Chirurgia (2010) 105: 831-834
Nr. 6, Noiembrie - Decembrie

A mediastinal germ cell tumor of Yolk sac type - case report

G. Tinica[1], D. Butcovan[2], C. Cîmpeanu[3], E. Târcoveanu[4]

[1]Cardiovascular Surgery Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iaşi
[2]Morphopathology Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iaşi
[3]Department of Surgery, 3rd Surgical Clinic, "Sf. Spiridon" Emergency Clinical Hospital, Iaşi
[4]Department of Surgery, 1st Surgical Clinic, "Sf. Spiridon" Emergency Clinical Hospital,
"Gr. T. Popa" University of Medicine and Pharmacy, Iaşi

Rezumat

Tumoră cu celule germinale tip Yolk sac - prezentare de caz

Obiectiv: Raportăm un caz extrem de rar de tumoră cu celule germinale localizată la nivelul mediastinului anterior. Este cazul unui bărbat de 36 de ani care s-a prezentat cu tromboză de venă subclavie stângă şi a fost admis pentru tratament de specialitate. Tomografia computerizată toracică a relevat o masă tumorală mare în mediastinul anterior. Intervenţia chirurgicală a evidenţiat o tumoră infiltrativă mediastinală cu implicarea venei subclavii stângi, care a fost biopsiată pentru examinare morfologică. Histologic, masa tumorală s-a dovedit a fi un carcinom, cu mod de creştere papilar şi tubular. Examenul imunohistochimic a relevat imunoreactivitate pozitivă pentru alfa-fetoproteina în celulele tumorale si negativă pentru antigenul carcinoembrionar şi fosfataza alcalină placentară. Nivelul seric al alfa-fetoproteinei la acest pacient a fost, de asemenea, ridicat. Acest lucru a susţinut diagnosticul de tumoră Yolk sac, care este o tumoră primară rară în mediastin. Post-chirurgical, pacientul a primit o combinaţie chimioterapică constând din cisplatină, vespezid şi bleomicină, fiecare timp de 3 săptămâni, în total 4 cicluri. În timpul tratamentului, nivelul alfa-fetoproteinei, a fost în scădere.
Concluzie: Tumora Yolk sac primară mediastinală este o tumoră rară. Diagnosticul ar trebui să fie făcut nu numai pe studii morfologice, dar, de asemenea, luând în considerare vârsta pacientului şi nivelul seric crescut al alfa-fetoproteinei. În ciuda chimioterapiei moderne, prognosticul tumorii Yolk sac mediastinale rămâne sumbru. Cel mai important indicator prognostic este excizia completă a masei tumorale înainte de chimioterapie.

Cuvinte cheie: tumora cu celule germinale, tumora Yolk sac, tumora sinusului endodermic

Abstract

Objective: We report an extremely rare case of germ-cell tumor localized at the level of the anterior mediastinum. Clinical presentation: A 36-year-old man who presented with left subclavial vein thrombosis was admitted to our hospital for specific cure. Computed tomographic scan of the chest showed a large anterior mediastinal mass. Surgical intervention revealed an infiltrative mediastinal tumor involving the left subclavial vein, which was biopsied for morphological examination. Histologically, the tumoral mass proved to be a carcinoma, with papillary and tubular growth patterns. Immunohistochemical stains for alpha-fetoprotein were positive in the tumor cells while stains for carcinoembryonic antigen and placental like alkaline phosphatase were negative. The serum level of alpha-fetoprotein of this patient was elevated, as well. This supported the diagnosis of Yolk sac tumor, a rare primary tumor within the mediastinum. Post-surgery, the patient received a combination chemotherapy consisting of cisplatin, vespezid and bleomycin every 3 weeks for a total of 4 cycles. During the treatment, the alpha-fetoprotein level, was decreasing. Conclusion: Primary mediastinal Yolk sac neoplasm is a rare tumor. The diagnosis should be

Corresponding author: Dr. Doina Butcovan
Catedra de Morfopatologie
U.M.F. "Gr. T. Popa"
Str. Universităţii 16, 700115, Iasi, România
E-mail: butcovan@yahoo.com

made not only by morphological studies but also the patient's age and the elevation of serum alpha-fetoprotein. In spite of modern chemotherapy, the prognosis of mediastinal yolk sac tumor remains poor. The single most important prognostic indicator is whether the tumor mass can be completely excised before or after chemotherapy.

Key words: germ-cell tumor, yolk sac tumor, endodermal sinus tumor

Introduction

Yolk sac tumors (YST), also known as endodermal sinus tumors (EST), are uncommon malignant germ cell tumors, which are histologically similar to the yolk sac and its derivatives and, like them, tumor produce alpha-fetoprotein (AFP) (1,2). Most authors (1,2) have suggested that these tumors originate from germ cells, although other theories of histogenesis have also been proposed (3). Whereas most YSTs occur in the gonads, about 20% arise in extragonadal sites, including the mediastinum, sacrococcygeal region, cervix, vulva, pelvis, liver, prostate and retroperitoneum (4,5,6). The present paper reports a case of primary YST of the mediastinum, which is a rare location for these tumors.

Case report

A 36-year-old man was admitted to our hospital because of persistent cyanotic swollen of the left arm of 15 days duration, without any other medical history. Physical examination on admission identified a painless mass in the upper left chest area, the presence of which was confirmed by chest X-ray. Serum AFP and ß-hCG were determined: AFP was 369,2 ng/ml (<8 ng/mL), whereas ß-hCG was within the normal range (<5 mIU/mL). At chest CT scan (Fig. 1) was found an upper-anterior mediastinal mass. Scans of the liver, spleen, pancreas, kidney, bladder, uterus and ovaries were normal. The patient underwent surgery, which revealed a voluminous infiltrative mass. Subsequently, incomplete full resection of the tumor was made.

Macroscopically, an irregular, infiltrative bulky mass, measuring 20 ×13 cm, was found within the anterior mediastinum together with few reactive nodules, of 0.8-4.5 cm in diameter. On the cut surface, the tumor disclosed mainly solid-necrotic and, only at the margins, grayish, mixed solid soft tissue.

Histologically, we evidentiated an irregular microcystic structures, aligned by spindle cells, of various sizes were often seen fusing with each other to form a sinus structure (Fig. 2). The characteristic finding consisted of enlarged blood vessels, with cuboidal cells aligned radially toward the inner space of those vessels (Schiller-Duval bodies) (Fig. 3). As shown in Fig. 3, the eosinophilic particles (often called hyaline globules) were seen scattered both inside and outside of the cytoplasm of the tumor cells.

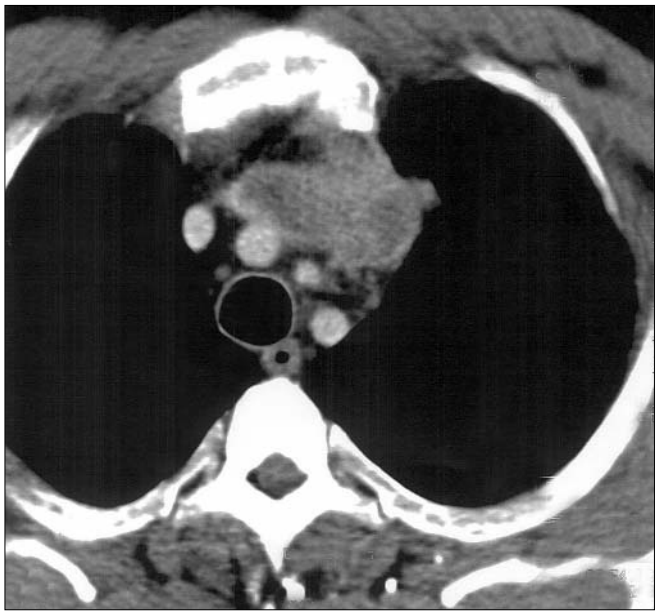

Figure 1. *Chest CT scan-mediastinal mass*

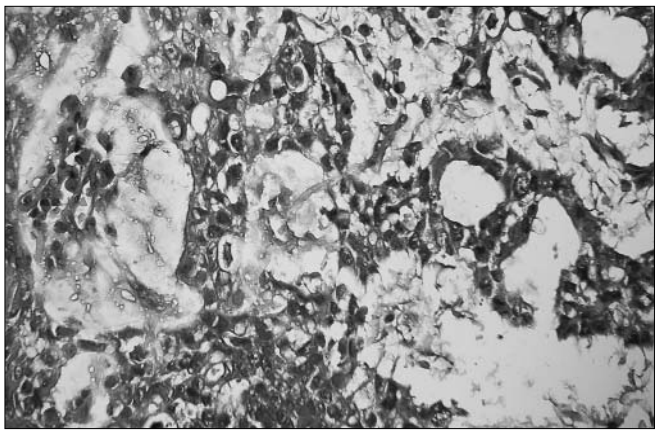

Figure 2. *YST reticular type, HE X 20*

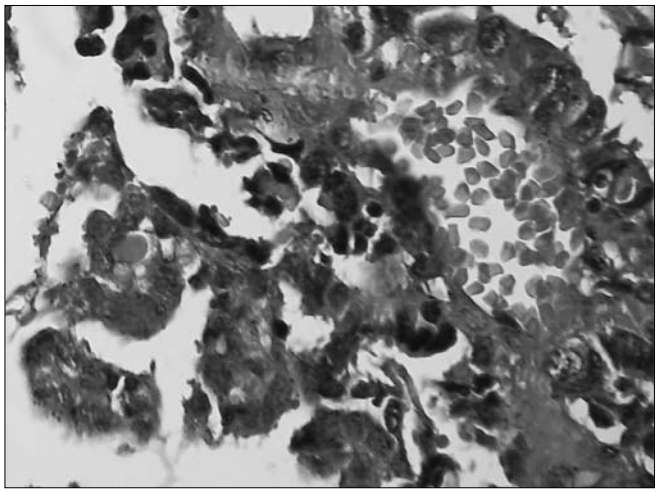

Figure 3. *YST endodermic sinus type, HE X 40*

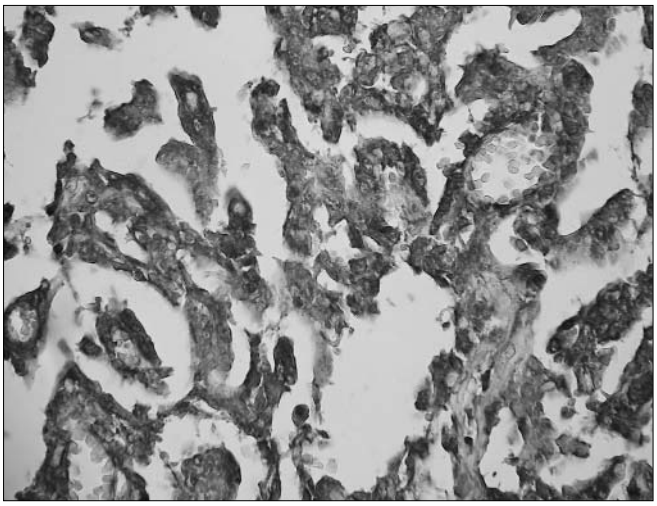

Figure 4. *Immunohistochimy - YST with AFP positive*

The immunohistochemical studies showed cellular positivity for AFP (Fig. 4), and focally for placental alkaline phosphatase, while vimentin, ß-hCG, antigen carcino-embrionar, smooth-muscle actine and CD34 were negative. The proliferation index, determined with Ki 67, was very high (about 70% in neoplastic cells).

Careful examination of the testis showed no neoplastic parenchymal involvement.

The final diagnosis was YST of the mediastinum with a predominant endodermal sinus histological growth pattern and some zones of reticular type, admixed with extensively necrotico-hemorrhagic areas.

One month after surgery, the patient underwent combined intravenous chemotherapy (PEB regimen) with cisplatin (20 mg/m 2 for 5 consecutive days), vespezid (100 mg/m 2 for 5 consecutive days) and bleomycin (18 mg on days 2, 9 and 16) every 3 weeks.

AFP determination before chemotherapy (34 days after surgery) was 129 ng/ml. After the first cycle, it dropped to 80 ng/ml and decreased more after the second.

Discussion

YST is a highly malignant neoplasm of germ cells that grows rapidly and metastasizes early via the lymphatic and hematogenous routes (7). Although it usually occurs in the gonads, it has been reported to arise primarily in structures within and outside of the genital tract (8). The anterior mediastinum is one the most common extragonadal locations (6).

Multiple histopathological sections studied showed a highly cellular tumor composed of round to ovoid cells with scant to moderate eosinophilic cytoplasm and prominent nucleoli (8,9). These cells are disposed in varying patterns: solid sheets, trabeculae, glandular arrangement, microcystic areas and with formation of Schiller-Duval bodies. Occasional intracytoplasmic and extracellular hyaline globules are present. Rare mitoses are observed. With these characteristic features and absence of other germ cell elements, a diagnosis of pur yolk sac tumor of the mediastinum can be made.

The histogenesis of extragonadal YST remains speculative and controversial. Three main hypotheses have been proposed to explain the existence of germ cell tumors in extragonadal sites (9,10). The first is an origin from germ cells that have been misplaced or arrested in their embryonic migration. During embryogenesis, the primitive gonadal ridge extends from the cranial cavity to the region of the external genitals. A remnant of tissue along the pathway of migration may be a site of a subsequent germ cell tumor. According to this hypothesis, the arrest of germ cell migration through the anterior mediastinum could explain the origin of the tumor in our case. A further hypothesis is that the tumor originates from an aberrant differentiation of somatic cells. This may be the case of YST occurring in the endometrium and stomach. The third mechanism is metastasis from an occult focus in the testis. In our case, histopathologic examination of the testis excluded this hypothesis.

Normal yolk sac and YST can synthesize keratin, albumin, AFP, alpha1-antitrypsin, transferrin and basement membrane components including fibronectin, type IV collagen, vimentin and laminin (9,10). In our patient, the tumor cells were positive for AFP, focally for placental alkaline phosphatase (PLAP), and negative for vimentin and CEA. Schiller Duval bodies were present being essential for the diagnosis (11).

Receiving the treatment, surgery alone is mostly unsuccessful in eradicating the tumor, even in stage I of the disease, and although YST do not respond to radiotherapy, they are sensitive to combined chemotherapy (12). Over the past 10-15 years, adjuvant treatment has produced better survival rates. Vincristine, actinomycin-D, cyclophosfamide, vinblastine, bleomycin and cisplatin have been used for the treatment of YST with good results. In our case, the patient received PEB regimen chemotherapy, which provided a marked improvement in the survival of patients with germ cell tumors.

Estimation of serum AFP is useful for diagnosis, monitoring the effectiveness of therapy and detection of recurrence prior to clinical manifestation (13). In our patient, it was still high before systemic treatment, but decreased to within the normal range after two cycles of therapy.

As regarding the prognosis, the patient is steel surviving. Previous studies in the literature reported a worse prognosis for extragonadal YST. The estimated event-free survival at 10 years after combined treatment is 80.4% (14). In our case, the quality of life 3 months after the surgical treatment is acceptable and there is no evidence of recurrence.

References

1. Truong LD, Harris L, Mattioli C, Hawkins E, Lee A, Wheeler T, et al. Endodermal sinus tumor of the mediastinum. Report of seven cases and review of the literature. Cancer. 1986;58(3): 730-9.
2. Talerman A, Haije WG, Baggerman L. Serum alphafetoprotein (AFP) in patients with germ cell tumors of the gonads and extragonadal sites: correlation between endodermal sinus (yolk

sac) tumor and raised serum AFP. Cancer. 1980;46(2):380-5.
3. Nogales-Fernandez F, Silverberg SG, Bloustein PA, Martinez-Hernandez A, Pierce GB. Yolk sac carcinoma (endoder-mal sinus tumor): ultrastructure and histogenesis of gonadal and extragonadal tumors in comparison with normal human yolk sac. Cancer. 1977;39(4):1462-74.
4. Hart WR. Primary endodermal sinus (yolk sac) tumor of the liver. First reported case. Cancer. 1975;35(5):1453-8.
5. Benson RC Jr, Segura JW, Carney JA. Primary yolk-sac (endodermal sinus) tumor of the prostate. Cancer. 1978;41(4): 1395-8.
6. Moran CA, Suster S. Primary germ cell tumors of the mediastinum: I. Analysis of 322 cases with special emphasis on teratomatous lesions and a proposal for histopathologic classification and clinical staging. Cancer. 1997;80(4):681-90.
7. Gooneratne S, Keh P, Sreekanth S, Recant W, Talerman A. Anterior mediastinal endodermal sinus (yolk sac) tumor in a female infant. Cancer. 1985;56(6):1430-3.
8. Moran CA, Suster S, Koss MN. Primary germ cell tumors of the mediastinum: III. Yolk sac tumor, embryonal carcinoma, choriocarcinoma and combined nonteratomatous germ cell tumors of the mediastinum - a clinicopathologic and immunohistochemical study of 64 cases. Cancer. 1997;80(4): 699-707.
9. Gooneratne S, Keh P, Sreekanth S, Recant W, Talerman A. Anterior mediastinal endodermal sinus (yolk sac) tumor in a female infant. Cancer. 1985;56(6):1430-3.
10. Hawkins EP, Finegold MJ, Hawkins HK, Krischer JP, Starling KA, Weinberg A. Nongerminomatous malignant germ cell tumors in children. A review of 89 cases from the Pediatric Oncology Group, 1971-1984. Cancer. 1986;58(12):2579-84.
11. Suster S, Moran CA, Dominguez-Malagon H, Quevedo-Blanco P. Germ cell tumors of the mediastinum and testis: A comparative immunohistochemical study of 120 cases. Hum Pathol. 1998;29(7):737-42.
12. Mönig SP, Schmidt R, Krug B. Yolk sac tumor of the anterior mediastinum: the role of palliative surgery. Am Surg. 1997; 63(11):948-50.
13. Sham JS, Fu KH, Chiu CS, Lau WH, Choi PH, Khin MA, et al. Experience with the management of primary endodermal sinus tumor of the mediastinum. Cancer. 1989;64(3):756-61.
14. Mann JR, Pearson D, Barrett A, Raafat F, Barnes JM, Wallendszus KR. Results of the United Kingdom Children's Cancer Study Group's malignant germ cell tumor studies. Cancer. 1989;63(9):1657-67.