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CASE REPORT Open Access

Spontaneous pneumothorax in metastatic osteosarcoma: a case series

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Abstract

Background: Malignancy-associated secondary spontaneous pneumothorax (MSSP) has an incidence of 1% with a risk for recurrence of 9.4% reported in association with sarcomas, histiocytoma, malignant thymoma, and cancers of the breast and thyroid.

Case presentation: We report a series of four patients who presented to us with MSSP associated with pulmonary metastasis of osteosarcoma, all four being young males with metastasis to the lungs. All four patients were non-smokers and had no family history of malignancy. Less than 2% of all spontaneous pneumothoraxes present with bilateral pneumothorax, and our series reports the same in three patients. The occurrence of pneumothorax in two of the patients was in the week following chemotherapy. As there was evidence of pulmonary metastasis in these patients along with the clinical presentation of pneumothorax following chemotherapy, tumor necrosis was considered the likely etiology of spontaneous pneumothorax in these patients. All four patients required intercostal chest drain insertion, and the ICD tubes had to be retained for a prolonged duration due to either persistent air leak or secondary infection. ICD tube insertion further compromised the poor mobility of patients with lower limb lesions due to increased pain and was detrimental to the emotional morale of the patient and caregivers. The 2-year survival in such patients with pneumothorax is less than 10%.

Conclusions: Our series highlights the need for respiratory evaluation and follow-up both clinically and radiologically in cases of osteosarcoma, especially in the immediate post-chemotherapy period.

Keywords: Intercostal chest drain, Osteosarcoma, Pulmonary metastasis, Secondary spontaneous pneumothorax, Malignancy-associated secondary spontaneous pneumothorax

Background

Malignancy-associated secondary spontaneous pneumothorax (MSSP) is diagnosed when patients present with pneumothorax in the presence of underlying metastatic lung disease, and it is not causally related to trauma or invasive procedures. MSSP has been reported in association with sarcomas, histiocytoma, malignant thymoma, and cancers of the breast and thyroid. Spontaneous bilateral pneumothorax is a rare clinical entity with a prevalence of 1.3% of all spontaneous pneumothoraces [1]. We report a series of four patients who presented to us with MSSP associated with osteosarcoma including three patients with bilateral spontaneous pneumothorax.

Case 1

A 20-year-old gentleman, diagnosed with osteosarcoma 18 months ago, with no distant metastasis at the time of diagnosis, received two cycleds of neoadjuvant chemotherapy with cisplatin and adriamycin and was lost to follow-up. A year later, he underwent excision of the tumor in the left distal femur. And 2 months later, CT (Fig. 1)

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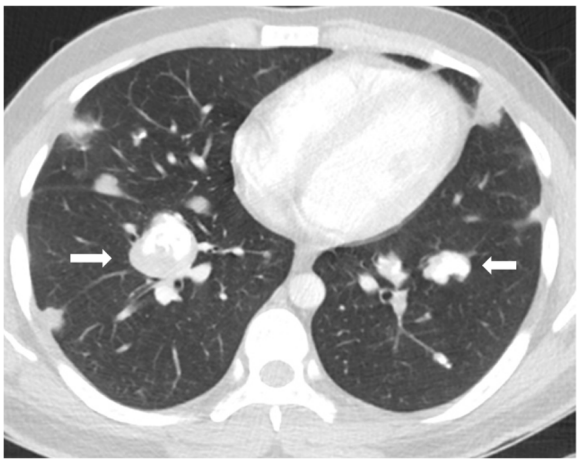

Fig. 1 Bilateral metastatic pulmonary deposits

showed multiple metastatic lung nodules and he was given palliative chemotherapy.

Eight days post-chemotherapy, he presented with right-sided chest pain, breathing difficulty of mMRC grade 4, and cough for 2 days. At presentation, he was tachycardic, hypotensive, and tachypnoeic with hyperresonance on percussion over the right hemithorax and decreased air entry. Chest X-ray (Fig. 2) confirmed right-sided pneumothorax, and a 24-French ICD was inserted. Follow-up chest X-rays showed lung expansion and resolution of pneumothorax. Subsequently, Talc pleurodesis was done and ICD was removed after 48 h.

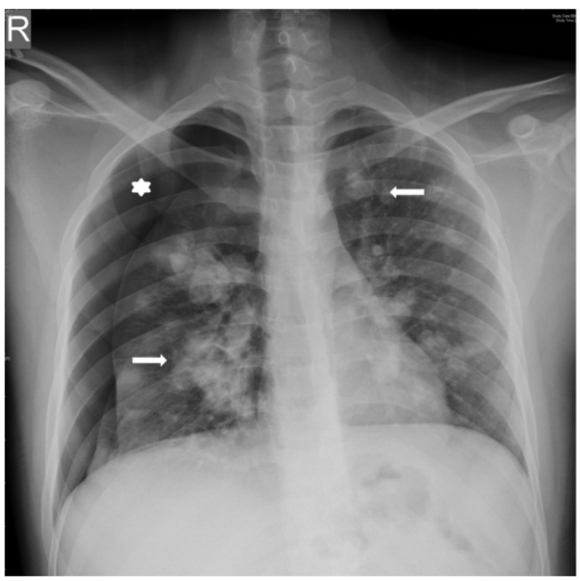

Fig. 2 Right pneumothorax, bilateral metastatic pulmonary nodules

He developed a secondary spontaneous pneumothorax on the left side after a week of the second cycle of palliative chemotherapy for which tube thoracostomy was done (Fig. 3). He developed febrile neutropenia during the admission, and pleurodesis was deferred due to active infection. He was discharged at request with the intercostal tube in situ and was referred to a palliative care centre in his hometown.

Case 2

A 16-year-old boy, diagnosed with high-grade osteosarcoma 2 months ago, presented with dyspnoea for 7 days and bilateral chest pain for 3 days. On examination, he was tachycardic and tachypnoeic and had normal blood pressure. His trachea was central with absent breath sounds bilaterally. Chest X-ray showed bilateral hydropneumothorax with rounded lesions suggestive of pulmonary metastasis (Fig. 4).

Emergency bilateral tube thoracostomy was performed, following which he improved clinically. Follow-up CT thorax showed partially expanded lungs (Fig. 5).

During his hospital admission, he developed persistent fevers and was initiated on antibiotic therapy. Pus swab taken from the site of debridement of the proximal tibial lesion grew *Pseudomonas stutzeri*, which was sensitive to Levofloxacin. F-18 whole body PET scan demonstrated bilateral lung parenchymal metastasis with the primary lesion in the tibia. Chemotherapy and radiotherapy were deferred due to the presence of active infection. An option of above knee amputation to prevent the local spread of tumour was considered, but his family was not keen to proceed with further treatment and was

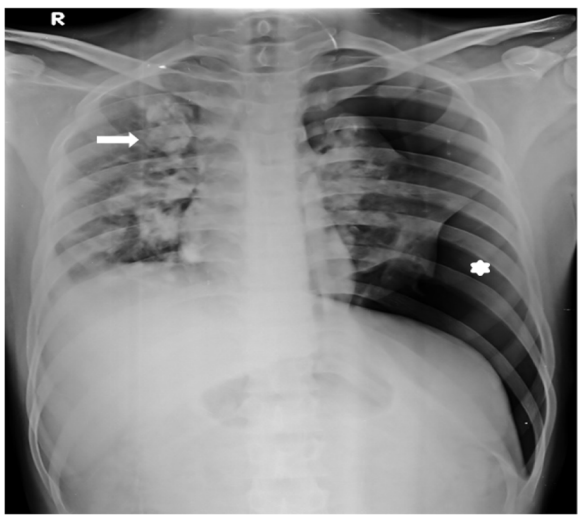

Fig. 3 Left pneumothorax with metastatic pulmonary nodules

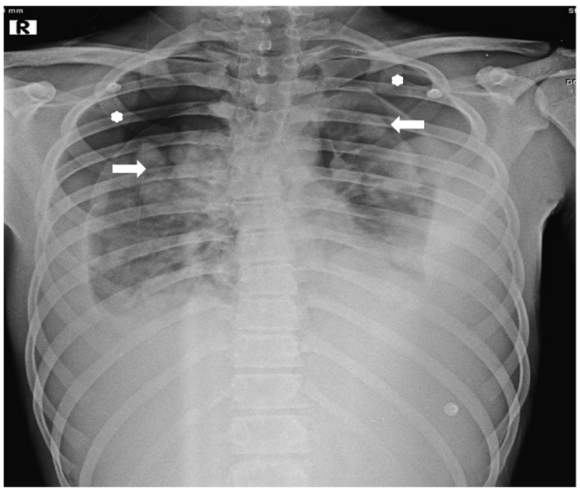

Fig. 4 Bilateral hydropneumothorax with multiple pulmonary metastatic nodules

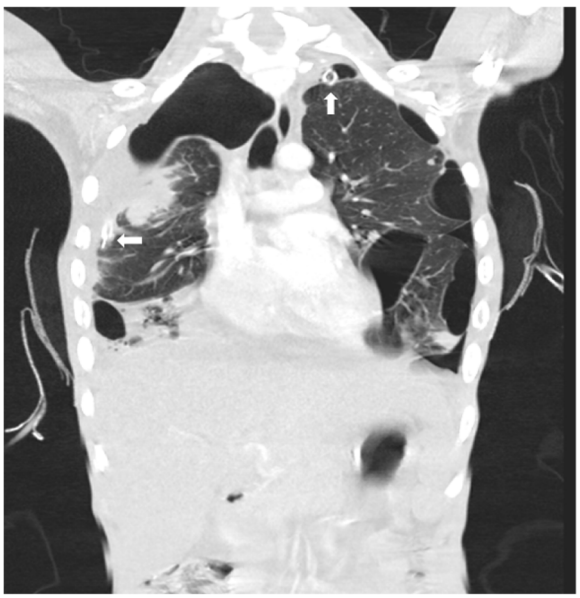

Fig. 5 Bilateral hydropneumothorax with multiple pulmonary metastatic nodules after bilateral ICD insertion

discharged at request with ICD in situ to continue treatment at a local center.

Case 3

An 18-year-old boy presented with progressive swelling over the right knee and difficulty in walking and weight bearing for 6 months. MRI of his right knee joint showed a well-defined multilobulated expansile mass lesion involving the mid and distal femur measuring 18.1×11.5×11.2cm in size. It was heterogeneously hyperintense on T2 with marrow involvement, involvement of growth plate in femoral epiphysis, and extension into upper tibia with skip lesions seen up to the mid tibial shaft. Lymph nodes in the popliteal fossa were found to be enlarged. These features represented the diagnosis of osteosarcoma.

At presentation, he had no respiratory complaints and his vitals were stable. The trachea was central, and breath sounds were decreased bilaterally. A chest X-ray was taken which showed incidental bilateral hydropneumothorax with multiple parenchymal nodules (Figs. 6) and an X-Ray of the Right Femur showed a mass lesion over the mid and distal Femur (Fig. 7).

Bilateral tube thoracostomy was done and follow-up X-rays showed partially expanded lungs. Both his ICD tubes had Cerfolio grade 1 air leak with purulent discharge. Pleural fluid culture grew *Staphylococcus aureus*. Pleurodesis was not performed due to active infection and was discharged at request to follow up at a local palliative centre on antibiotics.

Case 4

A 19-year-old boy, diagnosed with osteosarcoma with pulmonary metastasis 5 months ago, presented with right-sided chest pain and breathlessness for 3 days. He was treated with 7 cycles of chemotherapy with epirubicin and cisplatin, and the last cycle was received 6 days before presentation. On examination, he was tachycardic and tachypnoeic and had normal blood pressure. The trachea was central with hyperresonance on percussion and absent air entry over the

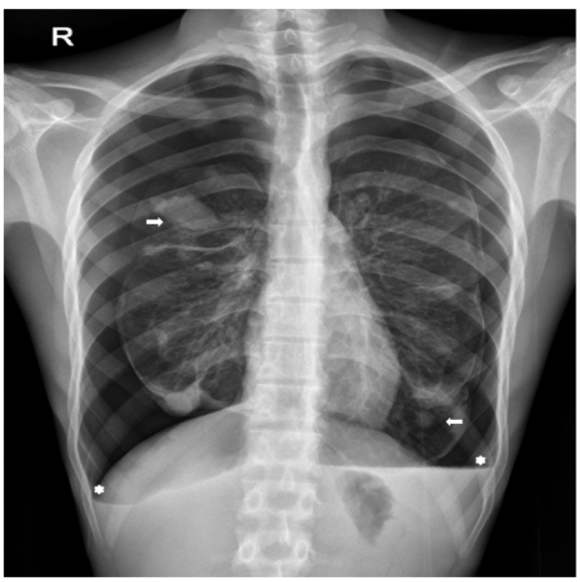

Fig. 6 Bilateral hydropneumothorax with pulmonary metastasis

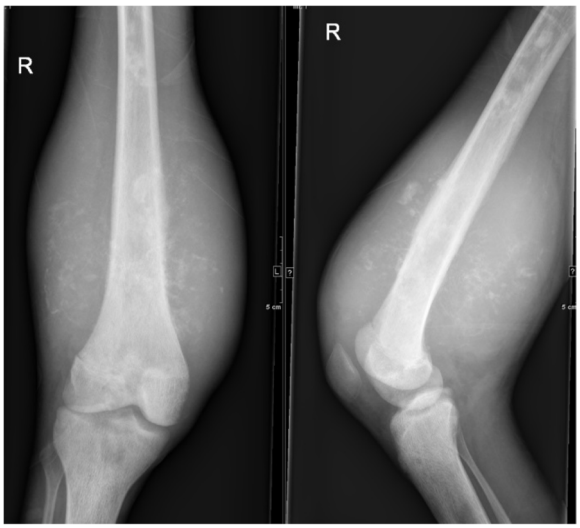

Fig. 7 Mass lesion over mid and distal femur

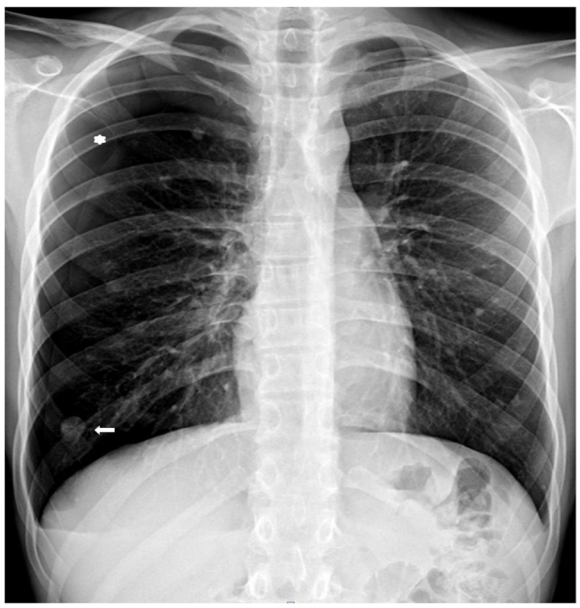

Fig. 8 Right pneumothorax with multiple pulmonary metastatic nodules

right hemithorax. Chest X-ray showed a right-sided pneumothorax (Fig. 8), and a 20-French ICD was inserted. Follow-up chest X-rays showed expanded lung but persisting Cerfolio grade 1 air leak. Hence, pleurodesis was deferred and he was discharged with an ICD tube in situ.

Discussion

Spontaneous pneumothorax usually originates from the rupture of apical bullae or subpleural blebs. However, in MSSP, the occurrence is associated with pulmonary metastasis, which contributes to 1% of all spontaneous pneumothoraces [2]. 2% of all patients with metastatic pulmonary deposits develop SSP. Eighty percent of patients with MSSP have metastatic sarcoma with osteosarcoma being the most common cause in 31.4% of these cases [3]. Osteosarcoma is the most common primary skeletal malignancy in young adults and the most common site for metastasis of this primary bone tumor is the lung [4]. Up to 50% of them develop lung metastasis. At the time of diagnosis, as high as 20% of the patients with osteosarcoma already have lung metastasis. The association of spontaneous pneumothorax in a patient with osteosarcoma is a known but rare complication occurring in less than 2% of cases with lung metastases [3]. There are reports of recurrent spontaneous pneumothorax in such cases even after remission, although the exact risk of recurrence is unknown [5, 6]. MSSP with recurrence of less than 10% has been reported in a cohort of patients with different malignancies and the median survival time was less than 8 months [7].

Of all spontaneous pneumothorax, only 1.3–1.9% of cases present with simultaneous bilateral spontaneous pneumothorax. MSSP has been reported in patients on radiation therapy, angiogenesis inhibitors, and pleural metastasis from breast carcinoma [8].

The proposed pathogenetic mechanisms in MSSP are as follows:

- Transpleural rupture of cystic lung metastasis [4]
- Rupture of necrotic lung nodules
- Pleural metastasis and
- Chemotherapy-induced tumor cavitation [9].

Alveolar wall rupture secondary to an airway obstruction caused by a tumor nodule impedes airflow by a ball valve mechanism and leads to the formation of subpleural blebs that can rupture. Metastatic nodules which are closely related to a pre-existing cavity can invade and/or erode the cavity wall and result in a pneumothorax. The formation of cystic lesions in the lungs predisposes to the development of a pneumothorax. There have been reports of chemotherapy-induced tumour necrosis increasing the risk of spontaneous pneumothorax in a patient with osteosarcoma by 7–14% [10]. Tumour emboli causing infarction and necrosis is

Table 1 Summary of cases

	Case 1	Case 2	Case 3	Case 4
Age (in years)	20	16	18	19
Smoking history	Non-smoker	Non-smoker	Non-smoker	Non-smoker
Family history of malignancy	Yes	Nil	Nil	Nil
Duration of symptoms of pneumothorax	2 days	7 days	Incidental finding	3 days
Location of the primary tumour	Left distal femur	Left proximal tibia	Right distal femur	Right proximal tibia
Time of first pneumothorax from diagnosis of osteosarcoma	18 months	4 months	6 months	5 months
Time of first pneumothorax from chemotherapy	8 days	Not applicable	Not applicable	6 days
Suspected pathology leading to first pneumothorax	Pulmonary metastasis Chemotherapy-induced necrosis of lung nodules	Pulmonary metastasis	Pulmonary metastasis	Pulmonary metastasis Chemotherapy-induced necrosis of lung nodules

another proposed mechanism for the development of this complication.

In this case series, we have presented four cases of MSSP with primary osteosarcoma with pulmonary metastasis. All of them were young, non-smoking, males who were symptomatic except one (Table 1). The most likely mechanism of pneumothorax in this series of patients seems to be trans-pleural rupture of the metastatic lesions. In two of the cases, it has been probably due to the necrosis of metastatic lung nodules secondary to chemotherapy. All four patients required ICD insertion with prolonged chest drainage due to the non-resolving nature of the air leak or due to superadded infection. None of these patients were suitable candidates for surgical intervention.

The survival rate of osteosarcoma patients with lung metastasis is dismal and influences therapeutic decisions. Five- and 10-year survival rates are around 29 and 26%, respectively [11]. The diagnosis of pneumothorax in these patients decreases 2-year survival to less than 10% [12]. So, the decision for aggressive surgical management is usually not accepted by most patients considering the postoperative complications. ICD insertion compromises the already poor mobility of patients with lower limb lesions, increases pain, and is detrimental to the emotional morale of the patient and caregivers.

Conclusion

- Osteosarcoma has a high predilection for pulmonary metastasis presenting with spontaneous pneumothorax, which can be unilateral, bilateral, and recurrent.
- This risk rises substantially with the initiation of chemotherapy and patients should be monitored for pneumothorax in the immediate post-chemotherapy period.
- A differential diagnosis of metastatic malignancy should be ruled out with history and imaging if a young patient presents with spontaneous pneumothorax.
- It would be prudent to keep patients with metastatic lung disease secondary to osteosarcoma under regular follow-up with chest X-ray.
- Patients with osteosarcoma should be evaluated with a CT scan, to rule out pulmonary metastasis and if present, the role of metastatectomy should be considered. In symptomatic patients, the use of lung ultrasound can be useful for establishing the diagnosis of pneumothorax.
- While managing these patients one should focus on pain alleviation, psychological support, effective ICD management, and informed decision-making to reduce morbidity.

Abbreviations

18F FDG: Fluorodeoxyglucose; CT: Computed tomography; ICD: Intercostal chest drain; mMRC: Modified medical research council; MRI: Magnetic resonance imaging; MSSP: Malignancy-associated secondary spontaneous pneumothorax; PET: Positron emission tomography; SSP: Secondary spontaneous pneumothorax.

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Authors' contributions

All authors were active participants in the drafting and revision of the case series. MV, TJ, AN, RG, and PJ were involved in the direct care of these patients. MV, AN, and TJ did the literature search and manuscript writing. PJ and RG were involved in the design, conceptualisation, manuscript review, and editing. AI was involved in the design, image selection, and image interpretation. The authors read and approved the final manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Written informed consent was obtained from the patients for publication of this case report and accompanying images.

Consent for publication
Signed consent was taken from all patients.

Competing interests
The authors declare that they have no competing interests.

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