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ORIGINAL ARTICLE

Prepubertal testicular tumors in China: a 10-year experience with 67 cases

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Abstract

Aim Prepubertal testicular tumors are rare in children. We aim to present clinical and histological features of prepubertal testicular tumors through the analysis of the long-term experiences of a single medical center of China.

Materials and methods A total of 67 children (≤ 14 years) treated for testicular tumor at our institution from 2005 to 2015 were retrospectively reviewed. Data relating the clinical characteristics, histopathology findings, serum tumor markers, treatment method, and outcome were collected.

Results The patients' median age at diagnosis was 18 months (range 3–168 months), and 49 cases (73.1%) were diagnosed at age younger than 3 years. The most common clinical presentation was a painless scrotal mass or swelling. Regarding histology, 32 (47.8%) were teratomas and only one of these tumors presents immature teratomas, 20 (29.9%) were yolk sac tumors, 9 (13.4%) were epidermoid cyst, 1 (1.5%) was a Leydig cell tumor, 1 (1.5%) was a mixed malignant germ cell tumor, and 4 (8.3%) were paratesticular tumors. For germ cell tumors, the mean preoperative serum α-fetoprotein (AFP) level was significantly higher in patients with yolk sac tumor than in those with teratomas (2,078 ng/mL vs 5.7 ng/mL). Of all these patients, 37 (55.2%) were treated with radical inguinal orchiectomy and testis-sparing surgery was planned and achieved in 30 (44.8%). Surveillance was performed in 60 patients. None of the patients developed recurrence or testicular atrophy after appropriate treatment.

Conclusions The majority of our cases were benign, with the most common histopathological subtype being teratoma. A testis-sparing procedure should be performed in children with a palpable testicular mass and negative tumor markers. This study shows a better outlook for prepuberty patient with testicular tumors than their adult counterparts.

Keywords Prepuberty testicular tumors · Germ cell tumors · Teratomas · Yolk sac tumors · Epidermoid cyst

Introduction

Prepubertal testicular tumors (PTTs) are uncommon in children, and account for 1–2% of pediatric solid neoplasm with an incidence of 0.5–2 per 100,000 children [1]. In the past, most PTTs were often treated as they would be managed in adults. However, recently published data indicate that pediatric and adult testicular tumors are distinct from each other both in clinical and biological features [2, 3]. For instance, PTTs are composed mainly of teratomas or yolk sac tumors, whereas seminoma is the dominant testicular tumor in adults. The distribution of histological types of PTTs remains controversial. In the Prepubertal Testis Tumor Registry of American Academy of Pediatrics, most (> 60%) are malignant yolk-sac tumors; about 25% are teratomas and around 40% are benign [4]. In contrast, recent reviews of single-center or multi-institutional studies have shown that benign tumors of the testis are more common in children [5–7]. Considering this, testis-sparing surgery is now advocated in appropriate situations [8]. According to previous reports, the incidence of PTTs was significantly higher in Asian boys than in other races [9, 10]. However, only a few cases have been reported in Asia, especially in China. To

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define criteria for high likelihood of testicular malignancy in a prepubertal boy with a testicular mass, we analyze the features of the primary testicular tumors and report our experience with relative frequency, histopathologic findings, treatment and outcome of these tumors.

Materials and methods

Following approval of the Institutional Review Board, we reviewed the records of 67 children aged ≤ 14 years who had primary testicular tumors and presented at Wenzhou Yu-ying Children's Hospital from 2005 to 2015. The parameters assessed were: age at diagnosis, clinical characteristics, scrotal ultrasonographic findings, preoperative serum tumor marker levels (alpha fetoprotein [AFP], human chorionic gonadotropin [HCG]), treatment methods, histopathological findings, and treatment outcome. Serum AFP in early infancy was assessed according to normal ranges reported by Blohm et al [11]. Radical inguinal orchiectomy with spermatic cord ligature was performed as the standard treatment, with testis-preserving surgery in the cases with a normal preoperative AFP and ultrasound that shows salvageable normal testicular parenchyma. Intraoperative frozen-section examination was performed and the resected tumor was sent for histologic analysis after surgery. All patients were followed with further management, including physical examination, measurement of serum AFP levels and regular testicular sonography.

All clinical parameters were reported as median values with ranges and analyzed by the Chi-square, Mann–Whitney *U* test by the SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

The clinical data of the 67 patients are summarized in Table 1. The median age at diagnosis was 18 months (range 3–168 months). 49 (73.1%) were 3 years or younger, 13 (19.4%) were older than 3 years but 10 years or younger, and 5 (7.5%) were older than 10 years but 14 years or younger (Fig. 2). All boys with a yolk sac tumor were < 5 years. The most common presentation is of a painless scrotal mass or swelling. A total of 38 boys (56.7%) tumors were detected in the right side, and 29 boys (43.3%) tumors were detected in the left side. 23.9% (16/67) of the patients presented with concomitant hydrocele and 7.5% (5/67) with cryptorchism. Testicular microlithiasis was diagnosed in three patients by scrotal US. A 2-month-old boy presented with a large right-sided abdominal mass and nonpalpable right testis, operative findings showed an intraabdominal testicular tumor (Fig. 1). Furthermore, there were two emergency cases of testicular torsion. All the children are Han Chinese ethnicity and no family history was reported.

According to age-specific normal range, serum α-fetoprotein (AFP) was increased in 20 patients with yolk sac tumor (2243.7 ng/mL) and in one patient with mixed

Table 1 Clinical characteristics of patients with prepubertal testicular tumors

Pathology	Number (%)	Age at diagnosis (months) Median (range)	Affected side Left/right	Concomitant findings (*n*)	Testis-sparing surgery (*n*)	Follow-up period (months) Median
Teratoma	32 (47.8%)	19 (3–168)	15/17	Abdominal mass and pain: Intraabdominal Undescended testis (2) Testis torsion (2) Hydrocele testis (6) Contralateral cryptorchism (1)	19	23
Yolk sac tumor	20 (29.9%)	14 (4–55)	10/10	Hydrocele testis (5) Contralateral cryptorchism (1)	0	36
Epidermoid cyst	9 (13.4%)	24 (3–167)	2/7	Ipsilateral cryptorchism (2) Testicular microlithiasis (1) Hydrocele testis (3)	8	27
Mixed malignant germ cell tumor	1 (1.5%)	23	0/1	N/A	0	56
Leydig cell tumor	1 (1.5%)	82	1/0	Scrotal swelling and Precocious puberty	1	26
Rhabdomyosarcoma	2 (2.9%)	86.5 (14–159)	1/1	Hydrocele testis (1)	0	42
Hemangioma	1 (1.5%)	15	0/1	N/A	1	14
Fibrosarcoma	1 (1.5%)	38	0/1	Hydrocele testis (1)	1	60
Total	67 (100%)	18 (3–168)	29/38	N/A	30	32

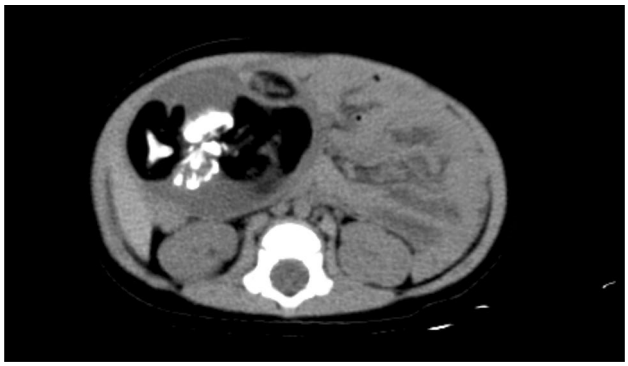

Fig. 1 Abdominal computed tomography showed a well-defined sizable cystic tumor with focal calcification in the lower abdomen. Operative findings show an intraabdominal testicular tumor

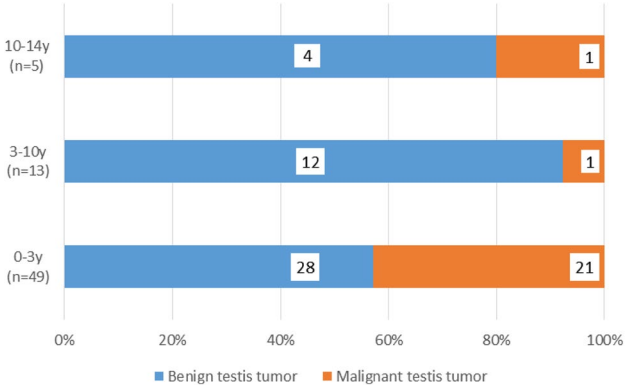

Fig. 2 Relative incidence of malignant vs. benign testis tumor at various ages

malignant germ cell tumor (23-month-old infant with an AFP concentration of 683 ng/mL). Table 2 shows the comparison of clinical variables between the patients with yolk sac tumors and those with teratomas. The mean preoperative AFP differed significantly between the two groups. All patients older than 6 months with yolk sac tumor had a preoperative AFP level greater than 100 ng/mL, whereas no patient older than 6 months with teratoma had a level greater than 100 ng/mL. Preoperative β-hCG level was normal in all patients (normal range 0–5.3mIU/mL). Serum AFP returned to normal levels after surgery.

Pathology revealed 32 teratomas (47.8%), 20 yolk sac tumors (29.9%), 9 epidermoid cysts (13.4%), 1 mixed malignant germ cell tumor (1.5%), 2 rhabdomyosarcoma (2.9%), 1 leydig cell tumors (1.5%), 1 hemangioma (1.5%), and 1 fibrosarcoma (1.5%). Overall, 44 (65.6%) of the tumors were benign, and the most common subtype was teratoma. Tumors that are likely to be benign based on AFP level, and that appear to have salvageable normal testis on ultrasound, should be managed initially with an excisional biopsy and frozen section analysis. Of these benign tumors, testis-sparing surgery was planned and achieved in 30(44.8%) tumors (Table 1). All patients were free of recurrence or testicular atrophy under a follow-up.

All 23 patients with malignant tumors underwent radical inguinal orchiectomy. Of 20 patients with yolk sac tumor, 5 underwent adjuvant chemotherapy due to the persistence or relapse of AFP levels after surgery. Chemotherapy was also administered to the two patients with rhabdomyosarcoma. The mean follow-up period was 34 months (range 3 to 136 months). All patients with yolk sac tumor and mixed germ cell tumor remained free of disease. One patient died from metastatic rhabdomyosarcoma.

Discussion

The incidence of testicular tumors in children is only 0.5–2.0 per 100,000 [1]. There have been a limited number of single institutional reports about PTT in China, because of the rarity of this entity. Prepubertal testicular tumors are distinct from those of adults in histologic characteristics, molecular biology, and clinical behavior. Although germ cell tumors are far more common than stromal tumors in both age groups, the vast majority of adult tumors are malignant with histologic features of either seminoma or mixed germ cell tumors. In contrast, the most common histologic features for prepubertal tumors are teratoma and pure yolk sac tumors. A review of the AAP Prepubertal Testis Tumor Registry showed that yolk sac tumors

Table 2 Comparison of yolk sac tumor and teratoma

	Yolk sac tumor	Teratoma	*P* value
No. patients	20	32	
Age (months)	14 (4–55)	19 (3–168)	> 0.05
Serum AFP (ng/mL)	2243 (62–74638)	2.09 (0.69–214)	< 0.05
Serum hCG (mIU/mL)	2.1 (0.2–5.0)	2.0 (0.3–5.2)	> 0.05
No. AFP levels greater than 100 ng/mL in infants older than 6 months (%)	18/18 (100%)	0/28 (0%)	< 0.001

Values are presented as median (range)

AFP alpha-fetoprotein, *hCG* human chorionic gonadotropin

accounted for 62% of all tumors, whereas teratoma comprised only 25% [4]. Maizlin et al. utilized the National Cancer Data Base to review all prepubescent patients with testicular neoplasms, and they found that yolk sac tumors accounted for 42.2% [12]. Moreover, a predominance of yolk sac tumors was reported in Japanese and Taiwanese studies, which suggests the predominance of yolk sac tumors in Asian populations [13, 14]. However, recent single-institutional reports of other countries suggest that teratomas are more common than yolk sac tumors [6, 7]. Consistent with previous reports, we confirmed that benign tumors formed the majority (65.6%) of all tumors, with the most common histologic subtype being teratoma. Our results are consistent with those of another single-institutional China study [5]. In that study, the reported rates of teratoma and yolk sac tumor were 50.8% and 33.3%, respectively, a distribution similar to ours. The reason for the discrepancy in histological distribution remains unclear, racial differences may be a possible cause.

Clinical manifestations of prepubertal testicular tumors are various, and with no specificity. There are no differences between the benign and malignant PTTs. In general, a painless testicular mass is the most common finding in a child with a testicular tumor. Once a testicular tumor is suspected, a thorough physical examination should be undertaken. Signs of androgenization should be sought. Acute abdominal pain could be the initial symptom with torsion of an abdominal undescended testicle containing a tumor. In our series, a 8-year-old child presented acutely with lower abdominal peritonism and a medical history of cryptorchism, operative findings showed torsed intraabdominal testicular tumor.

In a prepubertal child, evaluation of a testicular mass relies on the determination of serum tumor markers and ultrasonography. Of these, AFP is a yolk sac tumor specific marker, and its levels are high in some 80–90% of such tumors. And dozens of papers have indicated that AFP is useful in diagnosing testis tumors, monitoring the treatment response, and detecting recurrence, whereas β-hCG is not [4, 7, 15, 16]. The present study again confirmed these findings. In addition, no infant older than 6 months with teratoma had a preoperative AFP level greater than 100 ng/mL. Therefore, preoperative AFP level is considered to be very useful, even in infants with testicular tumor.

Ultrasonography has shown a sensitivity of almost 100% for the detection of testicular neoplasms. Testis-sparing surgery should be used in children with a testicular tumor in which the normal testicular tissue seems salvageable on ultrasonography and with a normal AFP concentration [17–19]. Two patients with malignant testicular tumors and one with epidermoid cysts had testicular microlithiasis. Whether testicular microlithiasis increases the risk of testicular cancer is still inconclusive. However, an overwhelming body of evidence shows a strong association between testicular microlithiasis and primary testicular neoplasia in pediatric population [20, 21].

Surgical resection has a central role in the management of PTT. Intraoperative frozen-section biopsy may be determinant in the choice of the appropriate surgical procedure [22]. Based on these histopathological characteristics, testis-sparing surgery has been reported for PTT. Sugita et al. reported 27 patients with teratoma, 17 of whom were treated with testis-sparing surgery. With a mean follow-up of 10 years, there were no cases of recurrence or testicular atrophy [23]. In another series of testis-sparing surgeries in 13 prepubertal boys with teratoma or epidermoid cyst, no patient had recurrent tumor after a mean follow-up of 7 years [24]. In our series, 30 patients were treated with testis-sparing surgery, no patient had no evidence of recurrence or testicular atrophy under follow-up of 23 months, supporting the excellent outcomes of this procedure.

This study improves current knowledge of the diagnosis and management for prepubertal testicular tumors. However, some limitations of this study should be mentioned, including its small size and retrospective nature. In addition, because we saw only the patients with localized yolk sac tumors, we do not know whether the changes in AFP following treatment might be as good in yolk sac tumors of other stages. Despite these limitations, we believe that our data will enhance knowledge about this rare tumor.

Conclusion

Our single-center 10 years of experience showed that most of the prepubertal testicular lesions were benign, and the most common histologic subtype was teratoma. Testis-sparing surgery should be considered if preoperative evaluation suggests benign PTT with salvageable normal testicular parenchyma. The outlook for prepubertal patients with testicular tumors is better than that for adults, and the emphasis in recent years has been on reducing the morbidity of both the surgical and the adjuvant therapies for these children.

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Compliance with ethical standards

Conflict of interest Dazhou Wu declares that he has no conflict of interest. Nannan Shen declares that she has no conflict of interest. Xiaokun Lin declares that he has no conflict of interest. Xiaoming Chen declares that she has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethic committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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