

Metastatic Osteosarcoma: A Case Report of Secondary Pneumothorax and Intravascular Tumor Emboli

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Abstract: Osteosarcoma is a primary bone malignancy that disproportionately affects young patients and often metastasizes to the lungs. We report a case of osteosarcoma with metastatic disease in the lungs of a patient who presented with a spontaneous pneumothorax. We briefly discuss the mechanisms of secondary spontaneous pneumothorax, the mechanisms of pulmonary tumor emboli, and the diagnosis of calcified lung nodules in patients with osteosarcoma.

Keywords: *metastatic osteosarcoma, secondary pneumothorax, intravascular tumor emboli, malignant calcified pulmonary nodules*

Introduction

Osteosarcoma is the most common type of primary bone malignancy.¹ The median age at diagnosis is 15 years.¹ It has a high rate of metastatic spread, with 15%-20% of patients with osteosarcoma presenting with metastatic disease.^{1,2} Of these patients, approximately three-quarters have distant disease that is limited to the lung.¹ On average, patients who develop metastatic disease in the lungs do so in young adulthood.² In a study by Alubran et al² of 247 patients with osteosarcoma, a subset of whom had metastatic disease, the median age at onset of either synchronous or metachronous lung disease was 29 years; over 80% of patients in that subset were 18 years old or older at the time of first lung metastasis. Their cohort had a five-year survival rate of 66%, with no significant difference between patients younger than 40 years of age and those older than 40 years of age. Patients with metastatic disease in the lungs had a survival rate of 30% at three years after the diagnosis of lung involvement².

Key Points

- Pneumothorax is a rare but well-known complication of sarcoma metastases. Mechanisms of secondary spontaneous pneumothorax include tissue necrosis, direct metastasis to a bulla, and intrabronchial tumor obstruction.
- Pulmonary intravascular tumor emboli are rarely captured on imaging; growing intravascular calcifications in a patient with metastatic osteosarcoma may make these presumed tumor emboli more conspicuous on imaging.
- Calcified lung nodules are often benign, but they should be considered as potential metastases in patients with osteosarcoma.

This case presented here illustrates rare but known complications of metastatic osteosarcoma. Our report highlights the fact that calcified pulmonary nodules are not always benign and discusses the incidence and mechanisms of secondary spontaneous pneumothorax and pulmonary tumor emboli. This case report was prepared following the CARE Guidelines.³

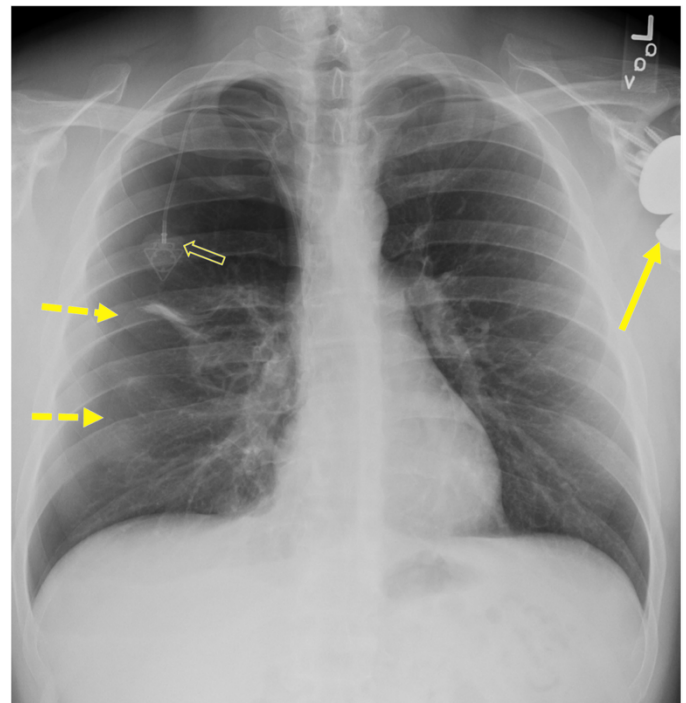
Case Presentation

A 26-year-old man was diagnosed in 2015 with osteosarcoma of the left proximal humerus and was treated with neoadjuvant chemotherapy (cisplatin, doxorubicin, and high-dose methotrexate), resection of the primary tumor, and subsequent adjuvant chemotherapy with the MAPIE regimen (doxorubicin, cisplatin, methotrexate, ifosfamide, etoposide). There were no metastases at the time of initial diagnosis. Thirteen months following the initial diagnosis, he developed a locally recurrent tumor in the left arm as well as 6 small pulmonary nodules. A fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) scan obtained at this time demonstrated intense FDG uptake in the lung nodules, which were therefore presumed to be metastatic, as well as additional small, intensely FDG-avid bone metastases in the sacrum and right iliac bone. The patient then began treatment with pazopanib and received radiation to the largest metastasis in the subpleural right lower lobe.

Sixteen months after his initial diagnosis, and 3 months after the identification of the nodules in his lung and the tumor in his arm, he presented to his oncologist for a regular follow up appointment with a dry cough and right chest pain with deep inspiration. A chest radiograph obtained at this time revealed a right pneumothorax (Figure 1). The pneumothorax was stable on serial imaging, but the patient elected to undergo a right video-assisted thoracoscopic surgery, pleurodesis, and wedge resection of multiple right lung metastases to reduce the chance of future pneumothorax. On pathologic examination, the irradiated dominant nodule was consistent with metastatic osteosarcoma and had a small area of internal necrosis.

The patient's subsequent oncologic course was complicated, with new and increased pulmonary metastases, additional pneumothoraces, and the development of additional osseous metastases. A CT of the chest performed 9 months after the initial wedge resections of the lung metastases (Figures 2A and 2B) showed a recurrent right lung metastasis with speckled calcifications at a prior resection site, new partially calcified nodules, and branching pulmonary arterial calcifications that

Figure 1. Chest Radiograph of 28-Year-Old Man with Osteosarcoma and Secondary Pneumothorax.



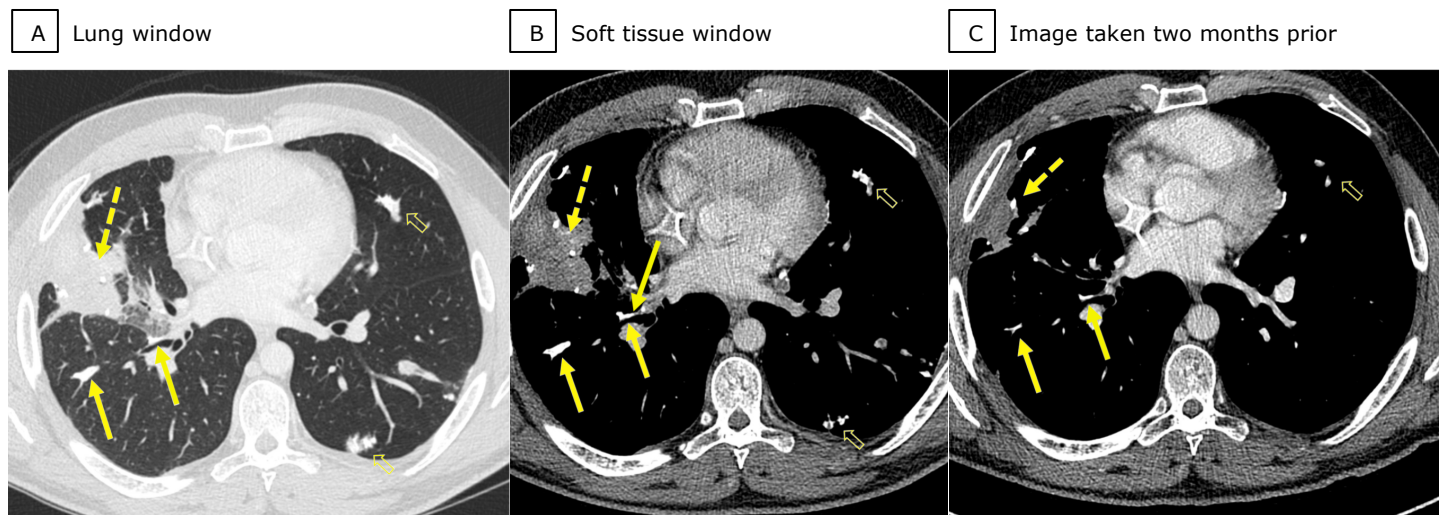
Chest radiograph shows a right pneumothorax (dashed arrows, visceral pleural edge) and left shoulder prosthesis (solid arrow) from the primary tumor resection and a port (open arrow).

were suspected to be tumor emboli. Comparison with a CT performed two months prior (Figure 2C) confirmed the growth of the suspected calcified intravascular tumor.

Discussion

Unlike many other solid tumor pulmonary metastases, osteosarcoma metastatic nodules may show calcifications.⁴ Although calcified pulmonary nodules are often considered benign, the differential diagnosis remains broad and includes both benign and malignant processes, such as calcified granuloma, hamartoma, carcinoid, bronchogenic carcinoma, and importantly metastases from sarcomas such as osteosarcoma.⁵ Patterns of calcification on imaging can help to distinguish benign and malignant nodules. Benign pulmonary nodules classically show dense central, laminated, or diffuse calcifications, whereas punctate or eccentric calcifications may indicate malignancy.

Figure 2. Contrast-Enhanced Axial Computed Tomography of the Chest of a 28-Year-Old Man with Osteosarcoma Metastases of the Right Lung with Growing Intravascular Calcifications and Calcified Pulmonary Nodules.



(A, B) Imaging was performed nine months after initial wedge resections and illustrates a recurrent right lung metastasis at a resection site (A, B dashed arrows), with speckled calcifications, branching pulmonary arterial calcifications (A, B solid arrows), and partially calcified nodules (A, B open arrows).

(C) Imaging acquired two months prior to images A and B demonstrates smaller branching calcifications (C, solid arrows), confirming the growth of the presumed calcified intravascular tumor emboli during the two-month period since the first imaging. A mass (C, dashed arrows) and pulmonary arterial calcifications (C, open arrow) are also partially visible.

When possible, follow-up imaging may best distinguish benign and malignant nodules; one of the most reliable imaging features of a benign lesion is a lack of interval growth on imaging for 2 years.^{5,6} As with any clinical assessment, the patient's age and clinical history are essential in the differential diagnosis of calcified lung nodules. As reported in our case, the patient's young age, his known progressive metastatic osteosarcoma with ongoing growth of a right lung metastasis (Figure 2B, 2C), and the interval growth of branching eccentric calcifications in his lung (Figure 2B, 2C) strongly suggest that these calcified nodules are metastases.

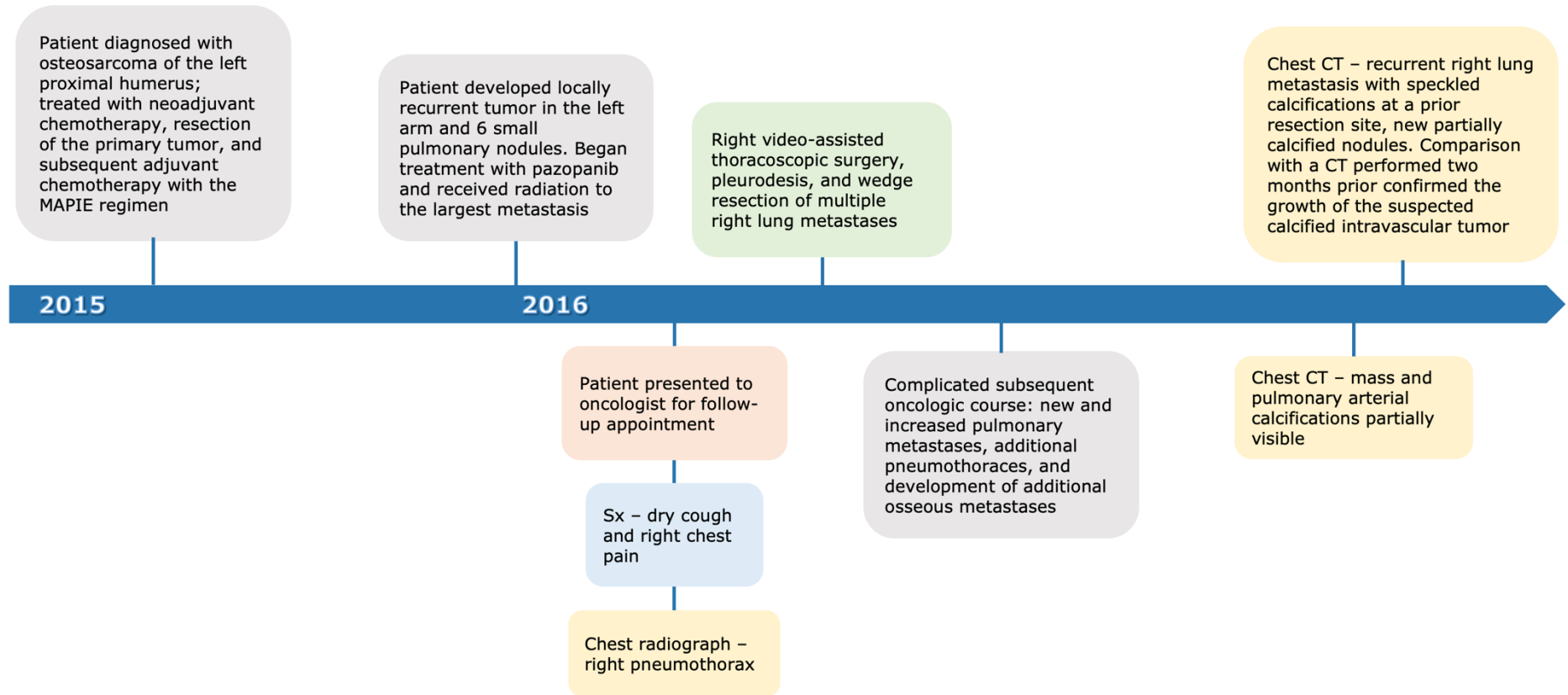
Pneumothorax is a rare but well-known complication of sarcoma metastases. In a review⁷ of 153 reported cases of metastatic sarcoma, approximately one-third of which were osteosarcoma, the incidence of pneumothorax was 1.9%. The mechanisms of spontaneous pneumothorax secondary to osteosarcoma include: tissue necrosis due to systemic or radiation therapy, direct metastasis to a bulla, or intrabronchial tumor obstruction resulting in a check-valve mechanism secondary to intermittent bronchiolar obstruction by tumor tissues.⁷ The

pneumothorax observed in this patient was suspected to be the result of necrosis of the peripheral metastasis, demonstrated at the time of resection. That necrosis was likely caused by treatment with pazopanib, a multitarget tyrosine kinase inhibitor with activity against vascular endothelial growth factor receptors and platelet-derived growth factor receptors⁸, but was possibly also exacerbated by the recent radiation.

Pulmonary tumor emboli occur when solid tumors seed pulmonary vasculature with individual cells, clusters of cells, or large tumor fragments. Emboli may cause vascular obstruction that ranges in severity from asymptomatic or subacute microvascular tumor emboli to large tumor masses that mimic massive pulmonary thromboembolism.⁹ Pulmonary intravascular tumor emboli are rarely captured on imaging.

Although autopsy series estimate that the incidence of pulmonary tumor embolism ranges from 3% to 26% in patients with solid tumors, retrospective autopsy reviews suggest that only 8% of patients with tumor emboli have documented disease prior to death.⁹ The majority of reported cases occur in association with breast, lung, or gastric carcinoma, which may reflect the

Case report timeline



Color-shading:

- patient visits
- signs & symptoms
- laboratory & imaging tests
- treatment
- medical history

Abbreviations: CT, computed tomography; Sx, symptoms

prevalence of those tumors.⁹ In our patient with metastatic osteosarcoma, growing intravascular calcifications made these presumed tumor emboli more conspicuous on imaging.

Conclusion

This case of metastatic osteosarcoma illustrates secondary spontaneous pneumothorax, a rare but well-known complication of sarcoma metastases, as well as calcified pulmonary intravascular tumor emboli, a sequela that is not often captured on imaging. We have briefly discussed the incidence and pathogenesis of secondary spontaneous pneumothorax and intravascular tumor emboli and have demonstrated that calcified lung nodules in patients with osteosarcoma are not necessarily benign.

Author Contributions

Conceptualization, J.A. and K.R.; Acquisition, analysis, and interpretation of data, A.G, J.A. and K.R.; Writing – original draft preparation, review and revisions, A.G., J.A., and K.R.; Supervision, J.A. and K.R. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Disclosures

None to report.

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