

Use of Intravascular Biopsy to Diagnose a Life-Threatening Giant Primary Anterior Mediastinal Yolk Sac Tumor

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Case Study

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ABSTRACT

We present here the case of a 26 year old man with a life-threatening and rapidly growing mediastinal yolk sac tumor. Chest contrast-enhanced computerized tomography (CT) scan and magnetic resonance imaging (MRI) revealed a giant anterior mediastinal mass with a rich surface blood supply that was invading the right atrium and superior vena cava. Because the severity of the superior vena cava syndrome (SVCS) made a traditional biopsy procedure risky, we performed an intravascular biopsy technique via the right femoral vein, successfully obtained biopsies from both the superior vena cava and right atrium, and identified an extragondal germ cell tumor.

INTRODUCTION

Mediastinal yolk sac tumor (YST, also called endodermal sinus tumor) is a highly malignant subtype of non-seminomatous germ cell tumors (NSGCT), predominantly diagnosed in children and young male adults. Primary YSTs of the anterior mediastinum are the least common germ cell tumors, and are associated with a poor prognosis. Here we describe the case of a patient with a rapidly growing giant mass in the anterior mediastinum, accompanied by life-threatening superior vena cava syndrome (SVCS). We successfully used an intravascular biopsy technique in this patient, to obtain the diagnosis necessary for initiating therapy.

CASE DESCRIPTION

A 26 year old man with no long-term medical history presented to our department, complaining of occasional cough, sputum production, right-sided chest pain for approximately four months, worsening dyspnea on exertion, facial and neck swelling and intermittent dysphagia for one week [1]. The patient had no fever, chills, night sweat, bloody sputum; he reported no contact with the sick or recent travel. He was obliged to stay recumbent on admission. Physical examination revealed cyanosis and edema of the face, neck, trunk and upper extremities, and collateral venous distension on the anterior chest wall. The patient showed right mid-posterior egophony and diminished breath sounds in the right lung base. SVCS was diagnosed, accompanied by coughing, pleurisy, facial edema and vessel dilation that resulted in a score of 3 by the Kishi Scoring system indicating severe disease [2]. Blood analysis revealed leukocytosis (white blood cell count 14.28×10^9 cells/L with 76.9% lymphocytes). Serum alpha fetoprotein (AFP) level was elevated to 528.5 ng/mL (normal value: <8.1 ng/ml), while levels of beta-human chorionic gonadotropin (β -HCG), lactate dehydrogenase (LDH) and thyroid-stimulating hormone (TSH) were normal.

Chest X-ray showed widening of the superior mediastinum and a massive infiltrative shadow in the right hilum, with elevation of the right diaphragm (Figure 1A). A contrast-enhanced CT scan of the chest revealed a mass measuring 6.2 cm \times 5.5 cm in the anterior superior mediastinum, with a rich surface blood supply (Figure 1B). A chest MRI showed marked invasion of the adjacent

tissues, involving the right sub-clavian vein, superior vena cava and right atrium. Partial collapse of the right inferior and middle lobes of the lung, with right-sided pleural effusion, was also detected (**Figures 1C and 1D**).

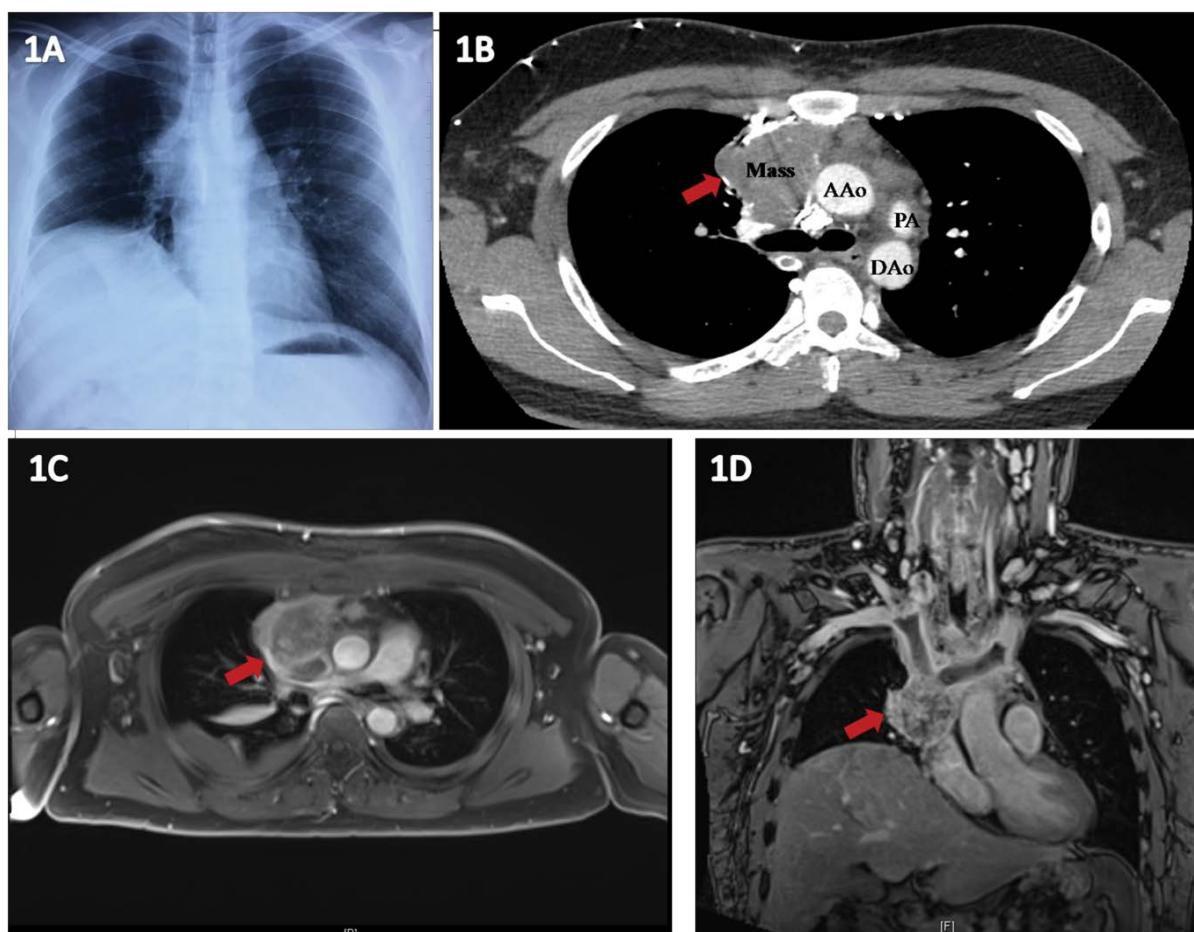


Figure 1. (1A) The chest X-ray that was taken on admission revealed widening of the superior mediastinum and a massive infiltrative shadow in the right hilum, with the elevation of right diaphragm. **(1B)** Contrast-enhanced Computed Tomography (CT) revealed a conglomerate mass measuring 6. 2cm × 5.5 cm in the anterior superior mediastinum. The mass shows abundant surface blood supply. Pleural effusion on the right unilateral is not observed. **(1C, 1D)** Magnetic Resonance Imaging (MRI) of the chest revealed a huge tumor in the anterior mediastinum, invading the surrounding tissue and extending markedly into the right sub-clavian vein and superior vena cava vessels. The right atrium is endovenously compressed, causing partial collapse of the right middle and lobes. Note the presence of pleural effusion in **Figure 1B**, taken 8 days after CT scans.

Based on radiological findings of the proximal compression and distal dilatation of the right subclavian vein and superior vena cava, we suspected thrombus formation; vascular ultrasound further verified the thrombosis, accompanied by severe superior vena cava dilation. The echocardiogram showed moderate right atrial compression and invasion by an external mass.

Following admission, the patient's dyspnea progressed rapidly to orthopnea. He presented with cyanosis. His respiratory rate was about 25-33 breaths/min and pulse rate was 110-120 beats/min. He had no fever, with a highest body temperature of 36.5°C. Oxygen was administrated with a *Venture* mask. Although the fraction of inspired oxygen (FiO_2) was about 50%, the peripheral oxygen saturation was less than 90%. The patients' facial and neck swelling worsened. His dyspnea cannot be alleviated by oxygen therapy, and the lowest partial oxygen pressure/fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) reached 144. The Kishi Score increased to 5 (including orthopnea 3, facial edema 1 and vessel dilation 1), indicating a life-threatening SVCS that required urgent intervention.

We considered use of palliative radiotherapy for the SVCS; however, despite the suspicion of malignant germ cell tumor or invasive thymoma, a definitive diagnosis needed clear evidence of pathological malignancy, in order to inform appropriate treatment for this anterior mediastinal mass. Even though the potential for complications associated with the use of fine needle aspiration biopsy is low, we decided against this procedure because of the likelihood that this approach would fail to yield enough diagnostic tissue. Other routine procedures such as ultrasound-guided core needle biopsy, cervical mediastinoscopy, anterior mediastinotomy, and video-assisted thoracoscopic surgery (VATS) were considered and rejected, because of the substantial risk associated with the use of each procedure in the presence of life-threatening SVCS and intensively vascularized tumor surface, and due to the need for use of further anticoagulant therapy. Fine needle aspiration and other routine biopsy procedures are

more likely to cause bleeding. Considering that the tumor had invading the superior vena cava and right atrium, we attempted an intravascular tumor biopsy with use of endomyocardial biopsy forceps (**Figure 2**).

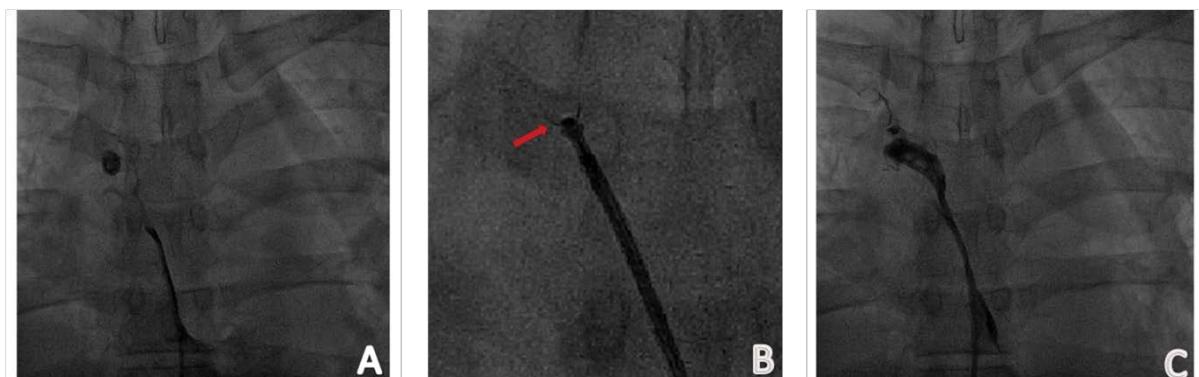


Figure 2. Vessel angiography, showing of tumor biopsy through the right atrium and superior vena. **A.** Angiography documented that the right atrium and superior vena cava were markedly compressed by the tumor. **B.** Endomyocardial biopsy forceps (ARGON Jawz) (red arrow) were used to obtain biopsy tissue at the junction of the atrium (top right) and the superior venacava: A Seldinger puncture was made in the right femoral vein and a 6F catheter (Judkin R4.0) was inserted via the percutaneous angiographic route to arrive at the site. **C.** No hemorrhage was detected following the procedure.

This procedure enabled a diagnosis of YST (**Figure 3**) without complications, and allowed us to initiate chemotherapy.

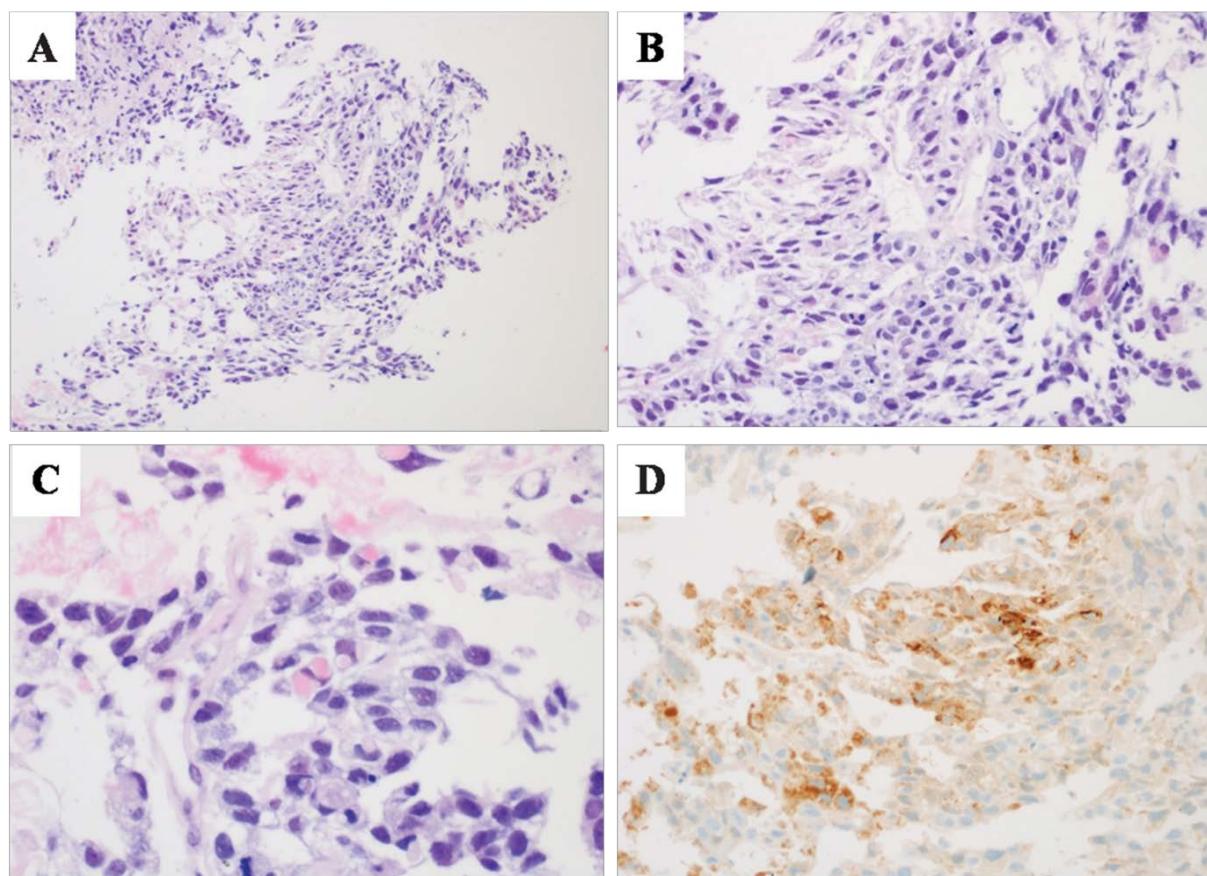


Figure 3. **(A)** The biopsy revealed abundant tumor cells arranged with reticular growth pattern forming microcapsules; (HE, x10) **(B)** The biopsy showed clusters of highly pleomorphic epithelial cells with hyperchromatic nuclei and mitotic cells. (HE, x20) **(C)** Transparent small bodies were evident both within and outside the tumor cells. (HE, x40) **(D)** Immunohistochemistry showing positive staining for alpha-fetoprotein (AFP).

DISCUSSION

Mediastinal YST is a highly malignant subtype of NSGCTs. Extranodal germ cell tumors have been detected in the retroperitoneum, in the sacrococcygeal region, and in the anterior mediastinum; mediastinal YST is the least common GCT. Also, YST is predominantly a disease of young adults, with the average age at diagnosis being 18 years; However, a few cases of mediastinal YSTs have also been reported in elderly patients ^[3]. Primary YSTs presenting in the anterior mediastinum respond

poorly to surgery, radiotherapy, and chemotherapy, and have a grave prognosis. The five-year overall survival rate for patients with mediastinal NSGCT is only 40%, with most YST patients already at an advanced stage at the time of diagnosis.

Here we present a rare case of a young male with a giant, unresectable, primary YST of the mediastinum, in whom pelvic and peritoneal cavity evaluations were negative. The patient was identified to have SVCS on admission, with rapidly progressing dyspnea. The Kishi Scoring system was used to evaluate the severity of the SVCS, to track symptom progression, and to inform therapy decisions [4], according to this scoring scheme, the patient's condition was determined to be life-threatening, and in urgent need of intervention - delays in diagnosis and treatment of life-threatening SVCS can result in poor outcomes or death. Blood tests revealed high levels of AFPs, potentially indicating NSGCT, which could include teratoma, choriocarcinoma, embryonal carcinoma and YST; teratoma is the most common type of YST in the mediastinum; mediastinal teratomas rupture in 36-41% of cases, and can lead to severe SVCS.

Different types of NSGCTs share certain clinical features, but are biologically distinct. NSGCTs arise from germ cells, and are clinically as well as biologically distinct from their testicular counterparts (the seminomas), in terms of their cell morphology and response to treatment. NSGCTs are insensitive to radiotherapy and have a poor prognosis compared to seminomas. Thus, accurate histopathological findings are of utmost importance in the diagnosis of the mass, and in determining the initial strategies to be used for treating the mass.

The patient we describe here presented a diagnostic challenge due to clinical features that contraindicated a number of approaches for obtaining a biopsy. We believed that a fine needle aspiration biopsy was the least likely to cause complications, but acquiring diagnostic tissue via this method was problematic; the rich vasculature on the surface of the invasive tumor, the severe SVCS and the need for anticoagulant therapy led us to reject the use of ultrasound-guided core needle biopsy, due to the risk of hemorrhage. And even though the Chamberlain procedure yields large biopsies from heterogeneous mediastinal masses, the procedure is not recommended for patients who cannot tolerate general anesthesia and ventilation [5]. Furthermore, cervical mediastinoscopy and VATS were also contraindicated in this patient.

Because the contrast-enhanced CT scan and the chest MRI both clearly showed that the tumor had invaded the superior vena cava and the right atrium, we explored the possibility of obtaining the biopsy through an intravascular pathway, using endomyocardial biopsy forceps. The intravascular forceps biopsy through a puncture in right femoral vein can obtain a tissue sample larger than that using fine needle biopsy, thus may allow a more definitive histological diagnosis and in turn supporting the initiation of chemotherapy. But the samples obtained by this intravascular way were still smaller than cervical mediastinoscopy, VATS and Chamberlain procedure; it is not fit for the diagnosis of lymphoma, especially for non-Hodgkin's lymphomas. Because this patient cannot tolerate the intubation and general anesthesia, intravascular forceps biopsy is feasible and may enable us to get an enough sample with fewer complications. Because of the tissue sample size and the possibility of tumor metastasis through blood stream, the intravascular biopsy should be considered with caution only when the classic methods of biopsy were problematic and the tumor invading the large vessels and/or the heart.

CONCLUSION

In conclusion, we show here the method of intravascular biopsy provides a safe and alternative approach to making the diagnosis of mediastinal endodermal sinus tumors. Due to the serious complications of the malignancy, such as severe SVCS, some patients cannot tolerate the general anesthesia and mechanical ventilation, therefore routine biopsy procedures are prohibited to perform. However, when the tumor invaded into the large vessels and/or the heart, intravascular biopsy can be an alternative procedure helping to make the diagnosis.

CONTRIBUTORS

WZ was a resident and wrote the first draft. WZ, FQH, WLF, JML and WW worked together and developed the therapy regimes and revised the manuscript. All authors had access to the data and played a role in writing this manuscript. FQH is corresponding author. Patient consent: Obtained.

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