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Case Report / Olgu Sunumu

# Primary posterior mediastinal germ cell tumor in a child

## Bir çocukta birincil posterior mediastinal germ hücreli tümör

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### Abstract

Yolk sac tumor is the most common malignant neoplasm of germ cell origin and usually occurs in infant testes or ovaries. On rare occasions, the tumor arises from extragonadal sites, including the sacrococcygeal region, uterus, vagina, prostate, retroperitoneum, liver, mediastinum (commonly in the anterior), pineal gland, and third ventricle. Yolk sac tumors have an unfavorable prognosis, if not treated aggressively. We report the case of a 3-year-old boy with a primary posterior mediastinal yolk sac tumor who was managed initially with surgery, followed by chemotherapy and had a favorable prognosis. In the literature on yolk sac tumors presenting as a mediastinal mass, pediatric germ cell tumors have been reported very rarely in the posterior mediastinum.

**Keywords:** Children, extragonadal, mediastinum, yolk sac tumor

### Öz

Yolk sac tümörü en sık görülen germ hücre kaynaklı malin neoplazmadır ve genellikle bebek testisi ya da overlerinde ortaya çıkar. Nadir durumlarda, tümör sakrokoksigeal bölge, uterus, vajen, prostat, retroperitoneal bölge, karaciğer, mediasten (sıklıkla önde), pineal bez ve üçüncü ventrikül gibi ekstragonadal bölgelerden kaynaklanır. Agresif olarak tedavi edilmezlerse, yolk sac tümörlerinin seyri kötüdür. Burada, başlangıçta cerrahi uygulanan, sonrasında kemoterapi alan ve olumlu bir seyir gösteren, birincil posterior mediastinal yolk sac tümörü olan 3 yaşında bir erkek çocuğunu sunduk. Mediastinal kitle olarak prezente olan yolk sac tümörleri ile ilgili dizinde, çocuk germ hücreli tümörler arka mediastende çok nadir olarak bildirilmiştir.

**Anahtar sözcükler:** Çocuklar, ekstragonadal, mediasten, yolk sac tümörü

### Introduction

Extragonadal yolk sac tumor (YST) is a very rare neoplasm that represents 3–5% of all pediatric malignancies, most frequently observed in infants and children under 4 years of age. It is a highly variable and aggressive tumor that requires immediate and definite diagnosis and treatment (1).

Mediastinal masses represent the most common thoracic masses in childhood, the majority of which (almost 90%) are of neurogenic origin. The differential diagnosis includes germ cell tumors (GCTs), lymphomas, bronchogenic cysts, pathologic conditions of the thymus gland, pulmonary malformations, enteric duplications and hernias, and pathologies of the spinal cord and vertebrae. Primary mediastinal GCTs constitute 10–15% of mediastinal masses and represent the most common site of primary extragonadal GCTs. Pediatric GCTs appear with a bimodal age distribution, with a small peak during infancy and then a higher incidence after puberty. A wide range of signs and symptoms can be observed in children with mediastinal GCTs that reflect the primary pathologic condition and the functional compromise (mostly compression) of the surrounding structures (2).

In this article, we describe a rare case of an extragonadal YST originating from the posterior mediastinum in a 3-year-old boy.

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## Case

A 3-year-old boy was referred to our department with a 5-day history of hyperpyrexia. At the physical examination, decreased respiratory sounds of the left lung were noted. The remaining physical and neurologic examinations were unremarkable. The child had an unremarkable perinatal and medical history, normal growth and development, and an unremarkable family history.

Full blood count, biochemical analysis, and arterial blood gases were found normal: $PCO_2$: 35 mm Hg, $PO_2$: 100 mm Hg, pH: 7.45, white blood cells (WBC): 11.0$^6$ x10$^3$/ µL, neutrophils (NEU): 66.3%, lymphocytes: 23.6%, red blood cells (RBC): 4.1 x10$^6$/ µL, hemoglobin (Hgb): 12.3 g/ dL, hematocrit (Hct): 36.8%, platelets (PLT): 491 x10$^3$/ µL, serum iron: 24 µg/dL, ferritin: 564.77 ng/mL, erythrocyte sedimentation rate (ESR): 44 mm/1h, serum glutamic-oxaloacetic transaminase (SGOT): 26 U/L, serum glutamic pyruvic transaminase (SGPT): 12 U/L, gamma-glutamyl transpeptidase (GGT): 12 U/L, alkaline phosphatase (ALP): 148 U/L, lactate dehydrogenase (LDH): 569 U/L, $K^+$: 4.9 mEq/L, $Na^+$: 140 mEq/L, $Ca^{+2}$: 9.9 mg/dL, P: 4.8 mg/dL, urea: 19 mg/dL, creatinine: 0.35 mg/dL, and uric acid: 3.7 mg/dL. Tumor markers were also measured: beta human chorionic gonadotropin (β-hCG): 0.1 mIU/mL, alpha-fetoprotein (aFP): 106.8 ng/mL, and carcinoembryonic antigen (CEA): 1.03 ng/mL.

Chest X-ray revealed extended right-sided pleural effusion. A computed tomography (CT) scan of the chest revealed extended right-sided pleural effusion, compression atelectasis of the right lower lobe, and a large paraspinal (T8-T12) lobulated mass (6.5x5.5 cm) (Fig. 1). For further evaluation, a magnetic resonance image (MRI) of the chest was obtained. The MRI showed a large right paraspinal soft tissue mass located in the posterior mediastinum extending from the T8 to T12 vertebrae, which did not cross the midline. The mass was lobulated, and heterogeneously enhancing with multiple internal necrotic-cystic lesions. MRI also revealed extended right-sided pleural effusion, and compression atelectasis of the right lower lobe (Fig. 2). No metastatic lesions were found in a bone scan.

A standard right thoracentesis was performed and antibiotic treatment with cefuroxime was started, which resulted in complete resolution of the pleural effusion. One week later, the patient was stable and afebrile. Thoracotomy and biopsy of the mediastinal mass was performed. Histologic studies showed a germ cell tumor with biochemical and morphologic characteristics consistent with YST. The patient received combination chemotherapy including bleomycin-etoposide-cisplatin

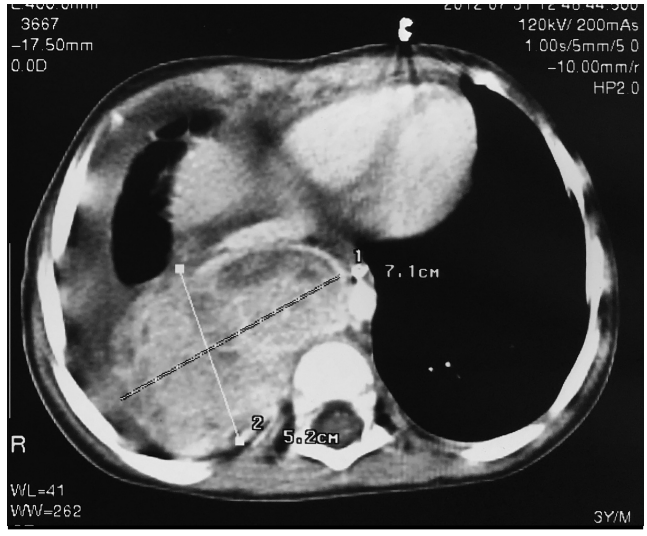


**Figure 1. Computed tomography scan of the chest revealing extended right-sided pleural effusion and a large paraspinal lobulated mass in posterior mediastinum**

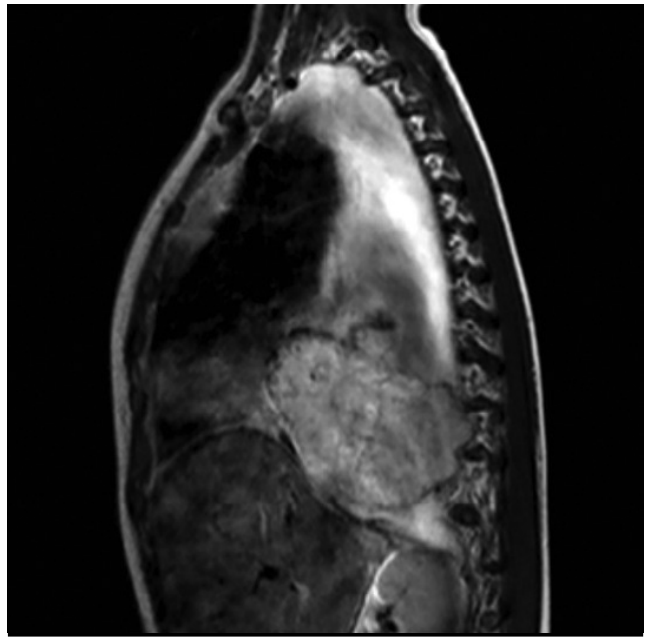

**Figure 2. Magnetic resonance image of the chest showing a large right paraspinal soft tissue lobulated mass heterogeneously enhancing with multiple internal necrotic-cystic lesions in the posterior mediastinum extending from the T8 to T12 vertebrae**

(BEP). In total, the boy received 4 chemotherapy cycles. Three months later, by the end of the protocol, aFP levels were found within normal limits (5.3 ng/mL) and a subsequent MRI scan revealed complete resolution of the tumor and pleural effusion. To date, the patient remains free of disease and complications 4 years after treatment. Written informed consent was given by the patient's parents.

## Discussion

Germ cells tumors (GCTs) comprise a heterogeneous group of very rare tumors that arise from primordial germ cells in a variety of sites, either in the gonads or, following aberrant germ cell migration, in extragonadal sites, from the brain to the sacrococcygeal region (1). Extragonadal GCTs are relatively uncommon representing 1 to 5% of all GCTs (3). The most common extragonadal sites are sacrococcygeal (78%), mediastinal, intracranial (pineal gland: 62%; suprasellar region: 31%; both areas: 7%), and retroperitoneal. Other locations include the pelvis, cervix or uterus, vagina, prostate, abdominal wall, bile duct, hernia sac and neck (1). Mediastinal GCTs usually occur within the anterior mediastinum, accounting for about 15% of all mediastinal cysts and tumors. Mediastinal GCTs can occur within the posterior mediastinum in very rare cases (4).

Yolk sac tumor (YST), also known as primitive endodermal tumor or endodermal sinus tumor, is the most common malignant GCT in the pediatric population, representing 20% of malignant GCTs. The tumor was not generally recognized until the 1960s, when Teilum described the tumor in the testes and ovaries of young children. YSTs represent 3–5% of pediatric malignancies, occurring in infants and children aged under 4 years. Most YSTs are diagnosed between 7 months and the third year of life (3). The most common sites of involvement are ovaries and testes, but rarely (about 20%) can occur in extragonadal sites such as the vulva, vagina, pineal region, broad ligament, prostate, cervix, mediastinum, sacrococcygeal, and retroperitoneum region. However, the commonest site for extragonadal lesions is the sacrococcygeal region. The pathogenesis of YST is unknown. The classic theory suggests that it arises from local transformation of misplaced primordial germ cells. YSTs are grey to yellow, solid and cystic tumors, with areas of hemorrhage and necrosis. They are highly malignant tumors characterized by tumor cells arranged in various patterns (3).

The three sensitive diagnostic markers for YST in immunocytochemistry are aFP, glypican-3, and SALL4. Serum aFP levels are elevated in patients with YSTs and usually decrease within 2 to 3 weeks after treatment. Assessment of serum AFP levels is useful for diagnosing YSTs and also in monitoring response to therapy and prognosis (5). The mean and standard deviation of normal serum aFP levels in infants at various ages are shown in Table 1.

The overall prognosis for mediastinal GCTs is unfavorable, partly because the tumors are far advanced at the time of diagnosis, but also because some tumors contain embryonal cell carcinoma, choriocarcinoma, and yolk sac elements, which are very aggressive (6). The prognosis of YST depends partly on its location. Although pure testicular YST in infants has at least a 75% 5-year survival rate, mediastinal YST is much more aggressive (7). There is a remarkable improvement in the survival of patients with YST because of the advent of chemotherapy. The single most important prognostic indicator is whether the tumor mass can be completely excised before or after chemotherapy. Primary mediastinal YSTs have worse survival compared with other extragonadal YSTs due to the large tumor bulk at diagnosis, resistance to chemotherapy, and difficulty in removing all residual disease after chemotherapy. Early detection and therapy is important because the tumor shows good response to surgery and chemotherapy (8).

**Table 1. Mean and standard deviation of normal serum aFP levels in infants at various ages**

| Age | Mean±SD |
|---|---|
| Premature | 134.734±41.444 |
| Newborn | 48.406±34.718 |
| Newborn – 2 weeks | 33.113±32.503 |
| 2 weeks – 1 month | 9.452±12.610 |
| 2 months | 323±278 |
| 3 months | 88±87 |
| 4 months | 74±56 |
| 5 months | 46.5±19 |
| 6 months | 12.5±9.8 |
| 7 months | 9.7±7.1 |
| 8 months | 8.5±5.5 |

SD: Standard deviation

In the past, YSTs were nearly uniformly fatal, regardless of the primary location. However, the survival rate of patients with YST has been significantly improved because of the application of cisplatin-based multi-agent chemotherapy. Currently, initial surgery followed by adjuvant chemotherapy including bleomycin, etoposide, and cisplatin (BEP) is considered the standard for the treatment of YST (9). Compared with other regimens, BEP appears to be the best active first-line option for primary, metastatic, or recurrent disease. It should also be stressed that secondary cytoreductive surgery could play an important role when tumors are limited and resistant to chemotherapy. Regarding the follow-up of chemotherapy, the determination of initially elevated markers (AFP) should be repeated before each cycle of therapy, soon after the end of the treatment and during the 2 years after the end of chemotherapy.

As mentioned above, the commonest site for extragonadal lesions is the sacrococcygeal region. The anterior mediastinum is the second most common extragonadal location for YSTs; the posterior mediastinum is a very rare extragonadal location (7, 10). Knapp et al. reported approximately 80 such cases, the vast majority occurring in young adult males (6). To our knowledge, there are no previous reports documenting the posterior mediastinum as a primary site for an extragonadal YST.

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