

Received: 2021.04.08

Accepted: 2021.11.16

Available online: 2021.12.09

Published: 2022.01.25

Yolk Sac Tumor in the Anterior Mediastinum Presenting as Acute Pericarditis

Authors' Contribution:

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

ABCDEF 1 **Beka Aroshidze**
ABCDEF 2 **Lakshmi Boyapati**
ABCDEF 1 **Akriti Pokhrel**
ABCDEF 2 **Vladimir Gotlieb**
BCDE 3 **Abdullah Khan**
AEF 2 **Burak Erdinc**
BD 4 **Muhammad Akhtar Cheema**

1 Department of Internal Medicine, One Brooklyn Health System, Brooklyn, NY, USA
2 Department of Hematology and Oncology, One Brooklyn Health System, Brooklyn, NY, USA
3 Department of Cardiology, One Brooklyn Health System, Brooklyn, NY, USA
4 Department of Pathology, One Brooklyn Health System, Brooklyn, NY, USA

Corresponding Author: Beka Aroshidze, e-mail: beqaaroshidze@gmail.com

Financial support: None declared

Conflict of interest: None declared

Patient: Male, 20-year-old
Final Diagnosis: Mediastinal yolk sac tumor • yolk sac tumor
Symptoms: Chest pain • cough • sensation of fullness in the neck
Medication: —
Clinical Procedure: Mediastinal biopsy
Specialty: Cardiology • General and Internal Medicine • Oncology • Pathology

Objective: Rare disease

Background: Mediastinal masses can originate from anatomical structures normally located in the mediastinum, or from structures that travel through the mediastinum during embryogenesis. Initial presenting symptoms usually vary from shortness of breath, cough, chest pain, and superior vena cava syndrome to nonspecific constitutional symptoms (eg, fever, weight loss, fatigue). However, the initial presentation of a mediastinal mass with acute pericarditis has not been reported in the literature as far as we know.

Case Report: A 20-year-old man presented to the Cardiology Clinic with chest pain and new pericardial effusion on echocardiography, both fulfilling the diagnostic criteria of acute pericarditis. The patient also had venous engorgement on the neck, and a chest X-ray followed by computed tomography imaging showed a large mediastinal mass. The serum tumor marker α -fetoprotein (AFP) was markedly elevated. The biopsy and immunohistochemistry revealed a high-grade malignant neoplasm – yolk sac tumor, which is a type of non-seminomatous germ cell tumor. The acute pericarditis resolved after administration of NSAID and colchicine. The patient was then started on chemotherapy.

Conclusions: The discussed case shows the rare presentation of an anterior mediastinal mass with acute pericarditis. This emphasizes the importance of a thorough review of systems and critical analysis of every sign and symptom at the time of initial presentation, which helps the physician to obtain appropriate imaging studies early in the course, leading to an early diagnosis and treatment of the disease, such as in this case of an extremely rare germ cell tumor.

Keywords: Mediastinal Neoplasms • Medical Oncology • Nonseminomatous Germ Cell Tumor • Pericarditis • Yolk Sac

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/932616>



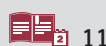
1815



—



4



11



Background

Mediastinal masses can originate from anatomical structures normally located in the mediastinum (eg, lymph nodes, the heart and its vessels, thymus), or from structures that travel through the mediastinum during embryogenesis (eg, esophagus, trachea, thyroid). However, many mediastinal masses are metastatic from extramediastinal malignancies. Regardless of the origin of the mass, presenting symptoms with mediastinal masses are generally due to extrinsic compression of structures in the mediastinum, such as dyspnea, chest pain, and cough. The anterior mediastinum is the most common location where mediastinal masses occur in adults. Thymoma, (“Terrible”) lymphoma, Teratoma/germ cell tumor, and intrathoracic Thyroid tissue (mnemonic: the “terrible Ts”) are examples of the most common anterior mediastinal masses.

We present the case of a rare germ cell tumor (GCT) of the anterior mediastinum in a 20-year-old patient. The patient presented with chest pain suggestive of pericarditis (which was demonstrated by its combination with new pericardial effusion) and engorgement of the neck veins. Later, he was diagnosed with a mediastinal yolk sac tumor, which is usually a highly malignant and aggressive germ cell tumor. Although clinical features of mediastinal GCTs have been well described (including chest pain and malignant pericardial effusion [1]), initial presentation with acute pericarditis has not been reported in the literature as far as we know.

Case Report

A 20-year-old man with no significant past medical/surgical history initially presented to the Cardiology Clinic reporting chest pain for 5 weeks. The pain was sharp, episodic (lasting for few hours), non-exertional, non-radiating, and gradually progressive (varying from 4 to 8 out of 10 in intensity), that was relieved on leaning forward and taking a non-steroidal anti-inflammatory drug (NSAID). Review of systems was positive for occasional dry cough and neck pain associated with some sensation of fullness on the left side of his neck. The patient was not on any home medications. He denied shortness of breath, paroxysmal nocturnal dyspnea, and orthopnea, and he denied having fever, chills, night sweat, diaphoresis, nausea, vomiting, fatigue, abdominal pain, diarrhea, hemoptysis, blurry vision, upper-limb edema or heaviness, facial swelling, or headaches.

A physical exam was significant for tachycardia (heart rate was 105 beats per minute and regular), low body weight, and engorged neck veins (**Figure 1**). The patient’s blood pressure was 125/87 mmHg. Cardiac auscultation showed normal heart sounds without rubs or murmurs. According to the patient and family members, “he has always been skinny.” There was no palpable adenopathy present in the neck, axilla, or groin.



Figure 1. Initial presentation of the patient: physical exam was significant for engorgement of the neck veins (shown by the arrows).

Laboratory findings were significant for elevated LDH (773 IU/L [reference range: 313-618 IU/L]), CRP (4.1 mg/dL [reference range: 0.5-1 mg/dL]), and AFP (15220 ng/mL [reference range: <6.1 ng/mL]). Thyroid function, β -hCG, and ESR were normal. EKG showed sinus tachycardia and mild ST elevation needing differential diagnosis between acute pericarditis and early repolarization. The persistence of findings after treatment supports the latter.

Transthoracic echocardiogram (TTE) revealed a left ventricular ejection fraction of 45-50%, with small pericardial effusion.

Since the patient was fulfilling 2 of 4 diagnostic criteria suggested by the guidelines of the European Society of Cardiology, he was started on naproxen (an NSAID) for 2 weeks and colchicine for 3 months. With this regimen, the chest pain resolved in less than 1 week. Of note, treatment guidelines suggest using ibuprofen as the primary NSAID.

Regarding other signs of pericarditis, his CRP ultimately decreased to 1.5 mg/d and pericardial effusion was absent on a subsequent TTE done 4 months later.

A chest X-ray was performed for evaluation of cough and neck vein distention. It showed a large mediastinal mass (**Figure 2A, 2B**).

A CT study of the anterior mediastinum demonstrated a large, heterogeneous, solid soft tissue mass in the retrosternal space measuring 8.4 cm in length, 8.1 cm across, and 5.1 cm in AP diameter (**Figure 3A**). There were enlarged lymph nodes: left supraclavicular lymph node (1.2 cm); Right hilar lymph node (1.4 cm) and left hilar lymph node (1.2 cm); left anterior mediastinal node (1.5 cm). The superior vena cava (SVC) in the right paratracheal space was extrinsically compressed and narrowed by the anterior mediastinal mass, with retrograde filling

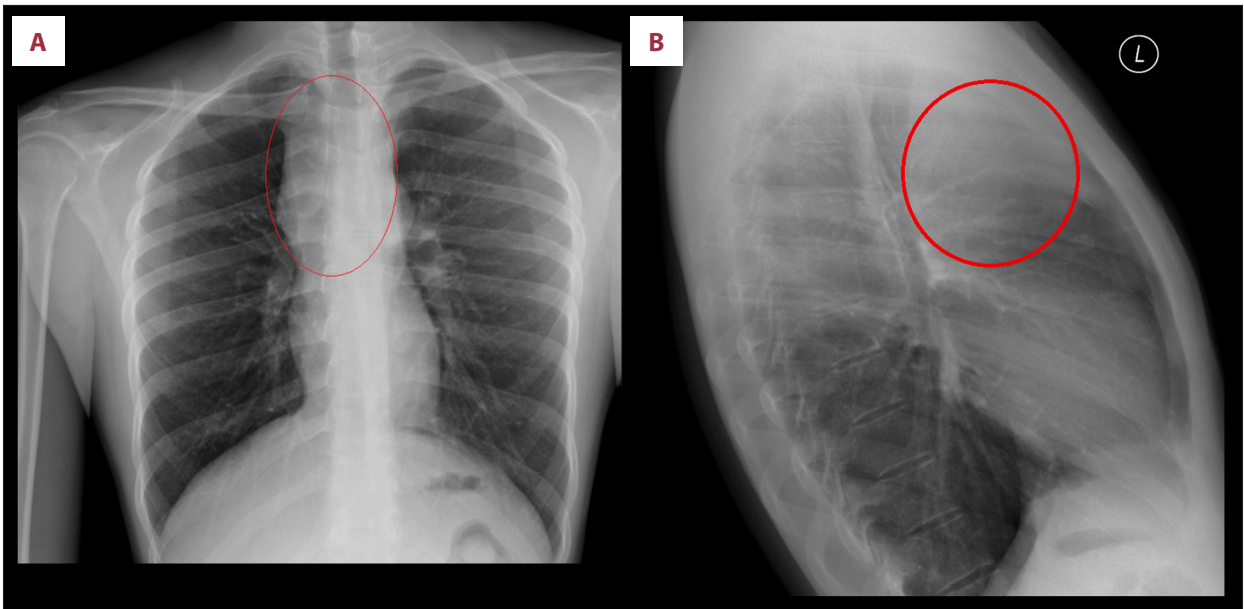


Figure 2. (A) Chest X-ray (PA view) showing large mediastinal mass (marked fullness in the right suprahilar, paratracheal, and anterior superior mediastinal region, predominantly right-sided). (B) Chest X-ray (lateral view), mediastinal mass outlined.

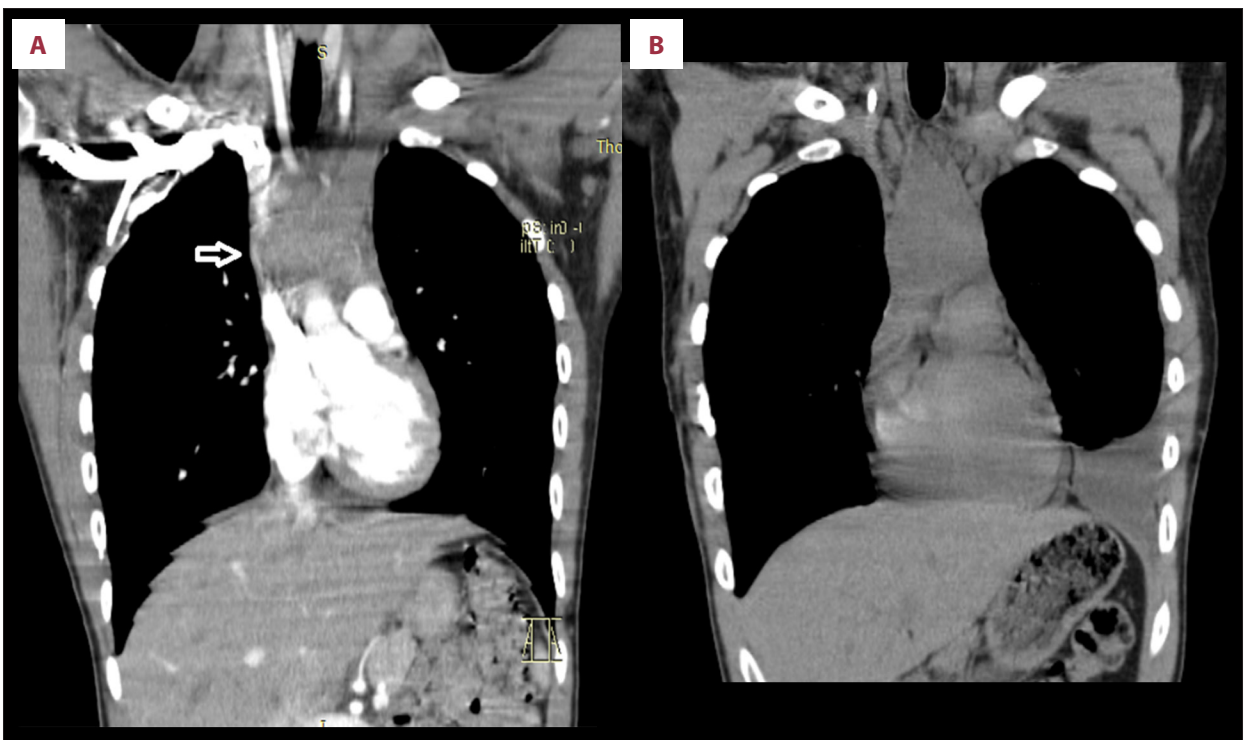


Figure 3. (A) CT scan of the chest with IV contrast showing large, heterogenous, solid soft tissue mass in the anterior mediastinum (8.4×8.1×5.1 cm) with extrinsic compression and narrowing of the superior vena cava in right paratracheal space by the mass. (B) Follow-up CT scan of the chest showing interval reduction in the size of mediastinal mass (4.6×4.0×7.5 cm, compared to 8.1×5.1×8.6 cm on the prior CT examination).

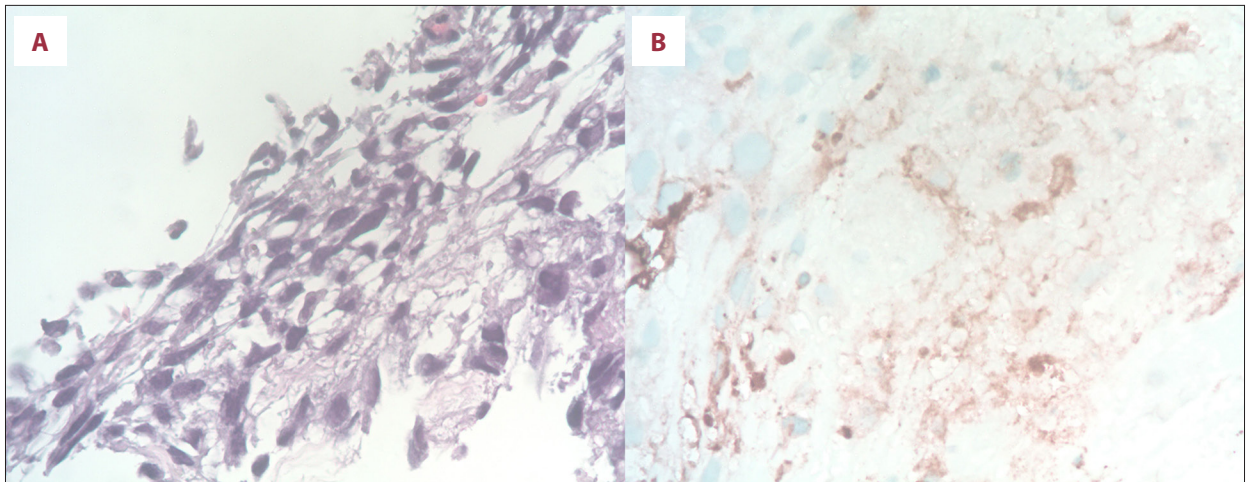


Figure 4. (A) H&E stain showing spindle features (40× mag). (B) PLAP positive stain (Immunohistochemistry, 40× mag).

of the SVC by the azygos vein. There was no hepatosplenomegaly or biliary dilatation. For further evaluation of the anterior mediastinal mass compressing the SVC, the patient was hospitalized and was seen by the Hematology-Oncology team. An endovascular stent was not placed, as the KISHI score was 2 (only cough and neck vein distention).

CT-guided core-needle biopsy of the primary substernal mass was performed and tumor markers were sent for analysis. Biopsy revealed a high-grade malignant neoplasm of uncertain type, evidence of marked cytologic atypia with spindle cell features (Figure 4A), and prominent tumor necrosis.

Immunohistochemistry staining was supportive of a germ cell tumor with positive staining with AE-1/AE-3; CAM5.2; PLAP (Figure 4B); SALL4; AFP and Glypican-3; negative staining with Desmin, S100, CEA, monoclonal CK5/6, TTF1, Napsin A OCT3/4, CD30, HCG, and Podoplanin. The Ki-67 proliferation marker result was 80% (suggestive of aggressive, increased cellular proliferation). Based on these results, the patient was diagnosed with a primary mediastinal yolk sac tumor (YST). Of note, testicular ultrasound (US) showed no mass.

The patient was planned for chemotherapy with 4 cycles of bleomycin, etoposide, and cisplatin (BEP regimen). He received 2 cycles of BEP, but pulmonary function tests showed a decrease in DLCO (44%). A subsequent high-resolution CT scan showed airspace opacities in the lingula and lateral basal segment of the left lower lobe, small left pleural effusion, and atelectasis likely as adverse effects of bleomycin. For this reason, the BEP regimen was stopped, although the tumor was getting smaller. CXR after 2 cycles of BEP showed improved widening of the superior mediastinum.

A CT scan of the chest without contrast showed an interval reduction in the size of the anterior mediastinal mass. It also

revealed the nodule in the right middle lobe and a new 3-mm nodule in the lateral basal segment of the right lower lobe of the lung (Figure 3B). The patient was then started on a VIP regimen (etoposide, ifosfamide, and cisplatin).

The patient completed a total of 2 cycles of the BEP regimen and 2 cycles of the VIP regimen. A PET scan was obtained after chemotherapy, which showed partial response with residual mediastinal mass and few lung lesions that increased in size. Post-treatment AFP was 335.4 ng/mL. Of note, the neck vein engorgement had also improved. The patient was re-started on the VIP regimen for further optimization for surgery.

Discussion

Most germ cell tumors (GCTs) develop in the testes and ovaries. Extragenital GCTs (EGGCTs) are rare and account for 1-5% of all GCTs [2]. They typically arise in midline locations from the pineal gland to the coccyx: the mediastinum, retroperitoneum, CNS, and sacrococcygeal region [3]. There is a theory that EGGCTs develop due to failure of the migration of primordial germ cell (PGC) remnants to the gonadal ridge [4].

GCTs account for approximately 10-15% of anterior mediastinal masses in adults [5]. Mediastinal GCTs are classified as seminomatous or non-seminomatous GCTs, with the latter including yolk sac tumor (YST), choriocarcinoma, embryonic carcinoma, and mixed GCTs [6].

Mediastinal YST is a rare, highly malignant, and aggressive GCT, that mainly affects young men and is visualized on chest X-ray or CT scan of the chest [7]. They can be locally invasive and can trigger early lymphatic and/or hematogenous metastasis. Our patient had regional lymph node involvement but no distant metastasis on initial presentation.

AFP levels can be used to support the diagnosis of YST and also as a marker, whether or not the treatment of YST was effective [7].

The immunohistochemical phenotype of mediastinal YSTs has similarities with testicular YST. The analysis of 14 cases of primary mediastinal YSTs by Weissferdt et al [8] demonstrated characteristic co-expression of CAM5.2 and SALL4 (strong and diffuse expression present in 100% of cases); Glypican-3 and AFP (expressed with a patchy pattern present in 71% of cases). Other immunohistochemical markers that can be expressed include placental alkaline phosphatase (PLAP), GATA-3, CDX2, CD117, and CD30.

By the time the diagnosis is made, mediastinal YST is frequently advanced, massive, and inoperable. According to Geng et al [9], “primary mediastinal locations of YST and distant Surveillance, Epidemiology, and End Results (SEER) Summary stage are associated with poor prognosis; receiving surgery is a good prognostic factor.” That study refers to the male patients.

According to Bokemeyer et al [10], international analysis of more than 600 cases of extragonadal germ cell tumors showed that the mediastinal GCTs usually present with the following symptoms: dyspnea (25%), chest pain (23%), cough (17%), fever (13%), weight loss (11%), superior vena cava syndrome (6%), fatigue (6%), non-chest pain (5%), and other less frequent symptoms. There have been cases of Horner syndrome (damage to sympathetic trunk), and hypotension (cardiac tamponade or cardiac compression). However, initial presentation with acute pericarditis (diagnosed with ≥ 2 out of 4 diagnostic criteria as per the European Society of Cardiology [11]) is extremely uncommon. It is unclear why our patient developed pericarditis. This can be related to the specific anatomical location of the tumor with resultant irritation of the pericardial layers or even some undiagnosed autoimmune phenomenon.

Our patient’s chest pain and tachycardia resolved a few days after starting NSAID and colchicine. However, the other EKG findings persisted after completing the course of treatment for pericarditis. This indicates that the ST elevations seen on

the initial EKG could have been related to the early repolarization abnormalities.

However, the rapid improvement of the characteristic chest pain, resolution of the pericardial effusion months later, and decrease in inflammatory markers as a result of the anti-inflammatory medications makes acute pericarditis a more likely cause of the chest pain in contrast to the local extension and compression secondary to the mass effect of the tumor.

Conclusions

Clinical symptoms with mediastinal masses are generally due to extrinsic compression of structures in the mediastinum. Our patient’s initial presentation of long-standing chest pain relieved by leaning forward and with NSAIDs, tachycardia, and small pericardial effusion on TTE led to the initial diagnosis of acute pericarditis. This eventually turned out to be a rare, highly malignant primary yolk sac tumor of the mediastinum.

The case shows the unusual presentation of an anterior mediastinal mass with acute pericarditis, thus emphasizing the importance of a thorough review of systems and critical analysis of every sign and symptom at the time of initial presentation; this helps the physician to obtain appropriate imaging studies and to make an early diagnosis of the disease, such as a rare anterior mediastinal neoplasm. Prompt diagnosis and appropriate treatment are the most important steps to avoid high morbidity and mortality from this condition.

Acknowledgments

We thank the patient for his cooperation and for consenting to publication of this case report.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Skelton WP, Mahtta D, Welniak S, et al. Pericardial effusion as an atypical initial presentation of extra-gonadal nonseminomatous germ cell tumor: A case report and literature review. *Oxford Med Case Reports*. 2018;2018(2):omx097
2. McKenney JK, Heerema-Mckenney A, Rouse R V. Extragonadal germ cell tumors: A review with emphasis on pathologic features, clinical prognostic variables, and differential diagnostic considerations. *Adv Anat Pathol*. 2007;14(2):69-92
3. Gao Y, Jiang J, Liu Q. Extragonadal malignant germ cell tumors: A clinicopathological and immunohistochemical analysis of 48 cases at a single Chinese institution. *Int J Clin Exp Pathol*. 2015;8(5):5650-57
4. Nakhla SG, Sundararajan S. A rare case of primary anterior mediastinal yolk sac tumor in an elderly adult male. *Case Rep Oncol Med*. 2016;2016:8961486
5. Beau V Duwe, Daniel H Sterman AIM. Tumors of the mediastinum. *Chest*. 2005;128(4):2893-909
6. Almeida PT HD. Anterior mediastinal mass. *Treasure Isl (FL)*. Published online 2020
7. Silva LLC da, Vergilio FS, Yamaguti DCC, et al. Yolk sac primary tumor of mediastino: A rare case in a young adult. *Einstein (Sao Paulo)*. 2017;15(4):496-499
8. Weissferdt A, Kalhor N, Rodriguez Canales J, et al. Primary mediastinal yolk sac tumors: An immunohistochemical analysis of 14 cases. *Appl Immunohistochem Mol Morphol*. 2019;27(2):125-33

9. Geng R, Zheng Z, Lin Y, et al. Clinical characteristics and prognostic factors of male yolk sac tumor: A Surveillance, Epidemiology, and End Results program study. *World J Urol.* 2021;39(4):1211-17
10. Bokemeyer C, Nichols CR, Droz JP, et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: Results from an international analysis. *J Clin Oncol.* 2002;20(7):1864-73
11. Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2015;36(42):2921-64