Peng, B.; Yang, C.; Cao, Y. (2023) Tissue type analysis of 122 pediatric testicular tumors. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (89) pp. 261-270
DOI: https://doi.org/10.15366/rimcafd2022.89.018

ORIGINAL

TISSUE TYPE ANALYSIS OF 122 PEDIATRIC TESTICULAR TUMORS IN YOUNG MALE PLAYERS

Bo Peng[1], Chao Yang[1], Yongsheng Cao[1]*

[1]Department of Urology, Anhui Provincial Children's Hospital, No.39, Wangjiang East Road, Baohe District, Hefei City, 230022,Anhui Province,China
*Correspondence:Yongsheng Cao,
Email: cysetyy@163.com

Spanish-English translators:

UNESCO Code / UNESCO Code:
Council of Europe classification / Council of Europe classification:

Recibido 30 de abril de 2020 **Received** April 30, 2020
Aceptado 26 de junio de 2020 **Accepted** June 26, 2020

ABSTRACT

Purpose: To study the association between various tissue types, benign and malignant proportion and preoperative serum alpha-fetal protein (AFP) value and benign and malignant testicular tumors, to provide help for clinical diagnosis and treatment in young male players. Methods: The clinical data of 122 pediatric testicular tumors of young players admitted to our hospital from October 2013 to December 2021 were collected for retrospective chart review. According to the pathological test results, the tissue type, age, benign and malignant proportion and preoperative AFP level and benign and malignant associations between testicular tumors were analyzed. Results: A total of 122 pediatric testicular tumors of young players aged 0.01 to 14 years old, 114 young players (93.4%) were primary testicular tumors, 8 young players were secondary malignant tumors (6.6%), and 7 of them were leukemic cell infiltration. Of the 114 primary testicular tumors, 84 were benign (73.7%), 43 left, 41 right, 0.01-12 median 3.29,60 teratas, 71.4% of primary benign tumors, 30 malignant (26.3%), 16 left, 14 right 0.44-4.33, median 2.81, including 26 yolk sac tumors (86.7% of primary testicular malignancy), 2 mixed cell tumors and two rhabdomyosarcoma tumors.In the primary testicular tumors, 100 young players cases were derived from germ cell tumors (87.7%).His children had preoperative serum AFP levels, including 19 children <6 months of age, including 11 mature teratoma, 4 immature

teratoma, and 4 yolk sac tumors, with an AFP range of 5.4-14424.12ng/ml, 46.1-713.26ng/ml, 2620.34-17597.67ng/ml.A total of 81 children over 6 months of age, including 43 mature teratoma (AFP range 0-92.18ng/ml), 2 immature teratoma (AFP 0.78-36.4ng/ml), 22 yolk sac tumors (AFP367.7-26630.3ng/ml), 12 dermoid cysts (AFP 0-4.6ng/ml), and 2 mixed germ cell tumors (AFP =5462.38ng/ml, 16018.65ng/ml, respectively).Conclusion: Most pediatric testicular tumors are primary tumors derived from germ cells; most pediatric testicular tumors are benign, among which teratoma account for the largest proportion, and most malignant primary testicular tumors are yolk sac tumors; for children older than 6 months of age, the significantly increased preoperative serum AFP value indicates the possibility of yolk cyst tumors, and AFP can be used as an important basis to judge the benign and malignant testicular tumors.

KEY WORDS: Testicular tumor; tissue type; children; teratoma; yolk sac tumor ;AFP

The incidence of testicular tumors in children is low, about 0.5 / 100000~2.0/100 000, accounting for 1% of pediatric solid tumors, and it has a higher trend in recent years in people aged <14 years (Stein et al., 2021). There are two high-incidence age groups of testicular tumors in children, respectively, around 2 years old and around puberty (Wu, Shen, Lin, & Chen, 2018). Children's testicular tumor classification is complicated and diverse, such as teratoma, yolk sac tumor, dermoid cyst, juvenile granulosa cell tumor, stroma cell tumor, Sertoli cell tumor, and mixed adenostromal cell tumor, etc., however, few scholars have studied its specific proportion and lack of specific data (Higioka, Martins, & Martinello, 2019).

AFP (serum alpha-fetal protein) is a serum glycoprotein whose half-life and age correlation peak at 12 to 15 weeks of the embryo, and then gradually drops to the normal adult level (<10 μg/ml) near 1 year of age. AFP in 6-month normal infants is often less than 100 μ g / ml. When developing hepatocellular carcinoma, yolk sac and embryo-like tumors and some extrahepatic tumors, the body can be re-synthesized. AFP is an important and valuable indicator in the diagnosis of germ cell tumors (Kumar, 2019).

The authors counted 122 cases of testicular tumors treated in our hospital from October 2013 to December 2021, and analyzed the epidemiological characteristics of the specific proportion of tumors of each tissue type, in order to provide help in clinical diagnosis and treatment.

1. METHOD

A total of 122 pediatric testicular tumors were admitted to our hospital from October 2013 to December 2021, and a retrospective chart review was conducted. According to the pathological test results, the tissue type, source,

age, benign and malignant proportion and the association between preoperative AFP level and benign and malignant degree of testicular tumors were analyzed.

2. RESULTS

In this study, there were 122 pediatric testicular tumors, aged 0.01-14 years, of which 114 (93.4%) were primary testicular tumors, and 8 were secondary malignant tumors (7 were leukemic cell infiltration). Of the 114 primary testicular tumors, 84 were benign (73.7%), left 43, right 41, aged 0.01-12, median 3.29 years, including 60 teratoma (71.4% of the primary benign tumors); 30 malignant tumors (26.3%), left 16, right 14,0.44-4.33, median 2.81 years, and 26 yolk sac tumors (86.7% of primary testicular malignancy). Specific data are shown in Figure 1 and Table 1.

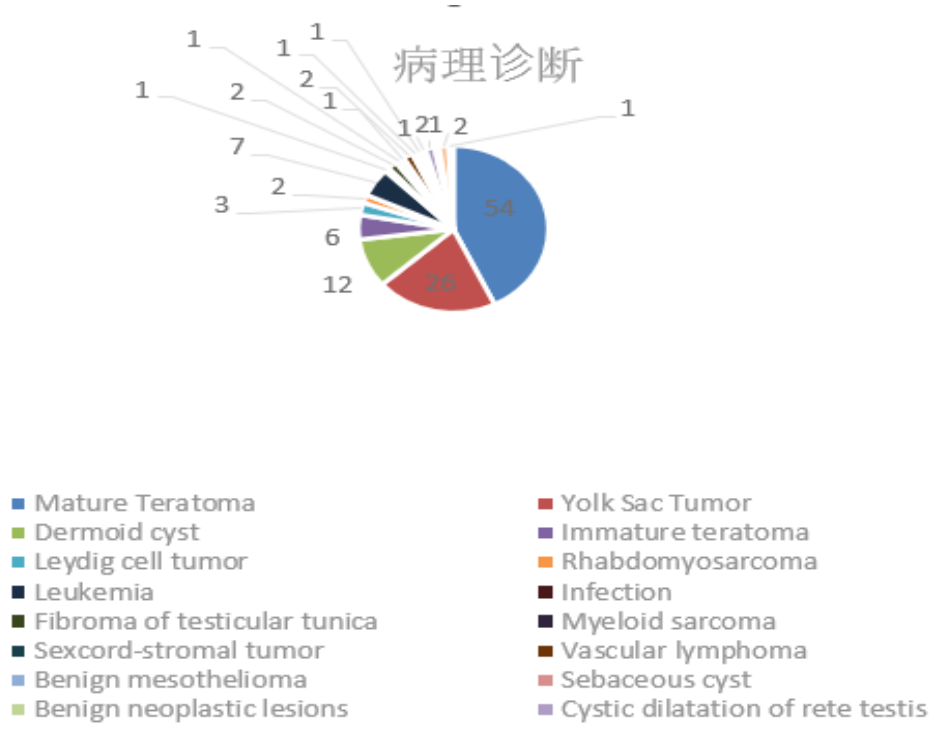


Figure 1: Pathological diagnosis of 122 testicular tumors

As shown in Figure 1, of these 122 cases, 100 were germ cell tumors (GCTs), with 72 (72%) benign, aged 0.01 – 12 years, median 3.36 years (0.01-12 years); 28 (28%) were malignant, aged 0.44 – 4.33, median 1.46 years (0.11-7). Tissue subtype: 54 cases of mature teratoma (54%), 26 cases (26%), 12 cases of dermoid cysts (12%), 6 cases of immature teratoma (6%), and 2 cases of mixed germ cell tumours (2%). L infiltration was the majority (87.5%).

These 122 children were divided into three groups by age, aged 0–4,5–

9,and 10– 14 years old. The most common histological types in each group were mature teratoma, yolk sac tumor, dermoid cyst, and immature teratoma (Figure 2)

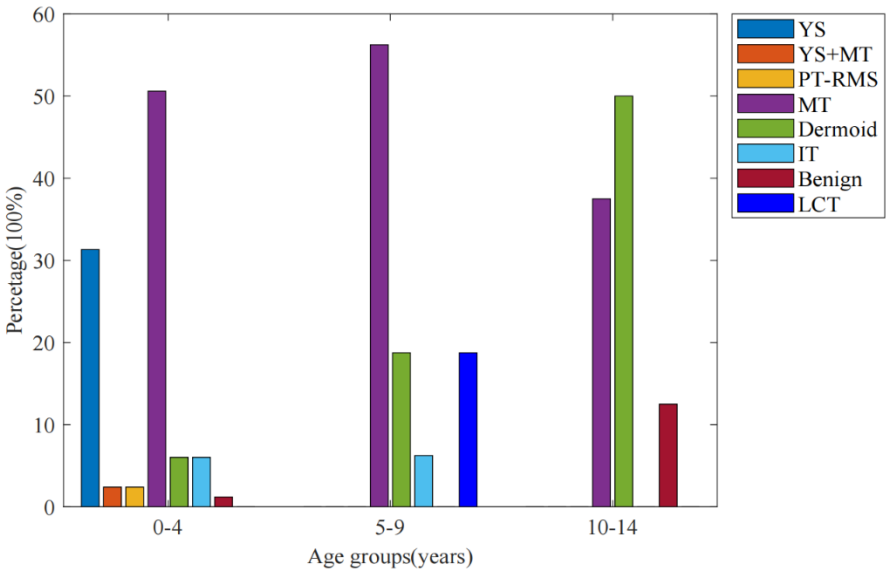


Table 1: Number and age of the histological types of some primary testicular tumors

	Number	Medium(year)	p25-p75(year)	Range(year)
Benign tumor				
MT（mature teratoma）	54	2.65	0.61-3.33	0.01-12
Dermoid cyst	12	6.60	2.84-11	1.33-12
IT（immature teratoma）	6	1.49	0.36-0.6	0.11-7
LCT（Leydig cell tumor）	3	8	7.25-8.75	7-9
Malignant tumor				
YS（yolk sac tumor）	26	1.44	0.92-1.83	0.44-4.33
PT-RMS（paratesticular rhabdomyosarcoma）	2	2.63	1.83-3.42	1.83-3.42
Mixed（YS+MT）	2	1.53	0.97-2.08	0.97-2.08

As shown in Table 1,84 pediatric primary testicular tumors were benign (73.7%), with teratoma, 71.4%; malignant minority (26.3%), and yolk sac tumor, the vast majority (86.7%).

Among them, 100 patients with germ cell tumors (GCTs) had preoperative serum AFP levels, with 19 children <6 months old, including 11 mature teratoma, 4 immature teratoma, and 4 yolk sac tumor, with an AFP range of 5.4-14424.12ng/ml, 46.1-713.26ng/ml, 2620.34-17597.67ng/ml. A total of 81 children over 6 months of age, including 43 mature teratoma (AFP range 0-92.18ng/ml), 2 immature teratoma (AFP:0.78-36.4ng/ml), 22 yolk sac

tumors (AFP:367.7-26630.3ng/ml), 12 dermoid cysts (AFP: 0-4.6ng/ml), and 2 mixed germ cell tumors (AFP: 5462.38ng/ml;16018.65ng/ml).

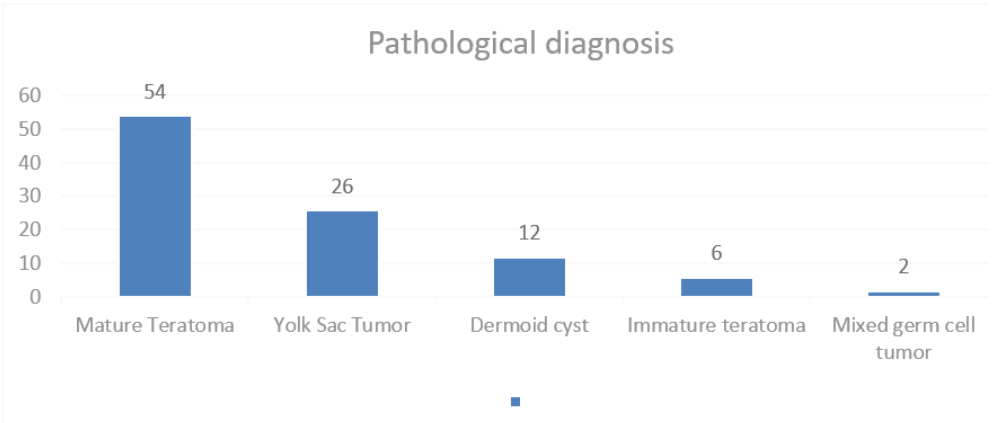
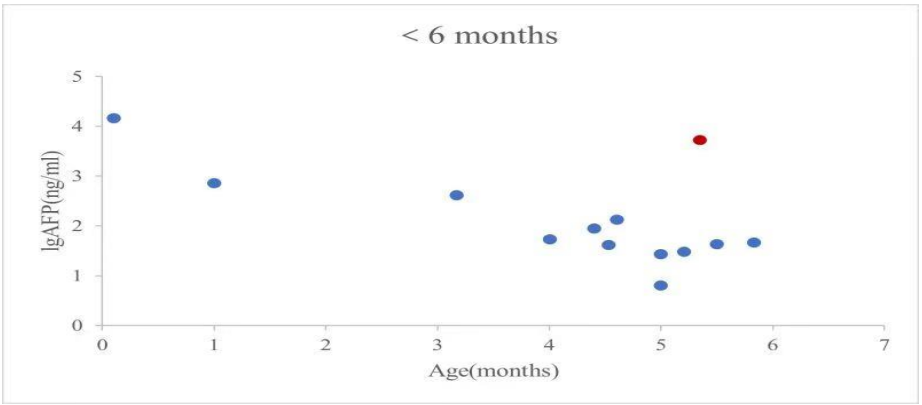


Figure 3: The portion of testicular germ cell tumors in 100 cases

Table 2: Range of AFP values in 100 germ cell tumors

	AFP <6months	**>6months**
Benign tumor		
MT（mature teratoma）	5.4-14424.12ng/ml	0-92.18ng/ml
Dermoid cyst	/	0-4.6ng/ml
IT（immature teratoma）	46.1-713.26ng/ml	0.78-36.4ng/ml
Malignant tumor		
YS（yolk sac tumor）	2620.34-17597.67ng/ml	367.7-26630.3ng/ml
Mixed（YS+MT）	/	5462.38ng/ml;16018.65ng/ml



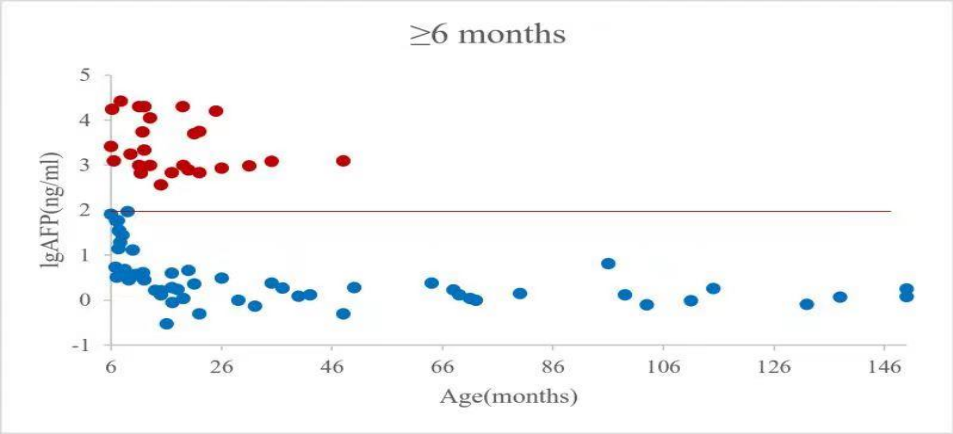


Figure 4: 5 Scatter diagram of common logarithm to AFP (ng/ml) in different age groups. Red dots represented malignant cases, and blue dots represented benign ones

3. DISCUSS

testicular tumor tissue types of children are complicated and diverse, and only a few scholars have reported the specific association between various tissue types, proportion of benign and malignant tumors, preoperative AFP value and benign and malignant tumors. Most pediatric testicular tumors are primary tumors (Zheng et al., 2015). We found that in this study, primary tumors accounted for 93.4% of testicular tumors. In pediatric secondary testicular tumors, most are leukemic cell infiltration (Nadanaka, Kinouchi, & Kitagawa, 2018). Our data show that most pediatric primary testicular tumors are tumors of germ cell origin (87.7%), among which teratoma is the most common, accounting for 71.4% of the primary benign testicular tumors, and yolk sac tumor is the most common malignant tumors, accounting for 86.7% of the primary testicular malignant tumors. Germcell tumors are formed by the transformation of primordial germ cells or pluripotent germ cells that differentiate from the yolk sac endoderm during embryonic development, move through the mesentery to the urogenital crest, and then form gonads (Aldrink et al., 2021; Iczkowski, 2022; Sung, Kim, Bae, Jo, & Park, 2020)。

Mature teratomas often contain well-differentiated tissues derived from the ectodermal, mesodermal, and endodermal germ cell layers。

Immature teratoma consists of the whole or part of immature tissues with different degrees of differentiation. Most of the immature components are ectodermal neural tissue, which is a rare benign germ cell tumor prone to occur in small infants(Hazan, Phillips, Qiao, Norton, & Aaronson, 2000; Wang et al., 2020). Immature teratomas accounted for 5.26% of pediatric primary testicular tumors in our study.

Epidermoid cyst belongs to testicular benign tumor, its incidence is not high, the cause is not clear. Epidermoid cysts occur mainly in the skin and

rarely in the testis. The pathogenesis of testicular epidermoid cysts may be squamous metaplasia of seminiferous tubules, epidermal inclusions or testicular web, and it has also been suggested due to the replacement of teratoma skin components or due to embryonic dislocation of the squamous epithelial content derived from the scrotal skin primordium (Liu, Ye, & Zhu, 2019; Satelli & Li, 2011). In our study, dermoid cysts accounted for 10.53% of primary testicular tumors.

Malignant germ cell tumors clearly contain malignant tissue of germ cell origin and rarely contain somatic cell-derived tissue. Isolated malignant components may constitute a small fraction of the major mature or immature teratoma, but do not affect the benign attributes of a pediatric teratoma. Pediatric malignant testicular tumors are usually composed of pure yolk sac tumor (also known as endodermal sinus tumor)(Chetty, Lakka, Bhoopathi, & Rao, 2010). Malignant testicular germ cell tumors can be histologically divided into yolk sac tumor (endodermal sinus tumor), embryonal carcinoma, seminoma, chorionic epithelial carcinoma, and mixed germ cell tumor. The yolk sac tumor is the most common testicular malignancy in the prepubertal population(Fernández et al., 2016). In our study, yolk sac tumor accounted for 24.56% of primary testicular tumors and 93.3% of primary testicular malignancies, indicating that yolk sac tumor is the primary pediatric testicular malignancy. In our study, there was no single case of embryonal carcinoma, seminoma, or choriocarcinoma, with an extremely low incidence of these germ cell-derived malignancies. Testicular mixed germ cell tumors are malignant tumors, containing endodermal sinus, villocarcinoma component of trophoblast cells, pure reproductive component of germ cells or teratoma component (Lu Liu et al., 2019)。

Embryonal rhabdomyosarcoma is rare, and testicular / paratesticular rhabdomyosarcoma accounts for 7 – 10% of genitourinary rhabdomyosarcoma, and testicular / paratesticular rhabdomyosarcoma originates from the distal spermatic cord, epididymis, and testicular sheath membrane, which can invade testicular tissue (S. Liu et al., 2019). The testicular / paratticular rhabdomyosarcomas accounted for 1.63% of patients with testicular tumors, consistent with 1.6% reported in other literature.

AFP is a glycoprotein that is mainly synthesized by fetal hepatocytes and the yolk sac. AFP has a higher concentration in the fetal blood circulation, which decreases after birth, and is more difficult to detect in the blood, and it is extremely low in the adult serum. When liver cells or gonad embryonic tissue undergo malignant changes, the genes related to the fexin are reactivated, so that the fexin can be re-synthesized and released into the blood, and the content is increased. In clinical work, AFP has been used as a tumor marker to diagnose and evaluate the therapeutic effect of testicular tumors producing AFP (Roskoski Jr, 2019)。

In newborns, serum AFP levels were significantly increased (term newborn: 41687ug / L, preterm: 158125ug / L). In infants, serum AFP levels decrease rapidly after birth. The serum half-life of AFP is age-related, with a half-life between birth and 2 weeks, about 10 days between 2 weeks and 2 months, and about 30 days between 2 months and 4 months. Most infants' AFP serum levels decreased to normal adult levels within the first 8 – 10 months. As AFP levels change in infancy vary with month age, this poses a challenge to the use of AFP as a tumor marker in infants. There are very few published reports in the literature on the normal upper limit of AFP values related to the malignancy of testicular germ cell tumors, especially in infants. As high AFP values are widespread in normal small infants, especially those less than 6 months, it should be prudent to conclude that elevated serum AFP in infants less than 6 months in testicular tumor cases is expressed as malignant. Our study showed that the benign and malignant preoperative serum AFP value of infants with malignant testicular tumors were less than June; while the preoperative AFP value of benign tumors was less than 100 ng/ml(0-92.18ng/ml), and the AFP value of germ cell-derived malignant tumors was significantly increased (367.7-26630.3ng/ml). For children with more than June, the preoperative serum AFP value has important reference value for judging benign and malignant tumors before surgery.

Significantly elevated serum AFP levels almost always show malignant testicular tumors, and the surgical approach is usually chosen for radical testicular resection with the inguinal approach. Testicular-sparing tumor enucleation has become the preferred treatment for benign testicular tumor cases in prepubertal children, and has been widely reported(Grogg et al., 2022; Roy & Thompson, 2006). However, in potentially malignant cases, inappropriate testicular-sparing surgery and preoperative biopsy surgery may improve the stage of the tumor, but may lead to unnecessary chemotherapy and even the metastasis of the tumor, especially the surgical method of the transscrotal approach (Chen, Fang, & Ma, 2021; Jurikova, Danihel, Polák, & Varga, 2016). In pediatric testicular tumors, when preoperative serum AFP values are significantly elevated, we recommend a radical orchiectomy with the inguinal approach without prior biopsy, while excluding elevated serum AFP values due to liver and other diseases.

4. CONCLUSION

Most prepubertal testicular tumors are primary tumors, among which germ cell tumors are the most common, and benign tumors account for the majority of pediatric testicular tumors. Teratoma is the most common benign pediatric testicular tumor, while yolk sac tumor is the most common malignancy. For pediatric testicular tumors older than 6 months of age, the preoperative serum AFP value has an important reference value for the judgment of benign and malignant tumors.

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