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PRIMARY MEDIASTINAL OSTEOSARCOMA: A RARE AND AGGRESSIVE TUMOUR IN AN UNUSUAL LOCATION

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ABSTRACT

Introduction: Mediastinal osteosarcoma is an exceptionally rare and aggressive malignancy arising in a location devoid of osseous structures. Unlike conventional osteosarcoma, which originates in the metaphyseal regions of long bones in younger individuals, mediastinal osteosarcoma develops within soft tissue, leading to a poorly understood pathogenesis and unpredictable clinical behaviour. Owing to its nonspecific symptoms and imaging overlap with other mediastinal tumours, early diagnosis is challenging. To date, around ten well-documented cases have been reported.

Case description: A 41-year-old man presented with progressive dyspnoea of 3 months' duration. Laboratory tests were unremarkable except for elevated alkaline phosphatase. Computed tomography revealed a 10 × 8.8 cm calcified anterior mediastinal mass with multiple calcified pulmonary nodules and lymphadenopathy. Robotic bronchoscopy of a minimally calcified right middle lobe nodule revealed a high-grade sarcomatoid malignancy forming malignant osteoid. Tumour cells expressed SATB2 (Special AT-rich sequence-binding protein 2) and were negative for epithelial markers (Pancytokeratin, TTF-1, Napsin A, and P40). The findings favoured a diagnosis of extraskeletal osteosarcoma. Positron emission tomography/computed tomography scan demonstrated distant metastases to the brain and the absence of any primary bone lesions. The case was discussed in a multidisciplinary tumour board, and combined chemotherapy with Cisplatin and Doxorubicin was initiated, along with radiotherapy targeting the intracranial lesion, followed by Regorafenib, a kinase inhibitor.

Conclusion: Mediastinal osteosarcoma should be considered in the differential diagnosis of calcified mediastinal masses. Accurate diagnosis depends on adequate tissue sampling and immunohistochemical profiling. Continued reporting of such rare cases is essential to improve understanding of clinical behaviour and optimize therapeutic strategies for these tumours.

KEYWORDS

Extraskeletal osteosarcoma, mediastinal osteosarcoma

LEARNING POINTS

- Primary mediastinal osteosarcoma is a rare disease.
- Calcifications within a mediastinal tumour should raise suspicion of osteosarcoma.
- Due to the rarity of mediastinal osteosarcoma, there is no consensus on how to treat this tumour.

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INTRODUCTION

Mediastinal osteosarcoma (OS) is an exceptionally rare and aggressive form of malignant tumour occurring in the mediastinum. Unlike conventional OS that typically arises in the metaphyseal regions of long bones in adolescents and young adults, mediastinal OS arises in a location that lacks osseous structures, making its pathogenesis and clinical behaviour poorly understood[1]. Due to nonspecific symptoms, such tumours often elude early detection and therefore pose a significant diagnostic challenge. They can radiographically resemble other mediastinal masses, further complicating the diagnostic process. Given the paucity of cases reported in the literature, knowledge about its etiology, optimal treatment strategies, and long-term prognosis remains limited. Here, we present a rare case of mediastinal OS and review its clinical presentation, radiologic findings, histopathological features, treatment strategy, and prognosis.

CASE DESCRIPTION

A 41-year-old male with a past medical history of ulcerative colitis was referred to our institute for evaluation of a mediastinal mass. He had a 3-month history of persistent progressive dyspnoea on exertion. He denied fever, night sweats, cough, haemoptysis, or weight loss. He denied any occupational exposure to asbestos or radiation.

On physical examination, vital signs were stable. Laboratory studies, including complete blood count and metabolic panel, were unremarkable, except for elevated alkaline phosphatase.

A non-contrast computed tomography (CT) scan of the chest demonstrated a large calcified anterior mediastinal mass measuring 10 × 8.8 cm *(Fig. 1)*, in addition to calcified mediastinal and hilar lymph nodes. There were bilateral calcified and partially calcified pulmonary nodules as well *(Fig. 2)*. No recent CT scans were available for comparison.

A robotic bronchoscopy was performed using an Intuitive ION bronchoscope (Intuitive, Sunnyvale, CA, USA), and a minimally calcified right middle lobe nodule was targeted *(Fig. 2)*. This was followed by an endobronchial ultrasound was performed during the same procedure to evaluate the mediastinal lymph nodes. Stations 11L, 4L, and 7 were sampled. However, calcification-induced acoustic shadowing limited safe sampling of the 4R station. This was followed by a bronchoalveolar lavage of the right upper lobe.

The examined tissue revealed a high-grade malignant neoplasm predominantly featuring sarcomatoid (fibroblastic) characteristics within an osteoid matrix. Additionally, there were polygonal cells with eccentric nuclei (osteoblasts) present in the osteoid matrix, along with rare scattered osteoclastic giant cells *(Fig. 3 and 4)*. The tumour cells tested positive for SATB2 and negative for carcinoma markers such as pancytokeratin, TTF1, NAPSIN A, and P40.

The differential diagnosis of these pathological findings includes carcinosarcoma of the lung with an unsampled carcinomatous component or OS. The sampled material is abundant and primarily consists of osteoid. In most cases of carcinosarcoma, the osteoid component is typically focal. Consequently, the lack of carcinoma components based on morphology and immunohistochemical stains, along with the predominance of the osteoid matrix, aligns with a diagnosis of OS.

A positron emission tomography (PET)/CT scan showed brain, liver, retroperitoneal, and multifocal skeletal muscle metastasis. Brain magnetic resonance imaging (MRI) revealed an enhancing mineralized intracranial lesion in the right hemisphere.

The case was discussed in the tumour board with a decision to proceed with systemic chemotherapy with

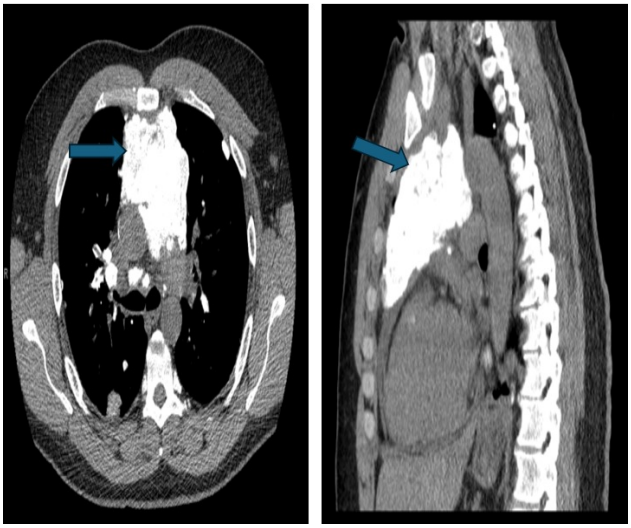


Figure 1. Mediastinal osteosarcoma: computed tomography scan showing a large mediastinal calcified mass (blue arrows).

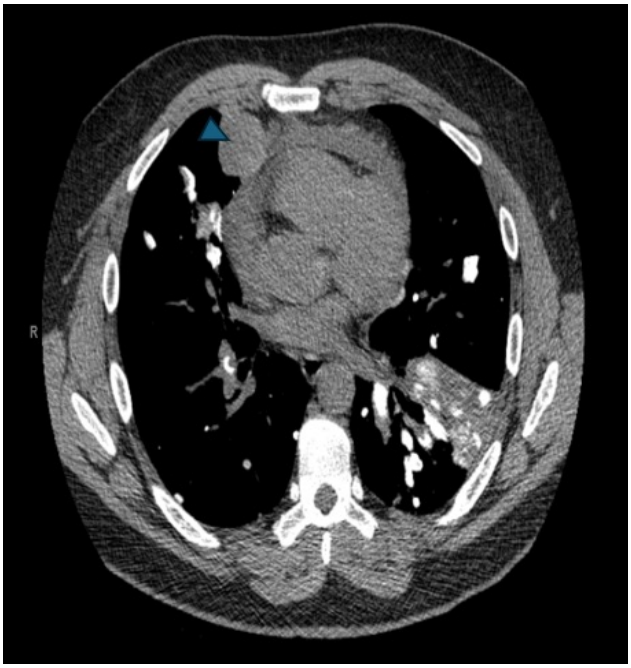


Figure 2. Computed tomography scan showing the bilateral calcified lung nodules. The blue arrowhead indicates the nodule targeted during robotic bronchoscope sampling.

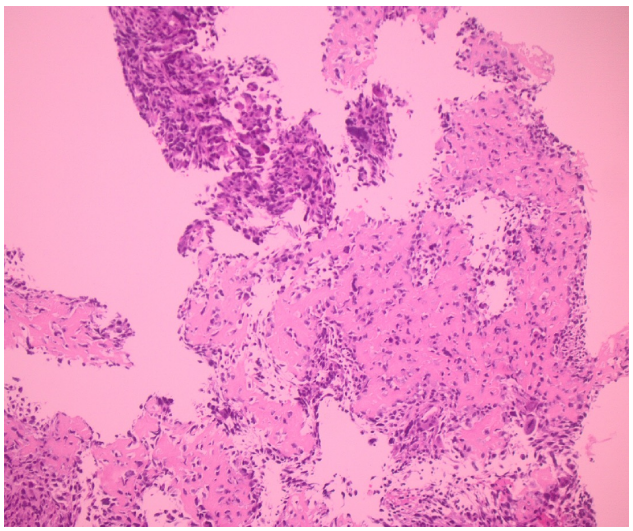


Figure 3. Microscopic examination of the tissue sampled shows hypocellular area of osteoid matrix and hypercellular area of malignant spindle cells (magnification 20×).

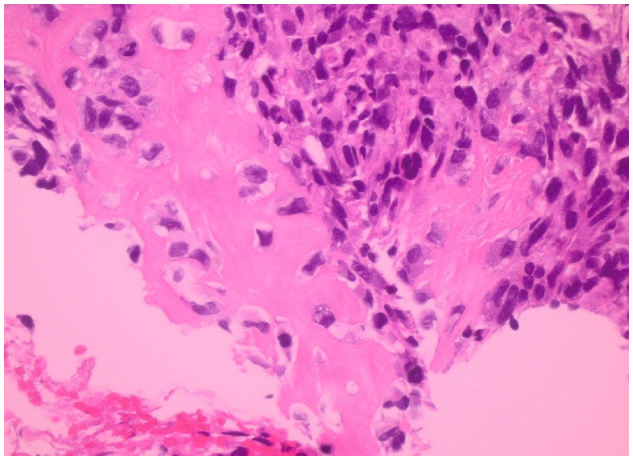


Figure 4. Microscopic examination of the tissue sampled x shows polygonal cells with eccentric nuclei (osteoblasts) and spindle cells (fibroblastic) embedded in the osteoid matrix (magnification 40×).

Cisplatin/Doxorubicin and radiation therapy for his brain metastasis. Nine months into therapy, imaging revealed a mixed response but indicated overall tumour stability. Consequently, Regorafenib, a kinase inhibitor, was initiated. Twelve months post-diagnosis, the patient was hospitalized due to hypoxemia secondary to pulmonary embolism requiring mechanical ventilation. He succumbed to his illness during the same hospitalization.

DISCUSSION

Extraskeletal OS is a rare and aggressive cancer characterized by the formation of osteoid tissue in soft tissues without any connection to bone or periosteum. It comprises roughly 1–2% of all soft tissue sarcomas and 2–4% of OS cases overall. Extraskeletal OS tends to occur most frequently in individuals over 30 years old, a demographic pattern that differs significantly from that of primary bone OS, which is more common in younger patients[1,2]. Mediastinal OS are even rarer; about 9 cases have been described in the literature[3]. Most patients were men, with a mean age of diagnosis of 44 years, and a median tumour size of 10 cm[3].

Patients with mediastinal OS usually present with nonspecific symptoms and physical examination findings that usually prompt imaging studies that reveal the mass. Common complaints include chest pain, persistent cough, and dyspnoea[3]. Due to such nonspecific symptoms, the sarcoma usually grows into large tumours. When the tumour compresses or invades the superior vena cava, patients may exhibit signs of superior vena cava syndrome, such as facial swelling, venous distention in the neck and upper chest, and cyanosis.

Imaging features are usually nonspecific, but the presence of ossification with malignant characteristics on a chest computed tomography scan is highly indicative of OS[4]. In addition, CT, helps delineate the size, margins, and extent of local invasion or metastasis. MRI offers superior soft tissue contrast and is valuable in assessing the involvement of adjacent cardiovascular structures, spinal elements, or pleura, if indicated[5]. PET-CT scan can be instrumental in assessing metabolic activity and ruling out distant metastasis, especially in the lungs or bones.

A definitive diagnosis necessitates histopathological confirmation. Similar to other mediastinal tumours, tissue biopsy can be performed via a percutaneous CT-guided method, mediastinoscopy, endobronchial ultrasound, video-assisted thoracoscopy, or through an open biopsy approach[6]. In the case discussed in this report, a robotic Bronchoscopic method was utilized for histological sampling, focusing on a minimally calcified nodule in the right middle lobe due to the extensive ossification of the mediastinal mass, in order to obtain a higher yield of tissue for diagnosis. Microscopically, mediastinal sarcoma, similar to other forms of extraskeletal OS, is characterized by the presence of a uniform morphological pattern of sarcomatous tissue and the production of malignant osteoid[7].

In addition, these tumours exhibit histopathological features akin to those seen in primary skeletal OS, which include conventional OS (osteoblastic, chondroblastic, fibroblastic), telangiectatic OS, low-grade OS, small-cell OS, parosteal OS, periosteal OS, and high-grade surface OS, with the conventional being the most common[8]. Immunohistochemically, nuclear expression of SATB2 is observed, however, this marker is not specific, but these tumours are uniformly positive for vimentin. Extraskeletal OS may also show weak smooth muscle actin, S-100 protein, and cytokeratin expression. Desmin may be present focally, though it is generally absent[9].

Given the rarity of mediastinal OS, little is known about the treatment approaches. Surgery is usually offered whenever possible, and/or radiation therapy[10]. If surgery is not feasible, chemotherapy with regimens including doxorubicin, cyclophosphamide, or cisplatin is an option. Overall, the prognosis is usually poor, and recurrence rates are high. The median overall survival is 4 months[3],

and, in contrast to the case presented in this report, most cases reported in the literature were locally invasive, with the majority treated with surgical resection followed by chemotherapy or radiation.

CONCLUSION

In conclusion, this case highlights the need to include mediastinal OS in the differential diagnosis of anterior mediastinal masses, especially when calcifications and unusual imaging characteristics are present. Definitive diagnosis depends on sufficient tissue sampling and comprehensive immunohistochemical analysis. Ongoing documentation and reporting of such rare cases are crucial for refining future diagnostic and therapeutic approaches.

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