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Pulmonary metastasis of osteosarcoma: multiple presentations in a single patient

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TO THE EDITOR,

Osteosarcomas are the most common primary bone tumors.[1] Approximately 20% of patients with osteosarcoma present metastatic disease at the time of diagnosis, with the lung being the main organ affected.[2] The early diagnosis of pulmonary metastasis may be critical for planning effective therapy.[3] For this reason, chest CT screening should be considered. Usually, pulmonary metastases appear as multiple rounded nodules of various sizes, predominating in the lower portions of the lungs and sparing the apices.[4] However, they may have an atypical presentation. Herein, we describe an unusual case in which multiple atypical lung metastases were detected during treatment in a young male with femoral osteosarcoma.

A 16-year-old male was admitted to an oncology referral service due to the presence of a tumor in the right distal femur. Right thigh radiography revealed a bone lesion with aggressive proximal periosteal reactions (forming a Codman triangle) and a large soft-tissue mass containing foci of ossification (Figure 1A). A biopsy was obtained, and the pathological diagnosis was osteosarcoma.

Staging chest CT revealed multiple peripherally located rounded nodules in both lungs, some with ground-glass opacities and one with subpleural excavation, suggestive of metastasis. Before neoadjuvant chemotherapy, the patient presented chest pain and dyspnea. Bilateral pneumothorax was evidenced on a chest radiograph and attributed to nodule cavitation. Thoracostomy with pleural drainage and right pleurodesis was performed. Neoadjuvant chemotherapy was administered after stabilization of the patient's clinical condition. However, he evolved with progressive pneumothorax, seen on daily X-rays, despite conservative treatment.

The cavitation of most of the pre-existing nodules and persistence of bilateral pneumothorax were observed on chest CT (Figure 1B). Surgical treatment was chosen, and left metastasectomy and pleurectomy were performed. Pathological analysis confirmed the metastatic nature of the nodules (Figure 1C).

After 3 months of neoadjuvant chemotherapy, the primary disease progressed. Surgical planning was postponed, and another chemotherapy regimen was initiated. During second-line chemotherapy, chest CT showed an alteration of the lung lesion pattern; nodular opacities with ground-glass halos, suggesting hemorrhagic metastasis, were observed (Figure 1D).

The patient's right lower limb was amputated, and an adjuvant chemotherapy cycle was restarted. Chest CT performed 2 months later showed increases in the number and size of the hemorrhagic metastatic nodules, with no lesion pattern modification. Therefore, palliative chemotherapy was initiated.

At the last follow-up, 13 months after the first examination, chest CT confirmed substantial disease progression, with multiple masses showing soft-tissue density and foci of calcification, measuring up to 7.0 cm, and moderate pleural effusion (Figure 1E). The patient died 7 days after this chest CT examination.

Osteosarcoma is a high-grade malignancy that occurs predominantly in the long-bone metaphyses of children and young adults, with a peak incidence in the second decade of life.[1] Microscopy shows the proliferation of spindle and epithelioid cells with marked nuclear pleomorphism, with features such as the presence of mitotic figures and osteoid matrix formation. In addition, non-neoplastic giant cells are seen in around 25% of cases.

Initial metastases of osteosarcoma are characteristically hematogenous. Microscopic metastases are present in almost all patients at the time of diagnosis, and lung metastases are clinically detectable in approximately 15–20% of patients.[2]

Surgical treatment may lead to the increased survival of patients diagnosed with osteosarcoma. In addition, survival rates increase significantly after chemotherapy. However, despite the development of new protocols and more effective treatments, some cases still show disease recurrence, most commonly in the lungs.[2]

Pulmonary metastases are characterized by multiple well-defined nodules in the lung parenchyma. However, unusual radiological features of these lesions are frequently encountered in patients with osteosarcoma. Examples of atypical findings include cavitation, calcification, atypical location in the lung, micronodular forms, hemorrhagic metastases, and tumor thrombi.[4,5]

The frequency of cavitation is much lower for metastatic nodules than for primary tumors. Cavitating lung metastases are associated most commonly with squamous cell carcinoma. Lung metastases of sarcoma can also cavitate, presumably due to chemotherapy-induced tumor necrosis or even neoplastic lesion behavior. Cavitation may also occur via a check-valve mechanism prompted by tumor infiltration of bronchial structures.[3,4]

Pneumothorax is a frequent complication in these cases and is usually the result of bronchopleural fistula

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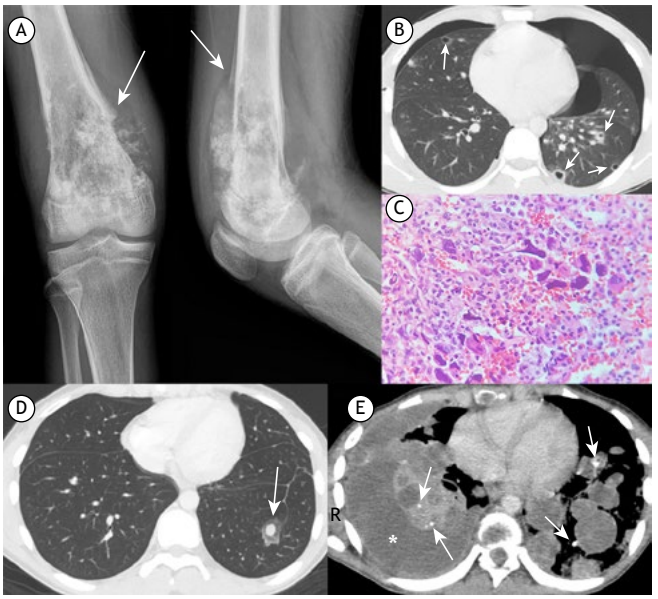

Figure 1. Frontal and lateral radiographs (A) of the right distal femur (taken in February 2019) showing a juxtacortical mass with a Codman triangle, periosteal reaction (white arrows), and calcification foci. The femoral metaphysis is involved and the tumor extends into the diaphysis. Chest CT image (B) obtained during neoadjuvant chemotherapy (in April 2019). Axial view showing multiple cavitated nodules, some of which are peripheral (white arrows). Bilateral pneumothorax can also be observed. Histological features (C) of a pulmonary nodule: a neoplasm composed of spindle cells and atypical epithelioid cells with an osteoid matrix surrounded by giant cells, similar to osteoclasts. Hematoxylin and eosin staining, original magnification ×40. Axial chest CT image (D) obtained during second-line chemotherapy (in October 2019) showing a nodular opacity in the left lower lobe with a ground-glass halo (white arrow), suggesting hemorrhagic metastases. Axial chest CT image (E) obtained with the mediastinal window during third-line chemotherapy (in March 2020) showing multiple bilateral masses with soft-tissue density. Note also the calcification foci (white arrows) and pleural effusion (asterisk).

formation due to tumor necrosis. For this reason, it is important to search for hidden lung metastases in patients diagnosed with osteosarcoma presenting with spontaneous pneumothorax.[5]

Hemorrhagic pulmonary metastases are lesions in which vessels have ruptured due to neovascular tissue fragility. They usually present as nodular opacities with ground-glass halos (the halo sign) or diffuse ill-defined margins. The halo sign is not specific, but the suspicion of hemorrhagic metastasis should be considered when it is present in patients with associated malignancies. Angiosarcoma and choriocarcinoma are the most representative causes of hemorrhagic pulmonary metastasis.[3,4]

Calcifications in primary nodules suggest a benign nature, generally corresponding to granulomas or hamartomas. Nevertheless, calcification or ossification may occur in metastatic nodules. Sarcomas and carcinomas, namely osteosarcomas, synoviosarcomas, chondrosarcomas, and mucinous and papillary adenocarcinomas, can produce calcified metastases. Lymph node involvement can also be seen with calcified metastases.[3,4]

Most cases of pulmonary metastasis present typical imaging features. Nonetheless, radiologists' knowledge of atypical presentations is essential for the differentiation of metastatic disease from synchronic primary lung cancer and benign lung conditions.

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