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Prepubertal testicular tumors: a single-center experience of 44 years

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ABSTRACT

Purpose: To present the clinical and histological features of prepubertal testicular tumors (PTTs), the long-term experience of a single institution was reviewed.
Materials and methods: A total of 62 prepubertal children who were treated for testicular tumors at Kanagawa Children's Medical Center from 1971 to 2014 were retrospectively reviewed. Histopathological findings, age at operation, clinical stage, and outcomes were analyzed. Clinical findings between the two eras, 1971–1990 and 1991–2014, were also compared.
Result: The median age at operation was 17 months. Pathology revealed 29 teratomas (47%), 26 yolk sac tumors (42%), 5 epidermoid cysts (8%), 1 Sertoli cell tumor (1.5%), and 1 benign cyst (1.5%). Teratoma was the most common tumor in this series, and children with immature teratomas were operated at a significantly younger age than those with mature teratomas. Yolk sac tumor was the second most common. The clinical stages of yolk sac tumors were stage I in 23 (89%) and stage II in 3 (11%). Clinical findings were not significantly different between the early and late eras.
Conclusions: To the best of our knowledge, this is the largest single-center study of PTTs in Japan. The most common PTT in this study was teratoma, followed by yolk sac tumor. There was no significant difference in the histological distribution of PTTs between the two eras. Compared with the current data of single-center series in North America, the incidence of yolk sac tumor was markedly higher in the present study. This discrepancy is possibly explained by racial differences.

Prepubertal testicular tumors (PTTs) are rare, representing 1 to 2% of all pediatric solid tumors, with an annual incidence of 0.5 to 2.0 per 100,000 children [1,2]. The American Academy of Pediatrics (AAP) Prepubertal Testicular Tumor Registry (PTTR) showed that the most common histology of PTTs was yolk sac tumors, representing 62% of 395 tumors [3]. Similarly, in the Armed Forces Institute of Pathology American Testicular Tumor Registry, yolk sac tumor was the predominant cell type in prepubertal patients [4]. In contrast, the recent data of 4 major pediatric institutions in North America showed that teratomas were the most common, and only 15% of 98 patients had yolk sac tumors [5]. The main reason for the high prevalence rates of prepubertal yolk sac tumors in the AAP PTTR was thought to be reporting bias, since benign tumors were less likely to be submitted to tumor registries. However, recent data from a single-center Korean cohort showed that yolk sac tumors were the most prevalent PTTs, accounting for 53% of 48 patients [6]. From the analysis of the Surveillance, Epidemiology and End Results Program (SEER) data for U.S. boys, the incidence of yolk sac tumors was significantly higher in Asian/Pacific Islander boys than in other races [7,8]. Racial differences might be present in the incidence and histological distribution of PTTs. As the tertiary pediatric urology center for a population of more than 8 million individuals in Japan, we reviewed our 44-year experience of PTTs.

1. Materials and methods

From the pathological database of testicular tumors of Kanagawa Children's Medical Center (KCMC), all records of children aged less than 12 years were extracted with the appropriate Institutional Review Board approval. A total of 62 records of children who were treated for testicular tumors at KCMC from 1971 to 2014 were retrospectively reviewed.

2. Exclusion criteria

Para-testicular tumor, non-primary testicular tumor, and patients referred to our institution after initial surgical treatment were excluded.

3. Study definitions

In the first study, histopathological findings, age at operation (months), clinical stage, adjuvant therapy, and outcome were analyzed

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in all children. The stage of the yolk sac tumor was determined according to the staging system used by the Children's Oncology Group [9]. In the second study, the effects of the different backgrounds of the early and late periods of this study were evaluated. Clinical findings of PTTs were compared between the two eras, from 1971 to 1990 and from 1991 to 2014. In the third study, to address the current controversy regarding the distribution of histological types of PPTs, the published data of 7 single pediatric institution series in North America, Korea, and Japan were compared.

In our institution, computed tomography was started for staging yolk sac tumors in 1984, and high-resolution scrotal ultrasonography was introduced for initial diagnosis of scrotal swellings from 1991. Before 1980, all children with stage I yolk sac tumors were managed with radiotherapy after radical inguinal orchiectomy. The first testis-sparing surgery for a benign tumor was carried out in 2009.

4. Data analysis

JMP ver.11 (SAS Institute Inc., Cary, NC) was used for the statistical analyses. All clinical parameters were analyzed by the chi-square test. A p-value of less than 0.05 was considered significant.

5. Results

The clinical data of the 62 patients were evaluated. The median age at operation was 17 months (range, 2 to 116 months). A scrotal mass was the most common presentation in these patients (Table 1). Two patients with testicular tumors were diagnosed at the time of evaluation of a concomitant undescended testicle. Two yolk sac tumors were found in children with Down's syndrome. No patients had disorders of sexual development.

Pathology revealed 29 teratomas (47%), 26 yolk sac tumors (42%), 5 epidermoid cysts (8%), 1 Sertoli cell tumor (1.5%), and 1 benign cyst (1.5%) (Table 2). The median follow-up period of all PTTs was 6 years (range, 0 to 42 years). Since 2009, testis-sparing surgery was carried out in 5 cases in which the AFP level was normal for age and the tumor border was clear on testicular ultrasonography.

Teratoma was the most common tumor in this series, and children with immature teratomas were operated at a significantly younger age than those with mature teratomas ($p = 0.002$). No patient with teratoma had metastatic disease during the follow-up period.

Yolk sac tumor was the second most common tumor in this series. The clinical stage of yolk sac tumors was stage I in 23 (89%) and stage II in 3 (11%). All three patients with stage II underwent scrotal needle aspiration before referral. Adjuvant therapy was performed in 9 patients; 7 patients treated in the 1970s underwent radiotherapy after radical orchiectomy, and 2 patients with stage I yolk sac tumors were managed with adjuvant chemotherapy because of microscopic vascular invasion of tumor cells. One stage I yolk sac tumor in a patient with Down's syndrome relapsed after normalization of AFP levels, and the patient died 35 months later. The five-year survival rate was 96%.

As for the comparison of the 2 eras, Fig. 1 shows the distribution of PTTs in each era. Although the numbers of teratomas and yolk sac tumors were quite similar in each era, teratoma was the most common tumor in both eras.

To compare the results of the histological distributions of PTTs with other single-center series, Table 3 lists the published data of 7 pediatric institutions in North America, Korea, and Japan. Although teratoma was the most common tumor in all series except the Korean series, the most striking finding was the preponderance of yolk sac tumors in Korean and Japanese pediatric institutions compared with those in North American institutions.

Table 1
Characteristics of prepubertal patients with testicular tumors.

Age at operation (mo) median (range)	17 (2–116)
Laterality (%)	
Right	25 (40)
Left	37 (60)
Presenting sign and symptoms (%)	
Scrotal mass	52 (84)
Hydrocele testis	6 (10)
Cryptorchidism	2 (3)
Incidental finding	2 (3)

Table 2
Clinical findings of patients with prepubertal testicular tumors.

Histologic type	Number (%)	Age at operation (Mo) Median (range)	Testis sparing surgery Number	Follow up period (yr) Median (range)
Yolk sac tumor	26 (42)	17 (2–35)	0	8 (2–42)
Stage 1	23	16 (2–35)	0	7 (2–42)
Stage 2	3	17 (9–29)	0	13 (4–14)
Teratoma	29 (47)	12 (3–116)	3	6 (0–35)
Immature teratoma	7	7 (3–10)	0	14 (6–25)
Mature teratoma	22	19 (9–116)	3	4 (0–35)
Epidermoid cyst	5 (8)	107 (11–127)	2	4 (0–22)
Gonadal stromal cell tumor	1 (1.5)	105	0	13
Others	1 (1.5)	4	0	5

6. Discussion

Pediatric testicular tumors are uncommon and account for 1–2% of pediatric solid tumors, which is approximately 1 per 100,000 population [1,2]. Because PTTs are rare in the world, the Prepubertal Testis Tumor Registry was established by the Urologic Section of the American Academy of Pediatrics (AAP) in 1980. In 2002, Ross et al. reported the registry data accumulating 395 prepubertal patients who had a primary testicular tumor [3]. In the AAP PTTR, yolk sac tumors represented 62% of all tumors, compared to teratomas, which comprised only 23%. Although the AAP PTTR was limited by the potential for selection bias and reporting bias, the registry offered a large sample size from which significant trends in epidemiology and behavior could be extracted. However, Pohl et al. studied the histopathologic features of all pediatric testicular tumors removed at 4 major pediatric centers (Toronto, Philadelphia, Washington D.C., Boston) in North America, and they found that the incidence of yolk sac tumors in children was even less than that described in the AAP PTTR [5]. Teratomas accounted for 48% of tumors, with yolk sac tumors accounting for only 15%. Overall, 74% of the tumors in that series were benign. The exact cause of this large discrepancy was unknown, but analysis of a single-center cohort may be useful in reducing not only reporting bias but also referral filter bias.

In the present study, 62 patients with PTTs were evaluated. To the best of our knowledge, this is the largest series of PPTs in Japan and also one of the largest single pediatric institutional studies of PTTs ever reported in the world [10–12]. Regarding histological distribution, the most common tumor was teratoma (47%), and the second most common tumor was yolk sac tumor (42%). The incidence of teratoma was similar to the pooled data of 4 major pediatric centers in North America, but there was a marked difference in the incidence of yolk sac tumors [5]. The period of review in this study was 44 years, and it was longer than any review of the 4 major pediatric centers. Because of the long period of this study, background on the diagnosis and management of PTTs was different in successive periods. In the 1970s, computed tomography was not used for tumor staging, and since 1991, high-resolution ultrasonography has been routinely used for initial diagnosis of any scrotal swelling. To evaluate the effects of the different backgrounds of the early and late periods of this study, the data were compared between the two eras, from 1971 to 1990 and from 1991 to