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Recurrent Spontaneous Pneumothoraxes as A Complication of Osteosarcoma Metastases: A Case Report

Nandish A L. Dr.Pentakota Lakshmi Bharat, Dr Asif Ibrahim Tamboli
Sr. Resident, Sr.resident, Associate professor

Department of Radiodaignosis Krishna institute of medical sciences, KVV, Karad (MS)
annandish2@gmail.com

ABSTRACT
The most prevalent primary malignant bone tumour in children and adolescents is osteosarcoma. Osteosarcomas are extremely aggressive tumours with a poor prognosis historically. However, with the addition of adjuvant and neoadjuvant chemotherapy, the survival rate has significantly increased. This case report describes a 18-year-old boy who had a left fibula osteosarcoma whose progress was worsened by recurring pneumothoraces associated with the tumour. Recurrent pneumothoraces are a relatively uncommon complication of osteosarcoma, but they provide a significant obstacle to patient care that improves outcomes and quality of life.

Introduction
The most frequent primary malignant bone tumour in children and adolescents is osteosarcoma, which affects 85% of all cases in high-grade intramedullary osteosarcoma, also known as conventional osteosarcoma. Long bones' metaphyses are where osteosarcomas often develop and spread, longitudinally, within the medullary cavity. They are extremely aggressive tumours with a poor prognosis historically; despite surgical intervention, 80% of patients die within 2 years. Traditional osteosarcomas still have a high risk of metastatic dissemination, notably through hematogenous metastasis to the lungs, despite treatment. Metastases to the lungs can mineralize and often occur in the periphery.

Case report
A 18-year-old boy in good health saw his primary care doctor to have his left knee ache, which had started after he attempted a layup during a basketball game. Physical testing revealed that his knee alignment was normal and that there was no palpable bulk, warmth, swelling, or redness. His motor function was still intact, and his neurovascular system remained unharmed. A radiograph revealed a expansile lytic lesion in the left proximal fibula that extended 5 cm distally along the shaft from the proximal growth plate (Fig. 1). An aggressive, marrow-replacing lesion that extended from the physeal to the distal fourth of the diaphysis was seen on a subsequent MRI and CT.
An aggressive, marrow-replacing lesion was found on a subsequent MRI that extended from the physeal to the distal fourth of the diaphysis. The proximal portion of the fibula metaphysis-diaphysis also showed signs of extraosseous dissemination, and a few enhancing soft tissue component. These results raised concerns about osteosarcoma with potential metastases. He underwent an open left fibula biopsy and histology revealed conventional high-grade osteosarcoma.
Before beginning the surgical resection, the patient underwent a course of doxorubicin-based neoadjuvant chemotherapy due to the degree of the involvement. A chest radiograph scan of the chest was negative at that time for metastases. He received a left above knee amputation following the end of chemotherapy. A 9 cm poorly differentiated osteosarcoma was seen on pathology.

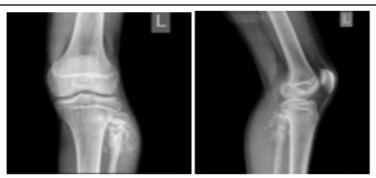

Fig. 1 – Knee radiograph showing a PERIOSTEAL RESPONSE IN OSTEOSARCOMA. A. AP Distal Femur. B. Lateral Distal Femur. The classic sunburst or spiculated periosteal response seen in the distal metadiaphyseal area of the femur (*arrows*). This sunburst appearance, the soft tissue mass, and the destructive lesion of the medullary portion of the fibula

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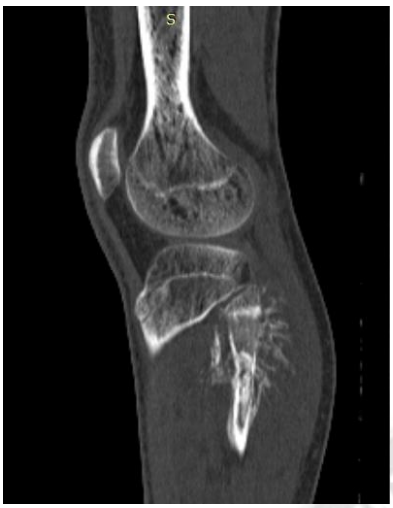
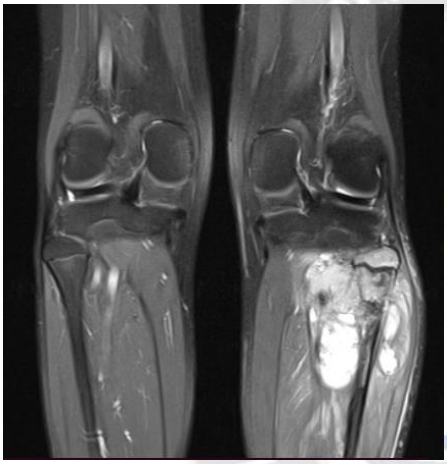
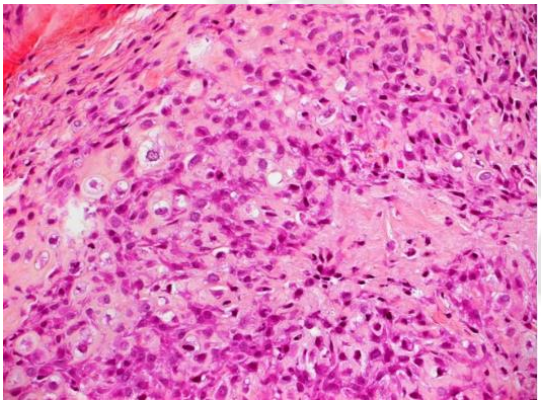


CT left knee showing ill-defined, destructive lesion assuming the mixed pattern of presentation in the metaphysis and proximal diaphysis of the fibula. Malignant spiculated periosteal response is observed on both sides of the fibular cortex.



Fat-saturated post contrast T1 weighted MRI image showing an enhancing mass with soft tissue component around the proximal fibula



Histologic image of bone biopsy. Hematoxylin and eosin (H&E)–stained sections show a hypercellular high-grade sarcoma with admixture of epithelioid, ovoid and plasmacytoid neoplastic cells, increased mitotic activity with atypical mitoses, and scattered clusters of multinucleated, non-neoplastic osteoclast-like giant cells.

The patient continued receiving doxorubicin-based adjuvant chemotherapy after having his tumour surgically removed. He visited the emergency room two years after his diagnosis with breathlessness, fever and chills. On assessment, his temperature was 99.8 degrees Fahrenheit, his tachycardia was in the 130s, his tachypnea was in the 30s, and his oxygen saturation on room air was in the low 90s. An imaging test of the chest revealed a significant pulmonary metastases and bilateral pneumothorax. There was concern that his pneumothorax, which had a history of osteosarcoma, might rupture.

He had a history of osteosarcoma, raising the possibility that metastases were the cause of his pneumothorax. A CECT Thorax revealed heterogeneously enhancing soft tissue density nodules on the both sides suggestive of metastatic disease. Pathological analysis revealed metastatic osteosarcoma in both the lobes.

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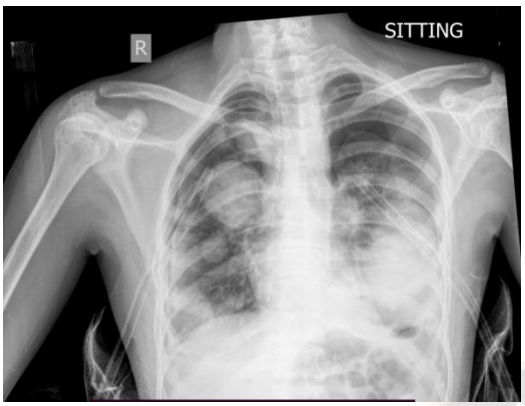
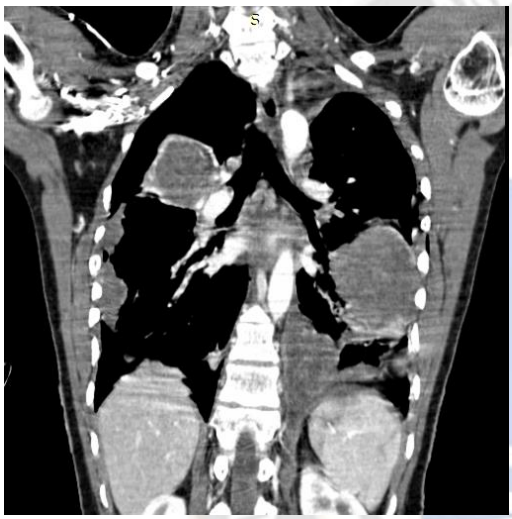


Chest radiograph showing a moderate bilateral pneumothorax with ICD tube insitu and bilateral lung metastasis; examination performed 2 years after initial diagnosis



CECT Thorax showing heterogeneously enhancing soft tissue density lesions noted in both lungs and subpleural nodules

He had multiple episodes of bilateral pneumothorax after that, everytime he was treated by ICD placement. Even while these treatments gave him temporary comfort, his illness kept becoming worse. He enrolled in hospital care, and 28 months after his initial diagnosis, he passed away.

Discussion

Osteosarcoma is distinguished by the development of osteoid by cancerous cells. It is the most prevalent primary non-hematologic cancer of the bone. Osteosarcoma can develop at any age, but it usually progresses in a bimodal pattern, with primary high-grade osteosarcoma typically appearing in the second decade of life, parosteal osteosarcomas peaking in the third and fourth decades of life, and other secondary osteosarcomas developing in older adults (>60), frequently in the context of Paget's disease or prior radiation therapy. The distal femur, the proximal tibia, and the proximal humerus are among the bones where primary osteosarcomas most frequently develop.

Osteosarcoma manifests itself in a very distinctive way. Most patients have localised discomfort when they first visit the doctor, and there is often a 8 to 9-week physician wait between the patient visit and the right diagnosis. Failure to collect radiographs on the initial visit was the primary cause of physician delay. Although conventional and secondary osteosarcomas cannot be distinguished histologically, these subtypes are diagnosed based on how they appear on radiographs. Conventional osteosarcoma frequently appears as a metaphyseal lesion on radiography. Radiographic appearances might range from completely lytic to completely sclerotic.

The medullary component most frequently has lytic osteoid or chondroid matrix. While chondroid matrix is frequently described as having a rings and arcs pattern, osteoid matrix is typically described as being "cloud-like" or "fluffy" . As a result of an active underlying process, tumour margins are frequently ill-defined and may appear lytic permeative or "moth- eaten" . The development of an eccentric extra-osseous soft tissue mass with typical osseous amorphous matrix mineralization is frequently caused by the frequent cortical disintegration. The periosteal new bone production, which is frequently complex-perpendicular, spiculated or "sunburst," or lamellated/onion skin, or reactive with Codman angles near the edge of the tumour, increases the density of the extra-osseous mass.

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Although an MRI is not necessary for the diagnosis of osteosarcoma, it is necessary for surgical staging because it can show the extent of the tumor's involvement in bone, soft tissues, joints, and neurovascular structures. In addition, intraosseous skip metastases, a known consequence of conventional osteosarcoma, are frequently assessed for using MRI. These skip lesions' presence emphasises the significance of covering the complete length of the affected bone and surrounding joints. The hematogenous spread of osteosarcoma is accompanied by the development of pulmonary metastases. Therefore, the most crucial prognostic factor for osteosarcoma is the presence of metastatic disease at the time of presentation.

Less than 20% of individuals with metastatic disease have long-term survival, which is a terrible prognosis. Less than 5% of patients with non-pulmonary metastases have a favourable prognosis, which is considerably worse. Larger tumour size, high lesion grade, a poor response to treatment (90% necrosis), and a more close-by lesion placement are further indicators of a bad prognosis. Historically, immediate broad or radical amputation was used to treat individuals with high-grade osteosarcoma. 80% of patients with an isolated illness died from distant metastases despite receiving this treatment. This statistic leads to the hypothesis that the majority of patients with high-grade osteosarcoma have non-detectable micrometastases at presentation, despite the absence of imaging abnormalities.

These micrometastases are the target of adjuvant and neoadjuvant chemotherapy. The current course of treatment for high-grade osteosarcoma includes neoadjuvant chemotherapy, surgical removal of the tumour, and adjuvant chemotherapy. Pulmonary metastases are removed if possible after adjuvant chemotherapy. A spontaneous pneumothorax is a common yet well-known symptom of metastatic lung cancer. Typically, the incidence of spontaneous pneumothorax resulting from malignancy is low, making up less than 1.5% of all spontaneous pneumothorax.

However, the incidence of spontaneous pneumothoraces caused by cancer varies depending on the type of malignancy. Pneumothoraces in particular seem to be more frequent in patients with sarcomas, particularly osteosarcomas. Approximately 11% of osteosarcoma patients in one study experienced a spontaneous pneumothorax. Numerous mechanisms have been put forth, but the precise mechanism underlying spontaneous pneumothorax in metastatic osteosarcoma remains unknown. The most frequent theory about the cause of spontaneous pneumothoraces in sarcomas and germ cell tumours is that chemotherapy-induced necrosis and haemorrhage of pulmonary metastases is to blame.

In particular, it is hypothesised that some peripheral, subpleural nodules are highly chemosensitive, resulting in fast lysis and necrosis after chemotherapy. When these nodules eventually break, air leaks into the pleural space and causes a pneumothorax. The use of chemotherapeutic drugs that cause nausea and vomiting is a different method that has been suggested. It is thought that increased intrathoracic pressure caused by emesis, along with the necrosis of subpleural nodules brought on by chemotherapy, causes the nodules to burst, resulting in a pneumothorax. Last but not least, some writers have suggested that some chemotherapy drugs (such Adriamycin and Doxorubicin) can directly extend metastatic lesions into the pleura or can hinder repair processes and responsible for spontaneous bilateral pneumothorax.

As previously stated, it is currently unknown what causes spontaneous pneumothorax in patients with pulmonary metastatic osteosarcoma. Also worth noting is that the previously suggested mechanisms are supported by observational data, case studies, and review articles. In fact, only 28 cases of spontaneous pneumothorax as a side effect of chemotherapy had previously been documented, according to a case study by Bini et al. from 2000.

Conclusion

This case examines pneumothorax as a consequence of osteosarcoma. Treatment options include chemotherapy, pleurodesis, wedge resections, and chest tube insertion. Despite the fact that pneumothorax recurrence is frequent in patients with osteosarcoma, it is unknown how to best treat this patient population. In the future, it will be critical to pinpoint the therapeutic approaches that give patients with recurrent sarcoma-related pneumotho- races the best results and quality of life.