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Concurrent Nontuberculous Mycobacteria Infection and High-Grade Anterior Mediastinal Extraskeletal Osteosarcoma (ESOS): Is There a Connection?

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 59
Final Diagnosis: High-grade anterior mediastinal extraskeletal osteosarcoma
Symptoms: Dyspnea • hemoptysis
Medication: —
Clinical Procedure: Biopsy
Specialty: Oncology

Objective: Rare disease

Background: Extraskeletal osteosarcomas (ESOS) of the mediastinum are extremely rare and may present with concurrent nontuberculous mycobacteria infection.

Case Report: We present the second documented case of high-grade anterior mediastinal extraskeletal osteosarcoma in a 59-year-old man with a history of treated, latent tuberculosis (TB). Sputum samples grew *Mycoplasma avium* complex and *Mycobacterium fortuitum*. Imaging showed a right-sided 7.6 cm mass with compression of the main bronchus. Subsequent biopsy with vimentin staining established the diagnosis of ESOS. Due to the patient's rapidly declining performance status, he was not deemed a candidate for surgery or chemotherapy. He subsequently expired within one month of presentation.

Conclusions: We present a unique case of high-grade anterior mediastinum ESOS and a review of the literature regarding all documented cases of ESOS to date. We suggest there is a possible link between mediastinal masses and nontuberculous mycobacteria infection.

MeSH Keywords: Mediastinal Neoplasms • Mycobacterium Infections, Nontuberculous • Osteosarcoma

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/898730

Background

Extraskeletal osteosarcoma (ESOS) is a very rare form of osteosarcoma (OS) that produces osteoids and is located in the soft tissues with no connection to the skeleton [1]. Whereas skeletal OS typically affects adolescents and young adults, ESOS affects mainly middle-aged adults and tends to have a poor response to chemotherapy [2]. Typical presenting symptoms of mediastinal sarcomas include chest or shoulder pain, dyspnea, cough, hoarseness, paresthesia, hemoptysis, and fever of unknown origin [3]. These symptoms closely mimic tuberculosis.

In this case report, we describe a patient who presented with signs and symptoms consistent with tuberculosis but was found to have a high-grade anterior mediastinal mass diagnosed as sarcoma.

Case Report

A 59-year-old African-American man presented with chief complaints of dyspnea and hemoptysis. The patient was currently an inmate and had been for 30 years. He was a former smoker, having smoked one pack-per day for 20 years, but he admitted to quitting 10 years prior to presentation. He was previously treated for latent tuberculosis with nine months of isoniazid therapy due to positive PPD skin test. He denied a history of HIV. For the past month prior to presentation, the patient complained of fever, chills, night sweats, and fatigue. He reported a 20-pound unintentional weight loss in a time span of 2 months. One week prior to admission, the patient complained of unremitting productive cough with blood-tinged sputum causing chest pain. He worked in construction prior to incarceration but denied any exposure to asbestos, silica dust, or radioactive materials. There was no history of mining, welding, sandblasting, or any other noxious chemicals or fumes. Chest x-ray showed a large pleural effusion on the right with a sizable mass medially (Figure 1). Sputum samples grew *Mycobacterium avium* complex (MAC) and *Mycobacterium fortuitum* in 3/6 bottles. Computed tomography (CT) scan of the patient's chest showed a right-sided mass measuring 7.6×7.6 cm with extension from the upper lobe to the lower lobe, compressing the main bronchus and generating atelectasis of the lung (Figure 2). A massive pleural effusion was present. Further evaluation of the effusion via thoracentesis, with removal of 1.2 L of fluid, showed malignant cells and by Light's criteria was found to be exudate. An ultrasound-guided biopsy was performed of the anterior mediastinal mass for further diagnostic confirmation. Histologic examination of the mass showed undifferentiated mesenchymal cells with small but pleomorphic nuclei consistent with a neoplastic process as well as osteoid production (Figure 3). Further characterization by immunohistochemistry showed cells diffusely positive for vimentin (Figure 4) and negative for cytokeratin. These findings strongly supported the diagnosis of high-grade ESOS. The patient's performance status deteriorated rapidly in a period of one week. He developed a pericardial effusion and subsequent atrial fibrillation with a rapid ventricular rate. Due to his rapid decline in performance status, he was not considered a candidate for surgery, chemotherapy, or radiation therapy. He died within a month of his initial presentation

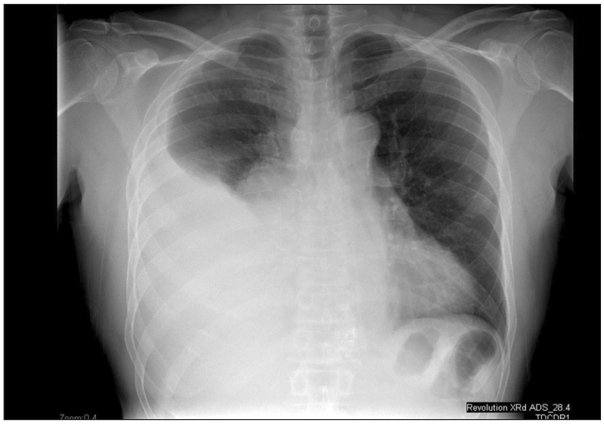

Figure 1. Chest x-ray AP view. Calcified anterior mediastinal structure. Large right-sided pleural effusion.

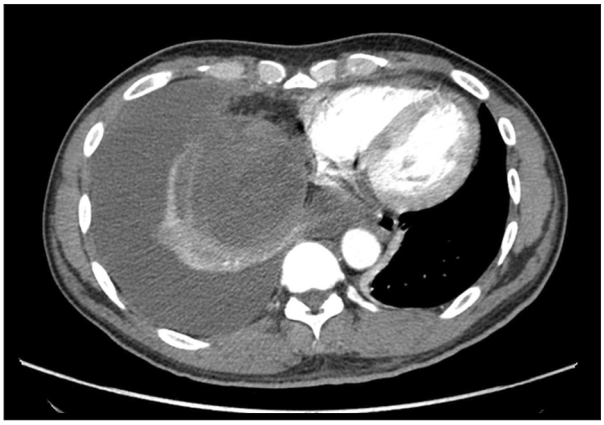

Figure 2. CT thorax with contrast. Right anterior mediastinal mass measuring 7.6×7.6 cm, which extends from the upper lobe to the lower lobe, causing compression on the main bronchus and atelectasis of the lung. Compressive pleural effusion/hemothorax is also seen. There is no pericardial effusion. Heart appears normal in size.

Discussion

Primary sarcomas of the mediastinum are rare (Table 1) [3]. Even more rare are extraosseous osteogenic sarcomas, which account for approximately 1.2% of all soft-tissue sarcomas [5]. The largest study to date discussing primary sarcomas of the mediastinum, a study by Burt et al. [3], described the most

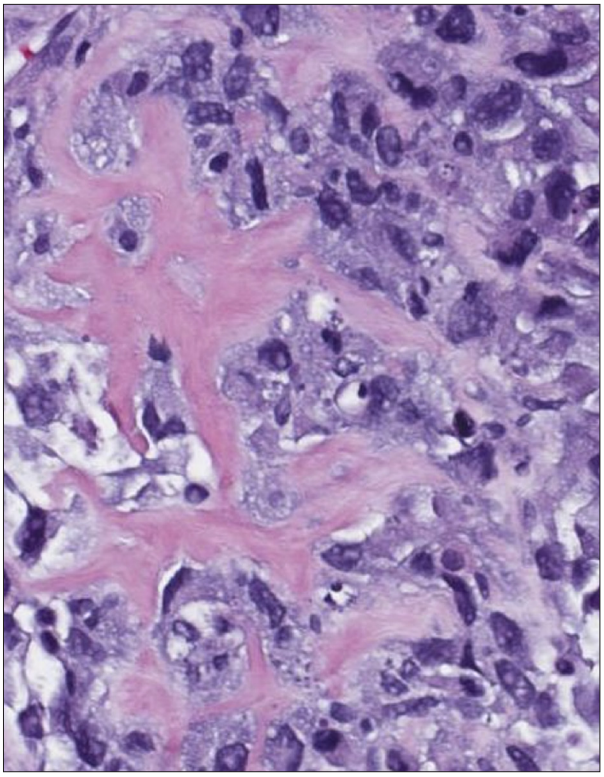

Figure 3. Photomicrograph showing undifferentiated malignant neoplasm in a background of osteoid material.

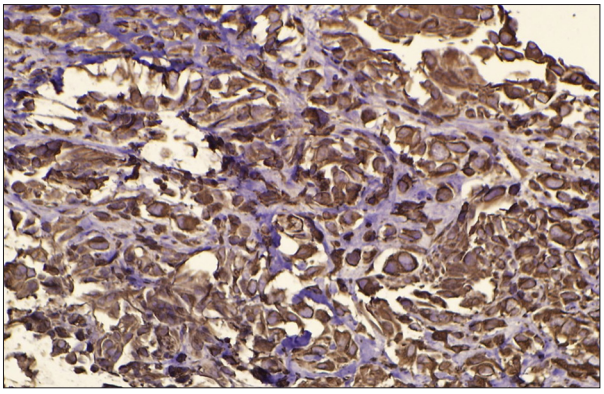

Figure 4. The undifferentiated malignant neoplastic cells are strongly positive for vimentin immunostain.

common histologic types as consisting of malignant peripheral nerve tumor (26%), spindle cell sarcoma (15%), leiomyosarcoma (11%), embryonal rhabdomyosarcoma (9%), and liposarcoma (9%). Each histologic type was further classified as high or low grade.

Although Burt et al. [3] did not mention osteogenic sarcomas as a histologic type, there have been 11 cases published in the literature since 1941. These cases are summarized in Table 2. Most cases occur in middle-aged men with a male to female ratio of 3:1, and range in size of sarcomas from 3 cm to 30 cm, with sarcomas mainly located in the anterior mediastinum and present with local metastasis. The overall prognosis is poor, with most patients not surviving past five months from diagnosis.

Table 1. Incidence of anterior mediastinal masses.

Tumor	Incidence (%)
Thymoma	20
Teratoma, seminoma	15
Lymphoma	10
Carcinoma	10
Parathyroid adenoma	
Intrathoracic goiter	
Lipoma	
Lymphangioma	
Sarcoma	<1
Extraskeletal osteosarcoma	
Leiomyosarcoma	
Liposarcoma	
Malignant peripheral nerve tumor	
Spindle cell sarcoma	

Burt et al. [3]; Baum and Crapo [4].

The most common presenting symptoms are dyspnea followed by chest pain. This can be explained by the vicinity of the tumor to the lungs and heart. The current case describes symptoms similar to tuberculosis: fever, night sweats, dyspnea, hemoptysis, fatigue, and weight loss. Symptoms were not supported by sputum cultures, which grew nontuberculous mycobacterium: *M. avium* complex and *M. fortuitum*. Nevertheless, the history of latent tuberculosis compounded with symptoms similar to infection were worrisome for reactivation.

Proposed treatment for mediastinal masses includes radiation, chemotherapy, and surgery. Patients that survive the longest usually undergo surgical excision. However, the close proximity of the sarcoma to vital structures in the thorax can pose a serious dilemma for treatment and thus add to a poor prognosis [3]. The aggressiveness of the tumor is evidenced by early metastasis and the relatively short period of survival after diagnosis.

To our knowledge, the current case is the second that describes a history of tuberculosis in a patient diagnosed with primary mediastinal sarcoma. There is no proven link between tuberculosis and mediastinal sarcomas. However, it is well known that there is a correlation between tuberculosis and lung cancer. Tuberculosis leads to chronic inflammation, which may orchestrate a tumor-supporting microenvironment that is

Table 2. Reported cases of mediastinal extraskeletal osteosarcoma.

Case	Author (year)	Age/ sex	Size (cm)	Location	Presenting symptoms	Metastasis	Treatment	Outcome
1	Wilson (1941) [6]	19/M	NA	Anterior mediastinum	Facial/neck/right arm swelling	Distant	SC	D (2 mo)
2	Ikeda et al. (1974) [7]	22/M	13	Superior mediastinum	CP, Dys, F	Local	S/RT	A (5 yr)
3	Catanese et al. (1988) [8]	30/M	NA	Mediastinum/ lung	Dys, DC	Local	S/CT/RT	D (1 mo)
4	Tarr et al. (1988) [9]	64/M	4,5	Anterior mediastinum	CP, Dys, WL	Local	S/CT	A (3 mo)
5	Greenwood et al. (1989) [10]	64/F	8,5	Anterior mediastinum	CP	Local	S	NA
6	Stark et al. (1990) [11]	30/M	3	Middle mediastinum	CP/arm pain, Dys, Syn, Fat	Local	NA	NA
7	Venuta et al. (1993) [12]	22/F	9	Posterior mediastinum	Parascapular pain, Dys, W	Local	S/CT/RT	D (7 mo)
8	De Nictolis et al. (1995) [13]	68/M	10	Anterior mediastinum	CP, DC, F	Local	S	A (3 yr)
9	Ulusakarya et al. (1999) [14]	21/M	7	Anterior mediastinum	Dys, painful gynecomastia	Distant	S/CT	D (4 mo)
10	Hishida et al. (2009) [2]	77/F	16	Anterior mediastinum	Dys	Distant	S	D (4 mo)
11	Sabatier et al. (2010) [1]	30/M	30	Anterior mediastinum	Cervical pain, left radial and cubital paralysis	Local	S/CT	D (5 yr)
12	Present case	59/M	7,6	Anterior mediastinum	CP, Dys, F, C, WL, NS	Local	SC	D (1 mo)

SC – supportive care; S – surgical resection; CT – chemotherapy; RT – radiation therapy; D – deceased; A – alive; NA – not available; CP – chest pain; Dys – dyspnea; F – fever; C – chills; DC – dry cough; W – weakness; WL – weight loss; Syn – syncope; Fat – fatigue; NS – night sweats.

indispensable to carcinogenesis [15]. The survival of patients with lung cancer is significantly shorter in subjects with a history of pulmonary tuberculosis [16]. An association between mediastinal sarcomas and tuberculosis has not been established due to the rarity of the illness.

However, several articles have been published which show nontuberculous rapid growing mycobacteria (RGM) infections in patients with cancer. The most common strains include *M. fortuitum*, *M. abscessus*, and *M. chelonae*. However, *M. kansasii* has been considered the most virulent and is that which closely resembles *Mycobacterium tuberculosis* [17]. Malignancies vary from leukemia to solid tumors involving the head and neck, lung, lymphatic system, and breast. Pulmonary RGM infections have been found to be associated with underlying structural lung defects [18]. Whether these structural abnormalities may be due to anomalies caused by gene predisposition, environmental pollutants, prior bacterial or viral infections, or are idiopathic, remains to be proven.

Conclusions

Our case represents the second documented case of high-grade ESOS of the anterior mediastinum reported in the literature. It is also the second reported case with a known prior history of tuberculosis, but the first nontuberculous mycobacteria infection. This case highlights the highly aggressive nature of ESOS in the mediastinum and concurrent nontuberculous mycobacteria infection.

Statement

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The authors have no statements or declarations regarding conflicts of interest.

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