study, report number 3,009, 002/2018, (CAAE (submission for ethical review 96279018.6.0000.5550) in compliance with Directive 466⁷, of December 12, 2012 of the National Health Council. The informed consent form was waived due to its retrospective nature.

CASE REPORT

Female patient, 19 years old, sought medical care in the city of Castanhal, state of Pará, in September 2016 complaining of intense pain at the right knee post blunt trauma. Initial radiology did not show bone alterations, she was prescribed analgesics for symptoms relief.

Regardless of the initial management, the patient evolved with persistent and continuous pain, refractory to analgesia and associated with progressive functional limitation. One month after the initial episode, a new radiological image revealed bone alterations suggestive of expansive process, prompting magnetic resonance performed in November 2016 for complementary investigation; the exam revealed expansive and infiltrative lesion on distal femur, compromising the diaphysis, metaphyseal and epiphyseal regions, extending to soft parts and subpatellar recess, in addition to periosteal reaction, compatible with sarcomatous lesion and indication of diagnostic biopsy.

The patient was referred to HOL for oncologic follow-up; bone biopsy was performed in October 2017 and confirmed the diagnosis of osteosarcoma. At initial physical examination, the patient presented edema at the right knee associated with significant reduction of muscle strength (Oxford scale grade 4) and articular range of motion. She reported moderate pain at rest, Visual Analog Scale (VAS) score 6 to 7 and Johns Hopkins Mobility Scale grade 3, indicating limited mobility and partial dependence for transferences and ambulation. On November 4, 2017, initiated outpatient treatment with MAP neoadjuvant chemotherapy – high-dose methotrexate, doxorubicin and cisplatin.

She was hospitalized in the same month at HOL oncologic unit to continue the neoadjuvant chemotherapy protocol (clinical staging III), being discharged in December 2017. Due to the necessity of primary tumor control, improvement of surgical resectability and micrometastasis control, she was readmitted on January 17, 2018 and submitted to segmentary resection of distal femur with implantation of endoprosthesis (Figure 1) on February 16, 2018. She received adjuvant chemotherapy post-surgery to consolidate the therapeutic response and reduce the risk of local and remote recurrence. It has been decided to keep MAP as the standard therapeutic protocol.

In April 2018, the patient was readmitted at HOL with persistent fever, overall malaise, dyspnea and phlogistic signs at the surgery site. Chest x-ray revealed pneumonia and diagnostic of postoperative wound infection. She was submitted to surgical debridement and ample lavage of the operation bed (Figure 2).

Despite the resolution of the local infectious conditions and initial clinical improvement, the patient evolved with persistent dry cough, thoracic pain, afternoon fever and dyspnea at rest. A contrasted thoracic computed tomography (CT) revealed metastatic pulmonary nodes and pleural bilateral, right pleural effusion, tuberculous cavity and alterations of the

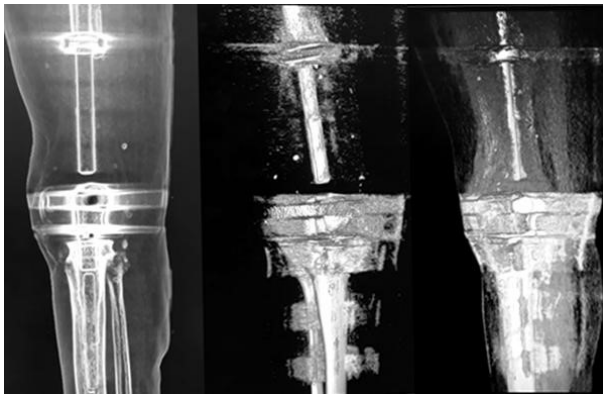


Figure 1. Postoperative immediate left thigh computed tomography (CT), showing position of endoprosthesis

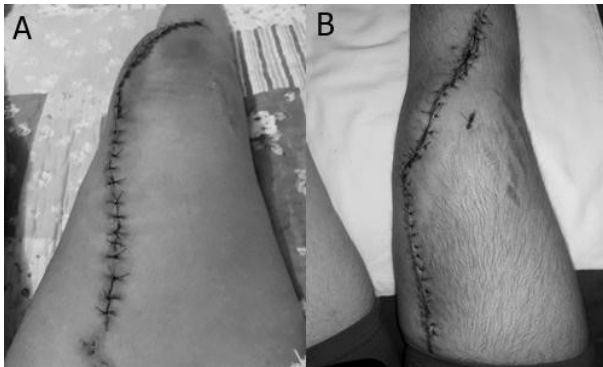


Figure 2. A) Phlogistic signs at surgical site; B) Postsurgical debridement

parenchyma consistent with pulmonary tuberculosis (Figure 3). Diagnostic hypothesis was clinically confirmed together with positive bacilli alcohol-acid-resistant (BAAR) test (3+) and imaging exam.

The patient began anti-TB treatment with good adhesion, presenting significant improvement: fever resolution, end of cough and regression of respiratory symptoms. In addition, there was no recurrence of infection at the surgical site. She was discharged on May 25, 2018 at stage IV of the disease due to confirmation of pulmonary metastasis.

On July 22, 2018, the patient died at home due to chemotherapy-related complications. The decision to provide home care was made by the palliative care team and the family, given the advanced stage of the disease and guarded prognosis. During this period, she was thoroughly followed up for symptomatic relief and comfort procedures according to palliative care guidelines focused to pain management and promotion of the quality of life. This approach respected the patient's autonomy, hers and her family wishes in addition to minimizing invasive interventions that did not contribute to improve the clinical condition.

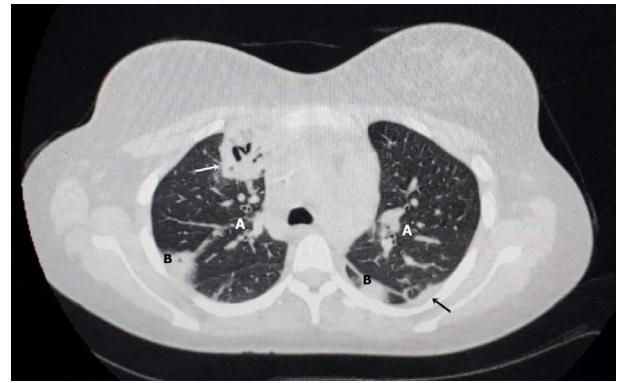


Figure 3. Chest CT: A) Diffuse metastatic nodes in pulmonary window; B) pleural nodes, tuberculous cavity (white arrow) and pleural effusion (black arrow)

DISCUSSION

The present case exemplified the multiple challenges related to diagnosis and treatment of osteosarcoma, moreover in the context of health systems and limited access and resources. There was nearly a 12-month gap between the onset of the symptoms and biopsy-based diagnostic confirmation, a considerable delay consistent with the national literature. Recent studies indicate that delayed diagnosis of osteosarcoma can significantly vary with negative impacts on prognosis⁸.

Frequently, osteosarcomas are insidious with unspecific symptoms as persistent bone pain, occasionally associated with minor trauma. The absence of significant alterations in initial radiology, as in the present case, can contribute to sub-diagnosis or delay of thorough investigation⁹. However, the persistence of pain and functional limitation should warn professionals for the possibility of bone neoplasm, especially in young patients.

Studies indicate that metastases at diagnosis are associated with dismal prognosis. Initial metastases in Brazil range between 18% and 30%, above international means^{8,10}. Although late diagnosis is a contributing factor, recent evidences suggest that tumor aggressiveness, intrinsic biologic features and molecular profile play an even more relevant role to determine the metastatic behavior and survival^{8,10,11}.

Additional relevance is warranted to this case due to coinfection by pulmonary tuberculosis diagnosed post metastatic progression. Overlapping of clinical and radiologic manifestations – fever, dyspnea, dry cough and lung cavitation – was a substantial diagnostic challenge. Concomitant malignant neoplasm and tuberculosis is rare although described in the literature, requiring clinical surveillance, most of all in endemic regions.

Adhesion to multidisciplinary treatment was critical for the patient's clinical stabilization, despite the advance stage of the disease at the end line. The patient and

multiprofessional team's involvement favored the correct management of infectious interventions, continuity of the oncologic protocol and early beginning of anti-TB treatment. Integrated and patient-centered approach contributed to functional improvement and quality of life in the context of palliative care.

The case reported contributes to the literature as it gathers in the same clinical scenario features as late diagnosis, lung metastasis, postoperative infectious complications and concomitant opportunistic infection. These elements reinforce the importance of early diagnosis strategies, continuous multidisciplinary follow up and surveillance for associated infectious diseases, most of all in vulnerable populations.

CONCLUSION

Notwithstanding significant advances of oncologic therapy, the prognosis of sarcoma remains directly associated with early diagnosis and timely implementation of multidisciplinary therapeutic plan. The present report clearly illustrates the obstacles encountered in actual clinical contexts as delayed diagnosis, evolution to lung metastasis and coinfections that brought additional complications to the course of the disease.

The singularity of this case lies on the rare association between metastatic osteosarcoma and active pulmonary tuberculosis, a setting that intensified the diagnostic and therapeutic complexity and strengthens the importance of a comprehensive clinical approach, most of all in endemic regions for infectious diseases. The favorable response to anti-TB treatment associated with effective management of postoperative complications highlights the relevance of the patient's adherence to the treatment and integrated action of the health team.

The case contributes to the literature while addressing an atypical clinical combination, emphasizing the necessity of elevated diagnostic suspicion even in face of unspecific symptoms and initial normal imaging findings. The relevance of warning signs as persistent pain and functional limitation in young patients should guide early investigation of bone neoplasms with potential impact on prognosis and survival.

It is recommended that primary and specialized attention health services are able to detect initial manifestations of osteosarcoma, choosing proactive conducts to screen and referral for reference centers to allow effective and early interventions.

CONTRIBUTIONS

Flávia Adrienne de Castro Grello and Adrielly Elane de Sousa Maia contributed to the conception and design of the study, acquisition and analysis of the data, drafting

of the manuscript and critical review. Katiane da Costa Cunha and Saul Rassy Carneiro contributed to the drafting of the manuscript and critical review. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

DATA AVAILABILITY STATEMENT

All content underlying the text of the article is contained in the manuscript.

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