



# Prepubertal Testicular Tumors in Children: Single Center 17 Years Experience

● Muhammed Hamidullah Çakmak, ● Serdar Moraloğlu, ● Ayşenur Celayir

University of Health Sciences Turkey, Hamidiye Faculty of Medicine, Zeynep Kamil Women and Children's Diseases Health Training and Research Hospital, Department of Pediatric Surgery, İstanbul, Turkey

## ABSTRACT

**Aim:** Testicular tumors are rare in children and have a bimodal distribution. The first peak is at two years of age in boys and comprises mainly non-GCNIS derived tumors (pre-pubertal teratoma and yolk sac lesions). Here, the clinical features and treatment of testicular tumors in pre-pubertal children in our center are presented.

**Materials and Methods:** The clinical records of those patients treated for testicular tumors younger than 18 years in our institution from January, 2006 to June, 2022 were reviewed retrospectively.

**Results:** A total of 12 patients were included in this study. All of the patients were younger than 3 years, except for one patient, who was 8 years old. The median age at primary diagnosis was 17 months (1-107 months). The most common clinical presentation was testicular swelling (n=9). Three patients were diagnosed incidentally. Serum  $\alpha$ -fetoprotein (AFP) was increased in 3 patients with yolk sac tumors (>1,000 ng/dL) and in one patient with mature cystic teratoma (1 month-old infant with an AFP concentration of 629 ng/dL). Preoperative  $\beta$ -hCG levels were normal in all patients (<1.2 mIU/mL). Of the 11 patients whose preoperative scrotal ultrasound could be obtained, 5 solid-cystic lesions, 3 cystic lesions, and 2 solid lesions were reported. Calcification was detected in 4 patients. All 4 patients with malignant tumors and 3 patients with benign tumors underwent radical inguinal orchiectomy. Of the 5 tumors removed by testis preserving surgery, 2 were mature teratomas, 2 were epidermoid cyst and 1 was a benign multi-cystic lesion. There was a patient with yolk sac tumor who died in the fifth month postoperatively while receiving chemotherapy. The remaining patients had no metastatic or local primary testicular tumor recurrence during a mean follow-up of 92 months (2-198 months).

**Conclusion:** Most pre-pubertal tumors are benign and testicular sparing surgery can be performed in patients with negative serum tumor markers. Inguinal radical orchiectomy is sufficient in the treatment of yolk sac tumor.

**Keywords:** Child, orchiectomy, organ sparing treatments, testicular germ cell tumor, testicular neoplasms

## Introduction

Testicular tumors in children are very rare lesions. These tumors represent 1-2% of all pediatric solid neoplasms with an incidence of 0.5-2 per 100,000 children (1,2). Pediatric testicular tumors have a bimodal distribution. The first peak is at two years of age in boys, and the second peak is seen after puberty (3).

Primary testicular tumors have been categorized into two main groups in the World Health Organization 2016 new classifications; germ cell neoplasia *in situ* derived (GCNIS) and non-GCNIS derived (Figure 1) (4). GCNIS derived tumors usually present in the post-pubertal age and are more aggressive than non-GCNIS derived tumors which are usually seen in the pre-pubertal age (5).

## Address for Correspondence

Muhammed Hamidullah Çakmak, University of Health Sciences Turkey, Hamidiye Faculty of Medicine, Zeynep Kamil Women and Children's Diseases Health Training and Research Hospital, Department of Pediatric Surgery, İstanbul, Turkey

Phone: +90 537 685 95 50 E-mail: dr.m.hamidullah@hotmail.com ORCID: orcid.org/0000-0003-1618-4783

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Traditionally, testicular tumors in children have been treated by radical high inguinal orchiectomy (1,6-8). As most pre-pubertal testicular tumors are benign (3,7-9), testis sparing procedures should be performed in selected cases especially with negative tumor markers (1,8). Here, we present the clinical and histological features and treatments of testicular tumors in pre-pubertal children in our center.

### Materials and Methods

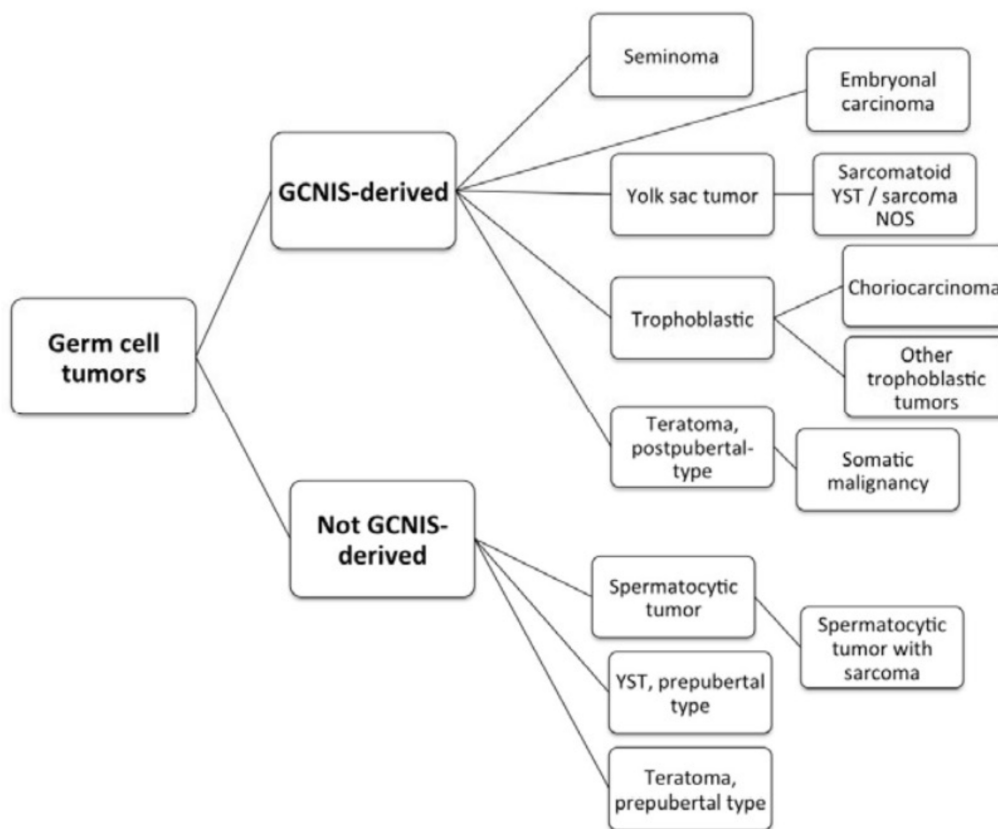
The clinical records of patients younger than 18 years treated for testicular tumors in our institution from January, 2006 to June, 2022 were reviewed retrospectively. Data were collected from the institutional electronic records. Their ages at diagnosis, clinical presentations, scrotal ultrasonographic findings, medical histories, tumor marker levels, surgical procedures, histopathological findings and outcomes were recorded.

Ethical approval was obtained from Zeynep Kamil Women and Children's Diseases Health Training and Research Hospital Clinical Research Ethics Committee (approval no: 202, date: 22.12.2021).

### Results

A total of 12 patients were included in this study. All patients were younger than 3 years, except for one patient, who was 8 years old. The median age at primary diagnosis was 17 months (range: 1-107 months). The mean time from initial clinical presentation to diagnosis was 162 days (range: 3-840 days). The most common clinical presentation was testicular swelling (n=9, 75%). Three patients were diagnosed incidentally. Eleven out of the 12 patients had a palpable mass on preoperative physical examination. All patients who were later diagnosed with yolk sac tumor had a hard palpable mass, and one patient who was later diagnosed with epidermoid cyst had a hydrocele on preoperative physical examination. The left testis was affected in 8 (66.6%) cases and the right in 4 (33.4%) cases. None of the patients had a history of cryptorchidism.

Tumor marker profiles were available for nine out of the twelve cases. The tumor markers of the remaining 3 patients were taken, but the results could not be obtained from the records. Serum  $\alpha$ -fetoprotein (AFP) was increased



**Figure 1.** WHO-2016 new classification of germ cell neoplasia  
WHO: World Health Organization, GCNIS: Germ cell neoplasia in situ derived

in 3 patients with yolk sac tumor (>1,000 ng/dL) and in one patient with mature cystic teratoma (1 month-old infant with an AFP concentration of 629 ng/dL). Preoperative  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) levels were normal in all patients (<1.2 mIU/mL).

Of the 11 patients whose preoperative scrotal ultrasound could be obtained, 5 solid-cystic lesions, 3 cystic lesions, and 2 solid lesions were reported. Calcification was detected in 4 patients. Preoperative ultrasound findings were variable, but there was hyperechogenic cystic areas within the solid matrix or hyperechogenic cystic lesions in mature teratomas (n=4) and in epidermoid cysts (n=2), and hypervascularization in yolk sac tumors (n=3). There were no cases of bilateral or multiple tumors. CT of the chest, abdomen, and pelvis was performed before surgery in two patients who were later diagnosed with yolk sac tumor, and they were reported as normal. No metastatic spread due to primary testicular tumor was found.



**Figure 2.** Patient with yolk sac tumor undergoing high inguinal radical orchiectomy

All surgical procedures were uncomplicated and the mean operation time of the patients for whom operation time records were available was 67.5 minutes (range 39-110 min). All 4 patients with malignant tumors and 3 patients with benign tumors underwent radical inguinal orchiectomy (Figure 2). Of the 5 tumors removed by testis preserving surgery, 2 were mature teratomas, 2 were epidermoid cyst and 1 was a benign multi-cystic lesion. They were treated by testicular-sparing surgery after frozen-section analysis (Figure 3).

Eight (66.6%) of the tumors were benign, and the most common subtype was mature cystic teratoma, and 4 (33.4%) of the tumors were malignant. Pathology revealed four (33.4%) yolk sac tumors, four (33.4%) teratomas, two (16.6%) epidermoid cysts, one (8.3%) hemangioma, and one (8.3%) benign multi-cystic lesion. The pathological characteristics and treatment outcomes are summarized in Table I.

There were no metastatic or local recurrences of the primary testicular tumor during a mean follow-up of 92



**Figure 3.** Patient with epidermoid cyst undergoing testis-sparing surgery

<b>Table I. Summary of results</b>			
<b>Histology</b>	<b>Number (%)</b>	<b>Median age at presentation (months)</b>	<b>Testis-sparing</b>
	<b>Non-GCNIS<sup>a</sup> derived</b>		
Yolk sac	4 (33.4)	16	-
Mature cystic teratoma	4 (33.4)	13	2
Epidermoid cyst	2 (16.6)	71	2
	<b>Others</b>		
Hemangioma	1 (8.3)	34	-
Benign multi-cystic lesion	1 (8.3)	7	1
Total	12	25	6

<sup>a</sup>: Non-germ cell neoplasia *in situ*

months (2-198 months), except for one patient who died. Especially those patients with yolk sac tumor were referred to a multidisciplinary center with a pediatric oncology department in the early postoperative period. One of the four patients with yolk sac tumor died and no recurrence was observed in the remaining three patients with yolk sac tumor in a mean follow-up of 103 months (26-188 months).

## Discussion

Testicular tumors are rare in children and they have a bimodal distribution. The first peak is at two years of age and comprises mainly non-GCNIS derived tumors (pre-pubertal teratoma and yolk sac lesions). Non-GCNIS derived germ cell tumors are the most common (77-85%) pre-pubertal testicular tumors and they are typically benign lesions (10,11). Patients with a prior history of undescended testis, a family history of testicular cancer or disorders of sexual development have been reported to have an increased incidence of testicular malignancy (12-14). Our patients had no history of undescended testis, family history of testicular cancer, or sexual development disorders. Similar to the literature, 83.4% of our patients were non-GCNIS-derived tumors.

The main symptom of pediatric testicular tumors is painless testicular mass. Hydrocele, hernia, bruising or precocious puberty are the less common findings (8). All patients in our series, except for those detected incidentally, presented with swelling in the testis.

Tumor markers are useful for the diagnosis and management of testicular tumors. Serum tumor markers include AFP,  $\beta$ -hCG and in some centers, lactic dehydrogenase. AFP (half-life 1-3 days) is secreted by the fetal yolk sac tissue and it is usually elevated in yolk sac tumors and some embryonal carcinomas (15). In infants, it is physiologically high and it returns to normal levels by the age of 1 year. Higher than age-related normal range of AFP suggests yolk sac tumor (90%) in pre-pubertal children with testicular tumors (16).  $\beta$ -hCG (half-life 5-7 days) is produced by syncytiotrophoblast tissues and it is elevated usually in choriocarcinoma or mixed tumor (15). In the present study, AFP was increased in 3 patients with yolk sac tumor ( $>1,000$  ng/dL) and in one patient with mature cystic teratoma.  $\beta$ -hCG levels were normal in all patients ( $<1.2$  mIU/mL).

The initial imaging method of a testicular mass is scrotal ultrasound. Ultrasound helps to predict tumor character. Ultrasonography has a sensitivity of almost 100% for the detection of testicular neoplasms (1).

Ultrasound will help to distinguish intra-testicular and extra-testicular lesions and identify the lesion as benign or malign and also it rules out contralateral testicular masses (17). Unilocular lesions with anechoic content, well circumscribed with sharp borders, and avascularity are usually ultrasound features of benign masses (3,5). Epidermoid cysts tend to be more cystic in appearance and usually have echogenic debris. Characteristically mature teratomas appear as a hyper-echogenic cystic area in a solid matrix, and yolk sac tumors are usually solid lesions in appearance (3,6,8). In our series, 5 solid-cystic lesions, 3 cystic lesions, and 2 solid lesions were reported in preoperative scrotal ultrasound. According to our experience, while hyperechogenic cystic areas in the solid matrix were notable in benign lesions, hypervascularization was especially evident in malignant tumors. However, it should be noted that hypervascularization is not a specific sign of malignancy. CT or MRI imaging of the abdomen and pelvis are used for pre-operational staging and treatment planning for patients at high risk of metastasis (18).

Surgery plays an important role in the treatment of pediatric testicular tumors. In the past, the treatment of pre-pubertal testicular tumor was based on the treatment experience of adults. Inguinal radical orchiectomy has been the historical approach for all testicular tumors. In recent studies, most of the pre-pubertal testicular tumors were reported as benign, with a low propensity for local recurrence, and as metastasis is rare, testicular sparing surgery is preferred in appropriate cases (1,7,8,16,18). Liu et al. (19) reported 70 patients with mature teratoma and 33 epidermoid cyst, all of whom were treated with testis-sparing surgery. With a mean follow-up of 5 years, there were no cases of recurrence or testicular atrophy. Testis sparing surgery may be appropriate for all potentially benign tumors in pre-pubertal children with normal preoperative serum AFP and  $\beta$ -hCG levels, and salvageable normal testicular parenchyma on ultrasound (10,20). The long-term outcomes of testis-sparing surgery for benign testicular tumors are favorable and recent studies have reported its efficacy in preserving hormonal functions and fertility (21). At the same time, preserving the testis is important for its physiological and psychological effects on pre-pubertal patients (22). High radical orchiectomy is still recommended as the initial treatment for pre-pubertal testicular tumors, especially with high preoperative serum AFP values (3). The guidelines recommend high ligation at the level of the internal ring with an inguinal incision, and vascular control of the testis before mobilization by reaching a 5 cm proximal spermatic cord (23). In accordance

with these principles, testis-sparing surgery is performed in our institution with an inguinal incision. The inguinal canal is opened and after the spermatic cord is separated from the cremaster at the level of the internal ring, it is clamped at this level with a non-crush clamp. The testicle is taken out of the incision while protecting the wound. The mass capsule is excised without damage. Excision material is sent for frozen. If it is benign, the tunica is closed and the process is terminated. In pathology, pubertal changes in the tissue around the tumor should also be excluded because post pubertal tumors can be malignant (17). In this study, 66.6% were benign tumors and testis-sparing surgery was performed on 62.5% of them. Our approach to our patients has changed over time.

In a systemic review published in 2021 (5), including 269 patients who underwent testicular-sparing surgery, tumor recurrence was reported in one patient with mature teratoma. Six Leydig cell tumors had a positive surgical margin microscopically, and 2 of these cases underwent subsequent radical orchiectomy after parenteral choice due to their possible malignancy risk. No recurrence was reported in the other studies examined in this review. In our study, there was a patient with yolk sac tumor who died in the fifth month postoperatively while receiving chemotherapy. The remaining patients had no metastatic or local primary testicular tumor recurrence during a mean follow-up of 92 months (2-198 months).

### Study Limitations

The limitations of the present study include its retrospective nature and its relatively small number of patients.

### Conclusion

Testicular tumors in pre-pubertal children are uncommon. Most pre-pubertal tumors are benign and testicular sparing surgery can be performed on those patients with negative serum tumor markers. Inguinal radical orchiectomy is sufficient in the treatment of yolk sac tumor, which is the most common malignant tumor in this age group.

### Ethics

**Ethics Committee Approval:** Ethical approval was obtained from Zeynep Kamil Women and Children's Diseases Health Training and Research Hospital Clinical Research Ethics Committee (approval no: 202, date: 22.12.2021).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Concept: M.H.Ç., S.M., A.C., Design: M.H.Ç., S.M., A.C., Data Collection or Processing: M.H.Ç., S.M., Analysis or Interpretation: M.H.Ç., S.M., A.C., Literature Search: M.H.Ç., Writing: M.H.Ç., S.M.

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