

CASE REPORTS

Extragenadal yolk sac tumor (endodermal sinus tumor) presenting with biliary tract obstruction in a woman

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Abstract

A 35-year-old woman presented to her primary care physician with early satiety, weight loss, nausea, vomiting, and pruritus. She was eventually found to have a pancreatic mass obstructing the bile duct. The mass was evaluated by endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) with biopsy. Histopathology results revealed a high grade malignant neoplasm of uncertain type. The tumor was further characterized by open biopsy, which revealed a yolk sac tumor (endodermal sinus tumor). Her disease was unresectable. Serum alpha-fetoprotein (AFP) levels were markedly elevated (693.3 ng/ml; reference range: 0-8 ng/ml). The patient was treated with bleomycin, etoposide, and cisplatin (BEP) with a partial response and a persistently elevated serum AFP of 139.7 ng/ml. She then received salvage chemotherapy with paclitaxel, ifosfamide, and cisplatin (TIP), with a minimal response (serum AFP, 68 ng/ml). She next received an autologous bone marrow transplant, with a decline in AFP to 19 ng/ml after the first of two tandem transplants. This case report illustrates a rare presentation of an extragenadal endodermal sinus tumor in a woman with biliary tract obstruction as the predominant manifestation.

Keywords

Extragenadal germ cell tumor, Yolk sac tumor, Endodermal sinus tumor, Biliary obstruction

1 Introduction

Extragenadal nonseminomatous malignant germ cell tumors are rare and include choriocarcinomas, embryonal carcinomas, endodermal sinus tumors (yolk sac tumors), malignant teratomas, and mixed germ cell tumors. In women, endodermal sinus tumors are extremely rare ^[1]. These tumors typically occur in men between the ages of 20-30 years ^[2] and arise in the testes (gonadal) or along the urogenital ridge (extragenadal). Extragenadal endodermal sinus tumors may cause symptoms including chest pain, cough, shortness of breath, fever, weight loss, night sweats or the superior vena cava syndrome ^[1, 3-5]. We present a unique case of a 35-year-old female with an endodermal sinus tumor adjacent to the pancreas presenting with biliary tract obstruction.

2 Case report

A 35-year-old previously healthy woman developed early satiety, a 30 pound weight loss, nausea, vomiting, and generalized pruritus. She was evaluated by her primary care physician and found to have an elevated total serum bilirubin level of 2.5 mg/dl, alkaline phosphatase of 526 U/L, AST 147 U/L, and ALT 291 U/L (see Table 1).

Table 1. Patient Laboratory Findings *

Serum Analyte	June 9, 2014	June 13, 2014	June 20, 2014	Reference Range (Outside Laboratory)	August 1, 2014	Reference Range
Bilirubin, Total (mg/dl)	2.5	4.8	9.4	0.0-1.5	1.4	0.2-1.2
Alkaline Phosphatase (U/L)	526	468	625	10 -130	101	0-98
AST (U/L)	147	215	198	5-34	28	< 30
ALT (U/L)	291	346	257	5-41	30	1-34
LD (U/L)					306	125-275
AFP (ng/ml)					693.3	0-8
beta HCG (IU/L)					< 1	0-5

* The following studies were nonreactive or negative on 6/13/2014 or 6/20/2014: hepatitis A virus IgM, hepatitis B virus core IgM, hepatitis B surface antigen, hepatitis C antibody, serum ferritin, antinuclear antibodies, Epstein Barr virus antibody and Monotest.

Abdominal ultrasonography showed a contracted gallbladder and a bile duct diameter of 2 mm with no intrahepatic biliary dilatation. She was referred to a gastroenterologist who recommended a liver biopsy. Three weeks later, she was scheduled for a sonography-guided percutaneous liver biopsy. However, the pre-biopsy ultrasonographic images now revealed a nearly 4 cm pancreatic mass (see Figure 1A); this mass had not been present on the earlier study. Liver biopsy was therefore deferred. CT scan revealed dilated intrahepatic bile ducts, two distinct masses adjacent to the head of the pancreas (see Figure 1B), and lymphadenopathy in the porta hepatis area. She underwent ERCP with biliary stenting and EUS-guided biopsy of the mass. Initial biopsy results showed a poorly differentiated carcinoma (non-small cell, non-squamous cell). She was subsequently admitted for port placement and laparoscopic biopsy of the mass for further histopathological characterization of the tumor.

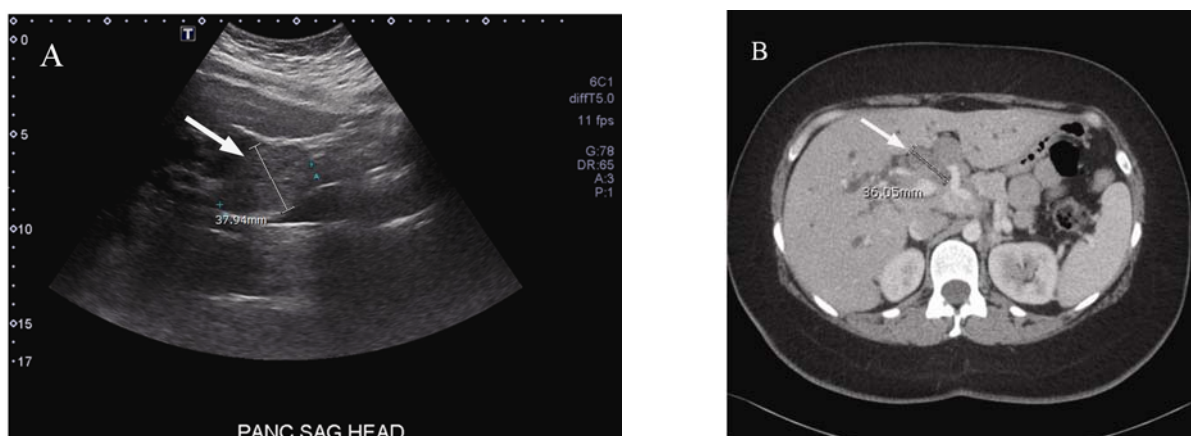


Figure 1. Tumor imaging. A: Ultrasonography of pancreatic mass (arrow); B: CT showing mass adjacent to the pancreas (arrow). The mass was nearly 4 cm in diameter

Physical examination revealed a well-developed female. Blood pressure was 116/60 mmHg, pulse was regular at 62 beats per minute, temperature was 97.8 °F, and oxygen saturation was 100% on room air. Her cardiovascular, pulmonary, and musculoskeletal exams were normal. Abdominal examination was significant for only mild epigastric tenderness without

hepatosplenomegaly. No masses were palpable. At the time of hospital admission on August 1, 2014, laboratory exam revealed a white blood count of 5,150 per mm³ and a hemoglobin level of 10.9 g/dl. The total serum bilirubin level was now 1.4 mg/dl, and the serum alkaline phosphatase, AST, and ALT levels were 101, 28, and 30 U/L, respectively (see Table 1). Renal function was normal. Her disease was unresectable due to significant portal vein involvement. Laparoscopic biopsy of the tumor showed a neoplasm that was immunoreactive to cytokeratin, alpha fetoprotein (AFP), glypican-3, and SALL4 (see Figure 2), diagnostic of an endodermal sinus tumor. After the biopsy result was obtained, a serum AFP was found to be elevated at 693.3 ng/ml (reference range: 0-8 ng/ml); the serum β -HCG level was undetectable (< 1 IU/L).

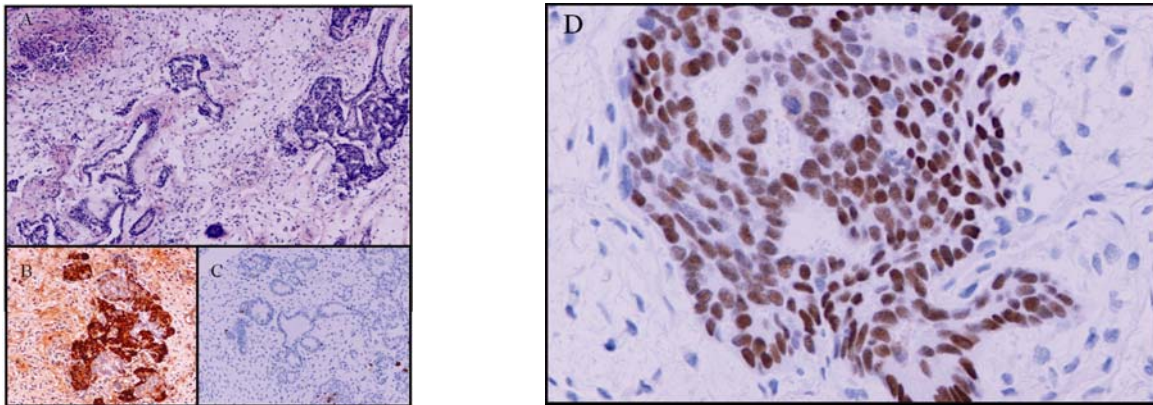


Figure 2. Tumor histopathology. A: Hematoxylin and eosin stain. High power view demonstrating formed glands and tubules with a myxoid stroma; B: Positive alpha fetoprotein immunostain; C: Negative Oct 3/4 immunostain; D: Positive SALL4 immunostain

She was treated with four cycles of bleomycin, etoposide, and cisplatin (BEP) with a partial response. However, tumor progression was seen on follow up imaging, in addition to a persistently increased serum AFP level of 139.7 ng/ml. She was then given salvage chemotherapy with paclitaxel, ifosfamide and cisplatin (TIP), with a suboptimal response (AFP, 68 ng/ml).

Given that she still had active disease with no further treatment options, she is currently undergoing tandem (2-step) autologous bone marrow transplantation and has already experienced a decrease in her serum AFP to 19 ng/ml after the first of two planned autologous stem cell transplants. The conditioning regimen used on both steps was G-CSF in combination with cyclophosphamide (G-Cy). The chemotherapy agents used on both steps were high dose cisplatin and etoposide.

3 Discussion

Our patient presented with signs of biliary tract obstruction from an extragonadal germ cell tumor located in the pancreatic head region, which has not previously been reported in endodermal sinus tumors. We are aware of only 3 cases of gonadal or extragonadal germ cell tumors involving the pancreas. In 2004, L. Wang *et al.* reported a 54-year-old man with a mixed testicular germ cell tumor (a seminoma with focal teratoma) with pancreatic metastases resembling a choriocarcinoma as the main clinical manifestation of his disease [6]. In 2010, Schmidt reported a 74-year-old man with obstructive jaundice due to an extragonadal embryonal cell carcinoma with periportal lymph node involvement; serum AFP and beta HCG were normal [7]. Finally, in 2013, J. Wang *et al.* reported a 12-month-old girl with a mixed extragonadal germ cell tumor (endodermal sinus tumor plus teratoma) arising in the head of the pancreas and causing obstructive jaundice and associated with a markedly elevated serum AFP level > 2,000 ng/ml [8]. Ours is the first case report of a woman presenting with biliary obstruction as the initial sign of an endodermal sinus tumor.

Extragonadal germ cell tumors typically originate along the midline. Presenting symptoms may include chest pain, cough, and shortness of breath in thoracic disease and abdominal pain, weight loss and fever in abdominal disease. Endodermal sinus tumors are a very rare type of nonseminomatous germ cell tumor, particularly in women^[9]. They typically occur in males between the ages of 20-30 years^[2]. Germ cell tumors much more commonly arise in gonadal tissues (ovaries or testes) while extragonadal germ cell tumors are hypothesized to originate from germ cells that do not undergo normal migration along the urogenital ridge or that undergo reverse migration^[2, 5, 10]. The most common site for extragonadal germ cell tumors is the anterior mediastinum, which can cause cough, chest pain, shortness of breath, fever, and weight loss^[1-5]. When the initial presentation appears to be extragonadal, evaluation must exclude a primary gonadal carcinoma in situ since extragonadal metastases are common at time of presentation^[2, 6, 11]. Primary gonadal tumors have been reported to undergo necrosis or “burn out”, with resultant presenting symptoms being extragonadal metastasis^[2, 3, 6]. Due to this concern, it is sometimes recommended that the affected patient undergo prophylactic oophorectomy or orchiectomy.

There is an increased risk of a variety of hematologic disorders in patients with extragonadal germ cell tumors including acute myelogenous leukemia, myelodysplasia, systemic mastocytosis, and histiocytosis X (Langerhans cell histiocytosis)^[12, 13]. These conditions may present synchronously or within the first 6 months after diagnosis of the extragonadal germ cell tumor. They are associated with isochromosome 12p^[5]. Endodermal sinus tumors contain AFP and, when more than one cell line is present (mixed tumors), the tumor may also produce β -HCG^[9, 11] (see Table 2). On microscopy, the tumors often have Schiller-Duval bodies, a glomerulus-like blood vessel surrounded by tumor cells. The tumor may demonstrate a microcystic or reticular pattern^[14].

Table 2. Extragonadal Germ Cell Tumor Markers^[14-17, 19]

	Serum AFP	Serum β -HCG	Tumor PLAP	Tumor Gypican-3	Tumor CD30	Tumor SALL4	Tumor Oct3/4	Tumor NANOG	Tumor SOX2	Tumor UTF1	Tumor TCL1
Seminoma	-	-	+	-	-	+	+	+	+	+	+
Yolk Sac Tumor	+	-	+/-	+	-	+	-	-	-	-	-
Embryonal Carcinoma	+	-	+/-	-	+	+	+	+/-	+	+	-
Pure Teratoma	+	-	-	-	-	+/-	-	-	+	-	-
Chorio- carcinomas	-	+	-	-	-	-	-	-	-	-	-

Nonseminomatous germ cell tumors are typically very sensitive to chemotherapy agents, and thus radiation therapy is not typically recommended as first line therapy. Endodermal sinus tumors are especially sensitive to cisplatin-based chemotherapy regimens^[2, 4, 7, 8, 15, 16]. Typical treatment regimens include bleomycin, etoposide, and cisplatin (BEP) for four cycles. Baseline pulmonary function tests must be obtained before using bleomycin and, if bleomycin is contraindicated due to underlying lung disease, alternate treatment regimens may include ifosfamide in place of bleomycin, with or without stem cell transplant^[4, 12, 17]. Patients such as our patient who are resistant to initial BEP therapy have a worse prognosis^[18]. Debulking surgery is not initially recommended^[15, 18], but if repeat serum tumor markers, such as AFP, remain elevated or increase with residual bulky disease on imaging studies, surgical resection, if the tumor is deemed resectable, and two additional cycles of chemotherapy are recommended^[19].

The utility of autologous stem cell transplantation is not well-established for chemotherapy-resistant disease. However, her disease seems to be responding to this therapy so far, although the response has not been brisk.

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