CASE REPORT

Pericardial effusion as an atypical initial presentation of extra-gonadal nonseminomatous germ cell tumor: a case report and literature review

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Abstract

Extra gonadal germ cell tumors have variable clinical presentations and locations. We report a case of an extra-gonadal germ cell tumor in a 26-year-old male who presented with chest pain. Imaging revealed a large pericardial effusion with underlying mass invading the pericardium. Pericardial effusion is an extremely rare initial site of diagnosis or site of metastasis for malignancy. This case illustrates the importance of a thorough history and physical examination, broad differential diagnosis, and to keep in mind serious complications from rare presentations of disease.

INTRODUCTION

First described in the mid-19th century, extra-gonadal germ cell tumors (EGGCT) are neoplasms displaying histological, serological and cytogenetic characteristics consistent with gonadal origin, but located outside the gonads [1]. This subset of germ cell cancers comprises of ~2–5% of all malignant germ cell tumors [2]. Similar to gonadal tumors, EGGCT neoplasms can occur in several different histological patterns which display the progression of normal embryonic development. These tumors can broadly be classified into seminomatous and nonseminomatous germ cell tumors. Seminomatous germ cell tumors mainly include germinoma and dysgerminoma whereas the nonseminomatous counterpart includes endodermal sinus tumor, yolk sac tumor, embryonal carcinoma, choriocarcinoma and teratoma [3].

Current hypotheses regarding presentation of EGGCT revolve around either aberrancy in migration of germ cells during embryogenesis or due to physiological extra-gonadal distribution of germ cells to provide hematologic and immunologic information [4]. The most common sites of extra-gonadal presentation include (from most to least prevalent) the mediastinum, retroperitoneum, pineal gland and sacral area. Very rarely do such neoplasms arise in the prostate, vagina, orbit, liver or the gastrointestinal tract [5]. Published series of >600 patients have shown that most common clinical presentations include dyspnea (25%), chest pain (23%), cough (17%), fever (13%), weight loss (11%) and superior vena cava syndrome (6%). Rare cases (<2%) cases have presented with hemoptysis, hoarseness or dysphagia [4]. Median age of presentation varies by the site of origin with a median age being 28–33 for retroperitoneal tumors and 30–41 for mediastinal neoplasms. Tumor markers that are commonly elevated include alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (b-HCG), lactate dehydrogenase (LDH) and

alkaline phosphatase. Extragonadal seminomatous tumors usually present with an elevated b-HCG and LDH whereas elevations in b-HCG and AFP are commonly seen with extragonadal nonseminomatous neoplasms. Although mediastinal germ cell tumors have been well described, invasion into the pericardium and resultant malignant pericardial effusion is a rare phenomenon which has been the topic of sporadic case reports involving mainly pediatric patients [6, 7]. We present a rare care of intrapericardial EGGCT and presented concomitantly with malignant pericardial effusion.

CASE REPORT

A 26-year-old white construction worker with a remote history of asthma presented to the emergency department with a chief complaint of chest pain. He had been seen 2 months prior with similar chest pain which was attributed to musculoskeletal injury versus costochondritis after acute coronary syndrome was ruled out, and he was discharged with non-steroidal anti-inflammatory medications (NSAIDs). On re-evaluation two months later, he also reported associated dyspnea on exertion, fever, night sweats, and weight loss. A computed tomography (CT) scan of the chest showed a large 10.5 cm mediastinal mass compressing the main pulmonary artery with a large pericardial effusion with invasion into the pericardium (Fig. 1). Transthoracic echocardiogram showed a large pericardial effusion without tamponade physiology. He underwent pericardiocentesis with pericardial drain placement and biopsy of the pericardium and intrapericardial mass. On the fifth day of hospitalization, the patient developed sudden onset dyspnea with associated hypoxia. CT angiogram of the chest to assess for acute pulmonary embolism was negative, but did show progressive compression of the pulmonary vasculature with 95% stenosis of the main pulmonary artery.

The patient underwent one fraction of emergent radiation therapy with symptomatic improvement. Labs revealed elevated AFP (341), elevated LDH (742), and normal hCG, CEA, and beta-2 microglobulin levels (Table 1). Cytology was consistent with a malignant pericardial effusion, and pathology resulted as a mixed malignant germ cell tumor with yolk sac tumor (70%), embryonal carcinoma (20%) and mature teratomatous component (10%). Immunohistochemistry (IHC) showed C-kit positive, SALL-4 negative, Calretinin negative, CD30 negative

Figure 1: CT chest with IV contrast on presentation, showing mediastinal mass of 10 cm with compression of main and left pulmonary arteries.

and OCT-4 negative. Further workup, including testicular ultrasound, CT abdomen and pelvis, and MRI brain showed no evidence of intratesticular tumor or metastatic foci, confirming the diagnosis of an EGGCT. The patient was promptly started on chemotherapy with bleomycin, etoposide and cisplatin (BEP) with the intention of surgical resection following reduction in the size of the tumor. Pre-chemotherapy pulmonary function tests (PFTs) revealed a moderate restrictive pattern, and subsequent PFTs showed no evidence of bleomycin-induced lung injury.

On completion of four cycles of BEP, a CT scan of the chest was done which showed interval decrease in size of the mediastinal mass with a new spiculated left upper lobe nodule concerning for metastatic disease (Fig. 2). Cardiac MRI showed pericardial and epicardial fat invasion along the anterior right ventricle abutting the main and left pulmonary arteries without evidence of myocardial invasion. He underwent cardiothoracic surgery for tumor resection, which revealed tumor invasion into the pericardium adherent to the epicardium, invasion into the left atrial appendage, invasion into the left hilum and invasion in the left pulmonary artery; and underwent tumor resection, lingular-sparing left upper lobectomy, pericardial resection with Gore-tex mesh reconstruction, left atrial resection and lung adhesionolysis.

Post-operatively, his course was complicated by acute hypoxic respiratory failure secondary to acute respiratory distress syndrome (ARDS), bleomycin-induced lung toxicity, and multidrug resistant pseudomonal pneumonia requiring intubation and mechanical ventilation. He was treated with high-dose steroids and *N*-acetylcysteine followed by imatinib, restrictive FiO_2 ARDSNET mechanical ventilation, and broad spectrum antibiotics. He continued to deteriorate, and extracorporeal life support management (VV-ECMO) was initiated on post-operative Day 11. His overall prognosis remained poor without suggestion of lung recovery after a prolonged period of VV-ECMO. Multiple goals of care discussions with the patient and family resulted in the patient opting to pursue comfort care, and he passed away comfortably on post-operative Day 50.

DISCUSSION

This case is an example of a nonseminomatous extragonadal germ cell tumor initially presenting as chest pain with a pericardial invasion and associated effusion. In young patients such as this one, musculoskeletal chest pain is a common etiology of chest pain, especially in patients without cardiovascular risk factors. In addition to thorough cardiac workup to evaluate for life threatening etiologies of chest pain, imaging with echocardiogram and CT scan are important in identifying pericardial or mediastinal mass lesions, especially in patients in whom the history suggests malignancy may be a possibility.

There are numerous malignancies which can be found in the mediastinum, and the differential diagnosis is affected by the area of the mediastinum (anterior, middle or posterior) in which the tumor is found [8]. The differential diagnosis of anterior mediastinal masses is quite broad, encompassing thymic lesions (most common), germ cell tumors (seminomas, nonseminomas, or benign such as dermoid cysts), teratomas, lymphomas and ectopic thyroid [8]. For mediastinal germ cell tumors, nonseminomatous germ cell tumors have the lowest 5-year survival rate (45–48%) [4], far less than seminomas or teratomas.

A review of the literature reveals that a pericardial effusion is an extremely rare initial site of diagnosis or site of metastasis for malignancy. There have been sporadic case reports of a variety of
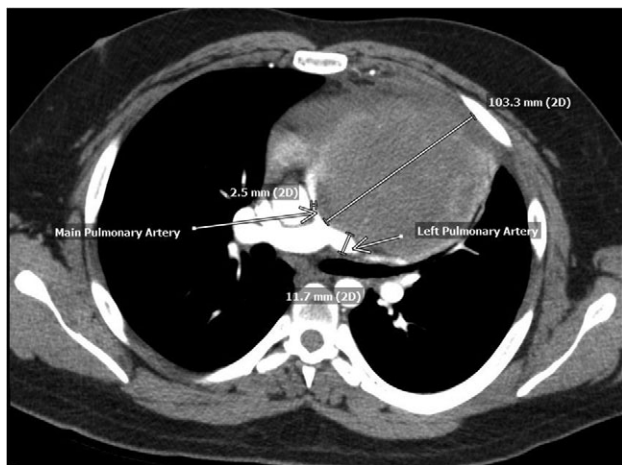
Table 1: International Germ Cell Cancer Collaborative Group (IGCCCG) risk stratification system for nonseminomatous germ cell tumors

	Primary tumor site	Serum beta-hCG (mIU/mL)	Serum AFP (ng/mL)	LDH
Good risk	Testicular or retroperitoneal	Beta-hCG < 5000$^\Delta$	AFP < 1000$^\Delta$	LDH < 1.5 × ULN
Intermediate risk	Testicular or retroperitoneal	Beta-hCG 5000–50 000	AFP 1000–10 000	LDH 1.5 to 10 × ULN$^\Delta$
Poor risk	Mediastinal primary with or without metastases$^\Delta$ or metastases to organs other than the lungs and/or LN	Beta-hCG > 50 000	Serum AFP > 10 000	LDH > 10 × ULN

AFP, alpha-fetoprotein; beta-hCG, beta-human chorionic gonadotropin; LDH, lactic dehydrogenase; ULN, upper limit of normal; LN, lymph nodes; mIU/mL, milliinternational units/mL.

$^\Delta$Indicates risk variables demonstrated by our patient's tumor.

Adapted from International Germ Cell Cancer Collaborative Group. International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol*. 1997;15:594–603.
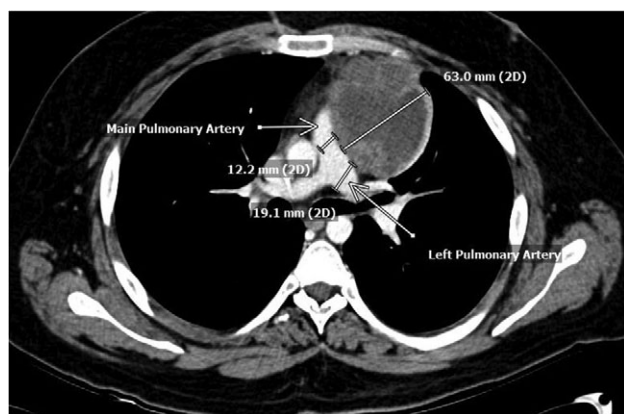
Figure 2: CT chest with IV contrast after cytoreductive radiation therapy and four cycles of BEP chemotherapy. Size reduction in the mass and a lesser mass effect on pulmonary vasculature is appreciated.

tumors involving the pericardium, most frequently teratomas. After teratomas, a multitude of tumors have been reported to cause pericardial effusions, including paraganglioma, leukemia, schwannoma, carcinoid tumor, primitive neuroectodermal tumor, rhabdoid tumor, pheochromocytoma, melanoma and extragonadal germ cell tumors [6, 9, 10]. It is important to that all of these, including nonseminomatous germ cell tumors, are extremely rare causes of pericardial effusion, with none of these having been shown to cause more than a handful of cases via literature review of case reports, retrospective analyses or meta-analyses. It has been shown that in patients with malignant pericardial effusions, 87% had a prior history of malignancy [11]. However, pericardial effusion is very rarely the first manifestation of malignancy. This highlights the importance of the fact that a proper workup and differential diagnosis are paramount in the evaluation of chest pain, especially with those in whom the history suggests that malignancy may be possible.

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None.

CONFLICT OF INTEREST STATEMENT

On behalf of all authors, the corresponding author states that there is no conflict of interest.

ETHICAL APPROVAL

N/A.

CONSENT

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

GUARANTOR

Dr Long H. Dang, MD, PhD.

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