

# Primary Mediastinal Embryonal Carcinoma Masquerading as Chronic Pancreatitis

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## ABSTRACT

Primary mediastinal embryonal cell carcinomas are aggressive tumors commonly presenting between the ages of 20-50 years with pulmonary symptoms (e.g., cough, chest pain, and hemoptysis), as well as extrapulmonary symptoms due to pressure on adjacent structures. Here we describe a 72-year-old man who remained undiagnosed for a prolonged period of time because of intractable epigastric pain. The patient was thought to have chronic pancreatitis for several months until a chest computed tomography scan demonstrated the mass. This case exemplifies that embryonal cell carcinoma may present in older age groups. It also illustrates the importance of including mediastinal tumors in the differential diagnosis of chronic epigastric pain and the need for further investigations to identify these tumors.

## CASE REPORT

A 72-year-old man presented with a 6-month history of multiple hospital admissions for epigastric pain associated with nausea and vomiting. The pain was dull, severe, intermittent, and radiated in a band-like fashion across the upper abdomen to the back. The pain was not associated with meals and was relieved only by oral morphine. The patient also complained of episodes of nausea and vomiting 2 days prior to the admission. He had regular bowel movements, and occasional reflux symptoms, but no hematemesis or melena. He denied any cough, chest pain, or shortness of breath. He had

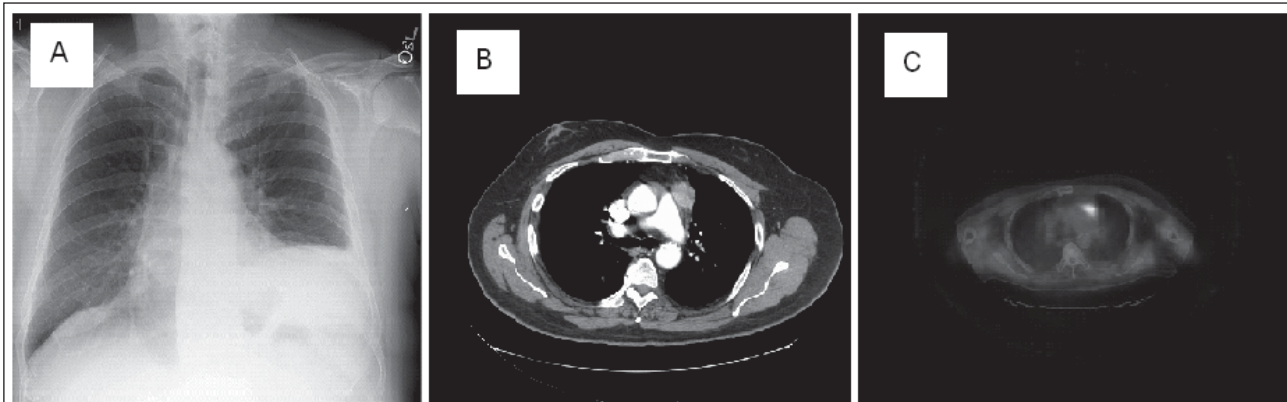
been worked-up in the previous months at 2 different hospitals in California, where he was visiting his daughter a few months prior. No computed tomography (CT) scan was done at either hospitalization, and as the results of prior tests were inconclusive, he was given different diagnoses including pancreatitis and referred spinal pain. As we did not agree with his prior diagnosis of pancreatitis due to lack of elevation in amylase or lipase in previous hospital admissions, we decided to do a complete work-up for epigastric pain.

The patient's past history included essential hypertension, diabetes mellitus type II, hyperlipidemia, paroxysmal atrial fibrillation, and a history of lower back surgeries. He had a 40-pack-a-year smoking history and had quit 15 years ago. He denied any alcohol or drug abuse. His family history was noncontributory. His medications included hydrochlorothiazine, lisinopril, metoprolol, coumadin, simvastatin, gemfibrozil, metformin, protonix, long-acting morphine pills, and oxycodone. The patient denied any weight loss prior to admission. His ECOG (Eastern Cooperative Oncology Group) performance status was 1, with limited ability for strenuous activity due to his chronic lower back pain.

Physical examination only revealed epigastric and right upper quadrant tenderness. Laboratory tests showed elevated blood glucose and a high serum triglyceride level of 400 mg/dl, but normal calcium, and normal liver and pancreatic enzymes (lipase 169, amylase 38). His hemogram, complete metabolic panel, and C-reactive protein levels were within normal limits. On comparison, these results were similar to his laboratory test results at the prior hospitalizations. An erythrocyte sedimentation rate (ESR) was not performed. A chest radiograph on admission showed elevation in left hemidiaphragm with a questionable left subdiaphragmatic abscess (Figure 1A). This finding was absent from his previous chest x-ray 2 months prior to admission. To better define the nature and location of this mass, an abdominal CT scan was ordered, which was negative

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**Figure 1A.** Chest X-ray PA (postero-anterior view) showing persistent left hemidiaphragm elevation. **Figure 1B.** Chest CT showing a 2.8 x 3.7 cm anterior mediastinal mass. **Figure 1C.** A transaxial PET scan image showing a markedly hypermetabolic mass in the prevascular space without metastasis.

for abdominal abscesses or pancreatic pseudocysts, and only showed hepatic steatosis (Figure 1B).

Fluoroscopy of the diaphragm (sniff test) confirmed left hemidiaphragm paralysis, and a chest CT scan was done (Figure 1B), which showed a 2.8 x 3.7 cm soft tissue mass in the left mediastinal prevascular space, with left lower lobe atelectasis. Due to the proximity of the mass to important vascular structures, it was decided to perform a whole-body positron emission tomography (PET) scan to identify other lesions before a biopsy was performed. The PET scan (Figure 1C) demonstrated a markedly hypermetabolic prevascular mediastinal mass, highly suspicious for malignancy. There was no other evidence of fluorodeoxyglucose (FDG)-avid malignancy or metastasis on the PET scan. Mediastinoscopy demonstrated that the mass was attached to the parietal pericardium and left upper lobe parenchyma, and encased the left phrenic nerve.

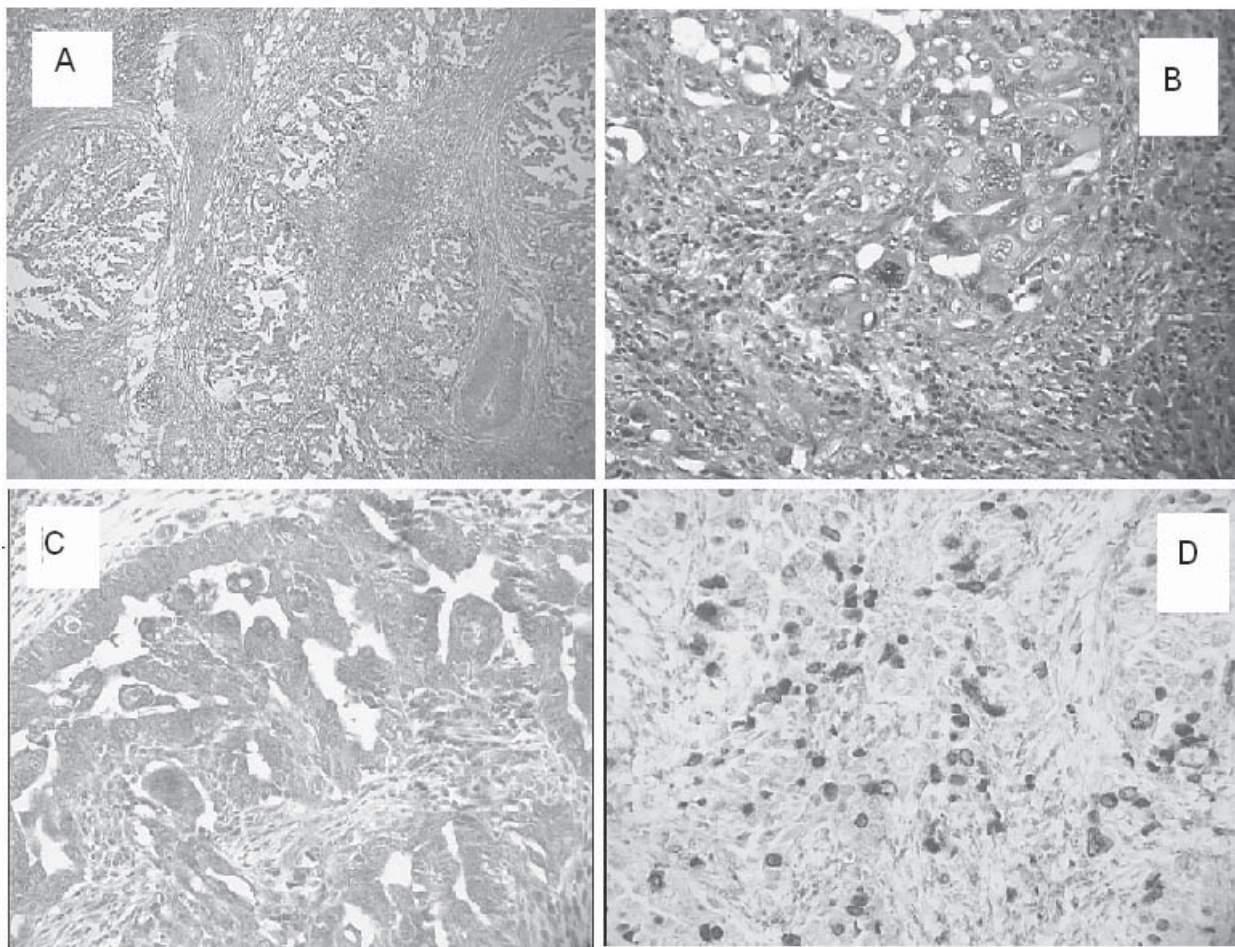
### **PATHOLOGIC FINDINGS**

An intraoperative frozen section of the mass on preliminary examination demonstrated adenosquamous cells of thymic origin, suggestive of primary thymic carcinoma. After complete surgical resection, the final pathology report determined that the tumor was 4 cm in greatest dimension, multinodular, and abutted but did not invade the pericardium or lung parenchyma. Microscopically (Figures 2A and B), the tumor demonstrated extensive necrosis, with irregular lobular aggregates distributed within small lymphocytic fibrous stroma. The tumor was composed of large, polygonal tumor cells arranged mostly in tubular papillary structures with vesicular, hyperchromatic nuclei and prominent nucleoli. Also seen were large multi-nucleated bizarre cells, and mitoses with focal atypical forms.

On immunohistochemical staining, the tumor cells were positive for placental-like alkaline phosphatase (PLAP; figure 2C), Ki-67 (figure 2D), CK-7, and AE1/AE3, and negative for Vimentin, CK-20, CD5, mucin, and alpha-fetoprotein (AFP). CD-30 staining was focally positive. PLAP and CD-30 are often positive in embryonal cell carcinomas, hence this result, along with the tumor morphology, was diagnostic of an embryonal carcinoma. However, a primary testicular tumor with mediastinal metastasis had to be ruled out. This prompted a testicular ultrasound, which was negative for any testicular mass. Serum lactate dehydrogenase (LDH) level was normal. Other serum tumor markers were also checked, including carcinoembryonic antigen (CEA), which was slightly elevated at 4.5, but AFP and beta-human chorionic gonadotropin ( $\beta$ -hCG) were normal. Thus the final diagnosis was primary anterior mediastinal embryonal carcinoma.

### **MANAGEMENT**

Due to the initial impression of thymic carcinoma from the frozen section, the patient underwent extensive primary resection of the tumor, along with partial thymectomy, resection of part of the left upper lung lobe and pericardium, and plication of the left hemidiaphragm. His postoperative course was complicated by pericardial tamponade, requiring a pericardial window. After resolution of his acute events, he was evaluated by the medical oncology service. As primary mediastinal non-seminomatous germ cell tumors fall into the poor risk category of the new International Germ Cell Consensus Classification,<sup>1</sup> adjuvant systemic chemotherapy using a cisplatin-based regimen was suggested to the patient. However, he refused chemotherapy and decided to have regular clinic follow-ups only. He had multiple follow-up CT scans that did not demonstrate any metastases,



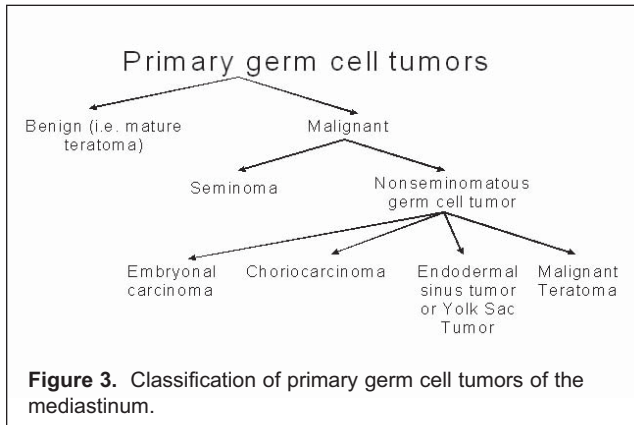
**Figure 2A and 2B.** Embryonal carcinoma. The tumor demonstrates glandular, tubulopapillary structures with focal necrosis (Fig. 2A. H&Ex40). Tumor cells are large and polygonal with vesicular nuclei, prominent nucleoli, and occasional bizarre giant cells and mitoses (Fig. 2B, H&E x200). **Figure 2C and D.** Immunohistochemical staining indicating that the tumor cells are positive for placental-like alkaline phosphatase (PLAP, Figure 2C x200), expressed in the cytoplasm, and Ki-67, which reacts in the nuclei (Fig. 2Dx200).

until his most recent scan (8 months after tumor resection), which showed a new left hilar lymph node suspicious for tumor recurrence. He was to continue with symptomatic management and follow up CT scans, as he still refused any systemic chemotherapy.

**DISCUSSION**

Primary germ cell tumors account for approximately 15% of anterior mediastinal tumors in adults and 24% in children.<sup>2-5</sup> Germ cells migrate from the urogenital ridge to the gonads during early embryonic development, and primary mediastinal germ cell tumors appear to arise from the rest of these cells that fail to migrate completely. Primary mediastinal germ cell tumors lack some elements of gonadal histology and are distinguishable from metastatic gonadal germ cell neoplasms in adults, or sacrococcygeal tumors in children.<sup>6-10</sup>

Primary germ cell tumors are classified into benign type including mature teratomas and malignant type tumors, which are further divided into seminomas and nonseminomatous germ cell tumors (Figure 3).<sup>11,12</sup> These are all usually seen between the ages of 20-50 years.<sup>4,13</sup> The different nonseminomatous germ cell tumors are grouped together due to similar therapeutic and prognostic implications. These include embryonal carcinomas, choriocarcinomas, endodermal sinus tumors, and malignant teratomas, and are 6 times more common in men than in women.<sup>11</sup> They usually contain multiple malignant cell types, probably due to the totipotent nature of the germ cell of origin.<sup>14,15</sup> These are aggressive tumors and are usually invasive and symptomatic at diagnosis, commonly presenting with chest pain, cough, weight loss, and hemoptysis,<sup>10</sup> none of which were seen in our patient.



The standard treatment for primary mediastinal non-seminomatous germ cell tumors is upfront chemotherapy using a cisplatin-based regimen such as bleomycin-etoposide-cisplatin (BEP) every 3 weeks. After 4 cycles of BEP regimen, the patient requires restaging with tumor markers and a CT scan. If the tumor markers are normalized, but the CT scan shows residual tumor, the patient needs to undergo complete surgical resection. If the resected tumor shows active disease, 2 additional cycles of chemotherapy are indicated, but if the resected tumor only demonstrates necrosis, no additional chemotherapy is needed. With this approach, 40%-45% of patients may have long-term survival.<sup>16-19</sup> For patients who undergo upfront complete surgical resection, there is no standard adjuvant treatment to follow. However, given that the risk of systemic involvement in primary mediastinal nonseminomatous germ cell tumors is very high, post-operative adjuvant cisplatin-based chemotherapy is a reasonable treatment option to follow.

**CONCLUSION**

This case is unique because the patient had an atypical presentation with epigastric pain, which was almost completely relieved after removal of the mass. This indicated it was possibly referred from the tumor. The patient was worked up several times for pancreatitis in the past. The lack of elevation of lipase and liver function tests, the absence of etiologic factors that could induce pancreatitis, and the finding of an elevated hemidiaphragm prompted us to work him up further for other etiologies of intractable epigastric pain. Although the embryonal cell tumor was small, it was aggressive and had already demonstrated local spread with phrenic nerve involvement. The elevation of tumor markers usually helps in the diagnosis, but our patient did not have any elevated tumor markers such as AFP or  $\beta$ -hCG, which are usually found in 80%-85% of patients with this tumor.<sup>20</sup> Thus, the case was a diagnostic challenge, and it illustrates the

importance of considering mediastinal tumors in the differential diagnosis of chronic abdomen pain.

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