[Chinese Journal of Cancer 27:11, 477-479; November 2008]; ©2008 Sun Yat-sen University Cancer Center

Clinical Research Paper

Clinical analysis of stage I pediatric testicular yolk sac tumors

A report of ten cases

Yun-Lin Ye,[1,2] Zi-Ke Qin,[1,2,*] Fang-Jian Zhou,[1,2] Hui Han,[1,2] Zhuo-Wei Liu,[1,2] Shao-Long Yu,[1,2] Yong-Hong Li[1,2] and Zhuang-Fei Chen[1,2]

[1]State Key Laboratory of Oncology in South China; Guangzhou, Guangdong P.R. China; [2]Department of Urology; Cancer Center; Sun Yat-sen University; Guangzhou, P. R. China

Key words: children, pediatric testicular neoplasm, yolk sac, diagnosis, treatment

Background and Objective: At present, pediatric testicular yolk sac tumor is hard to diagnose in the early stage, and the treatment strategy for this disease after radical inguinal orchiectomy is uncertain. This study summarizes our experience in diagnosing and treating clinical stage I pediatric testicular yolk sac tumors. Methods: Clinical data from ten patients with clinical stage I pediatric testicular yolk sac tumors treated from July 2001 to June 2007 were analyzed. Results: Testicular masses with low or uneven echoes were detected by B ultrasound in 11 testes of ten patients. The serum level of alpha fetoprotein (AFP) was increased in nine patients. Radical inguinal orchiectomy (RIO) was performed for all patients, whereas chemotherapy was not administered preoperatively. Pathology examination was used to confirm the diagnosis of yolk sac tumor. One patient with vascular invasion and another one with bilateral testicular yolk sac tumor received cisplatin-based adjuvant chemotherapy. Retroperitoneal lymph node dissection (RPLND) was not performed in these patients. No recurrence was found in nine patients during follow-up with a mean of three years. The patient with bilateral testicular tumor had retroperitoneal and lung metastases at 23 months after adjuvant chemotherapy, and achieved complete remission after salvage chemotherapy. Conclusions: With the combination of B ultrasound and the serum level of AFP, we can assess and diagnose stage I pediatric testicular yolk sac tumor. RIO can be used to treat it with good outcomes, while RPLND is not necessary. Chemotherapy is recommended to treat patients with a high risk of relapse.

*Correspondence to: Zi-Ke Qin; State Key Laboratory of Oncology in South China; and Department of Urology; Cancer Center; Sun Yat-sen University; Guangzhou, P. R. China; Tel.: 86.20.87343309; Fax: 86.20.87343295; Email: qinzike@263.net

Submitted: 03/13/08; Revised: 05/06/08; Accepted: 06/25/08

This paper was translated into English from its original publication in Chinese. Translated by: Beijing Xinglin Meditrans Center (http://www.58medtrans.com) and Wei Liu on 08/25/08.

The original Chinese version of this paper is published in: *Ai Zheng* (Chinese Journal of Cancer), 27(11); http://www.cjcsysu.cn/cn/article.asp?id=14750

Previously published online as a *Chinese Journal of Cancer* E-publication: http://www.landesbioscience.com/journals/cjc/article/8004

Pediatric testicular yolk sac tumor is rare in clinic, yet the most common tumor among all the primary tumors in children's reproductive systems. Testicular primary tumors have diverse pathological types, and early diagnosis of yolk sac tumor is difficult. In addition, the only established therapeutic regimen to treat it is radical inguinal orchiectomy. Our hospital treated 11 cases from July 2001 to June 2007, losing follow-up with one after discharge. Here we report 10 cases to explore the diagnosis and therapy strategies for pediatric testicular yolk sac cancer in its early stage.

Patients and Methods

Clinical data. From July 2001 to June 2007, our hospital treated ten cases of stage I pediatric yolk sac tumor. The patients were four months to three years old, with a median age of 11.5 months; eight cases were younger than two years old. The study included six cases of left side tumor, three cases of right side tumor and one case of bilateral tumor. All patients sought treatment because of painless testicular mass with no history of cryptorchidism. The patients' mothers had no special medication history during pregnancy. One patient was born in a silver-aluminum mine area. Physical examination identified swollen and hard testicles in the affected sides in nine cases and preoperative B ultrasound showed low or uneven echoes. In one case of bilateral testicular cancer, the neoplasm of the right testicle was palpable and the left testicle was non-palpable. B ultrasound showed uneven echo in both testicles; biopsy during operation found bilateral testicular yolk sac tumor. Chest X-rays were normal and no swollen retroperitoneal lymph nodes were identified by abdominal and pelvic CT or ultrasound. Alpha fetoprotein (AFP) levels; detected by electrogenerated chemiluminescence method, ranged from 12.79 μg/L~>121,000 μg/L, (normal value range 0.00~25.00 μg/L). There were nine cases with increased AFP, four cases >1,000 μg/L, 3 cases >10,000 μg/L, normal human chorionic gonadotropin (HCG) and lactate dehydrogenase (LDH) levels. Preoperative routine tests of blood, liver and kidney function were normal. All clinical diagnoses were stage I testicular yolk sac tumor.

Treatment. Ten patients received radical inguinal orchiectomy. Pathology confirmed yolk sac cancer, no invasion at spermatic

Table 1 **Clinical data of ten patients with clinical stage I pediatric testicular yolk sac tumor**

Case No.	Age(months)	Tumor site	AFP(μg/L)	Tumor size (cm)	Postoperative adjuvant chemotherapy	Follow-up (months)	Outcome
1	4	Left testis	63	1.5×1.5	No	79	No relapse
2	10	Right testis	215	4.0×3.0	No	77	No relapse
3	24	Left testis	2 054	3.0×2.5	BEP regimens,2 cycles	56	No relapse
4	36	Both testes	5 825	R:5.0×4.0; L:2.0×1.0	EP regimens,3 cycles; BEP regimens,4 cycles	54	Retroperitoneal and lung metastasis after 23 months
5	30	Left testis	>121 000	2.0×2.0	No	49	No relapse
6	8	Right testis	1 009	3.0×2.0	No	43	No relapse
7	11	Left testis	13	4.0×3.0	No	27	No relapse
8	24	Left testis	1 572	2.5×2.5	No	17	No relapse
9	12	Right testis	22 857	4.0×3.0	No	10	No relapse
10	5	Left testis	20 917	3.0×2.0	No	8	No relapse

AFP, alpha fetoprotein; RIO, Radical inguinal orchiectomy.

cord and tunica vaginalis. One case had tumor invasion in blood vessels. No retroperitoneal lymph node dissection was performed after surgery. In one case of bilateral testicular yolk sac tumor, after radical orchiectomy on right side, yolk sac tumor tissue was detected from contralateral testicle during biopsy, thus we changed into bilateral radical orchiectomy. Tumor diameter ranged 1.5~5.0 cm, average 3.2 cm. The bilateral testicular yolk sac tumor patient was given adjuvant chemotherapy using EP regimen (VP-16, 100 mg/m^2, d1-5; DDP, 20 mg/m^2, d1-5; administered at three week intervals) for three courses. Patient with vascular tumor invasion was treated by BEP regimen (BLM, 10 mg/m^2, d1, d5; VP-16, 100 mg/m^2, d1-5; DDP, 20 mg/m^2, d1-5; administered at three weeks intervals) for two courses.

Follow-up procedure. Ten cases were all followed-up by phone interviews until March 23, 2008. Follow-up questionnaires included children's overall status, growth and development, examination and treatment after discharge and the latest exam results.

Results

Ten pediatric patients were cured and discharged; their serum AFP levels declined markedly at the time of discharge and all returned to normal after one month. Patients were followed-up for eight to 79 months (average 42 months). For the bilateral testicular yolk sac tumor case, at the time of the 23rd month of follow-up after adjuvant chemotherapy, peritoneal and lung metastases were found. Complete remission was achieved after four courses of BEP regimen salvage chemotherapy, and no recurrence or progression was found after another 25 months follow-up. The one case of yolk sac tumor patient with vascular invasion had no recurrence after chemotherapy during 53 months' follow-up. In four cases followed-up for less than three years, no tumor recurrence or progression was found (Table 1).

Discussion

Yolk sac tumor is also known as endodermal sinus cancer, and has a relatively low incidence rate of about 0.1/100,000, but it is the most common tumor type among all pediatric malignant testicular cancers.[1,2] Guang-Hui Wei et al.[3] report 66 cases of pediatric testicular cancers. Among the 48 cases of primary tumors, 34 cases were yolk sac tumor, which amounts to (34/48) 70.8% of all testicular primary tumors. Data from U.S. Surveillance Epidemiology and End Results (SEER) show that pediatric yolk sac tumor accounts for 93/124 (75.0%) of testicular cancers,[4] while tumor registration data from multi-centers in Germany record the percentage of pediatric yolk sac tumor in pediatric testicular primary tumors at 117/173 (67.6%).[5] Our hospital treated 19 cases of children with primary testicular cancer from December 2001 to June 2007, among which there were 11 cases of yolk sac tumor (57.9%). This is consistent with previous literature reports worldwide.

The preoperative diagnosis of pediatric testicular yolk sac tumor is non-specific, since all cases present as scrotal mass. Scrotum B ultrasound can identify between scrotum cystic or solid tumor. Our B ultrasound results for all yolk sac tumors showed mixed or low echo solid neoplasm. Increased serum AFP level suggests possible pediatric testicular yolk sac tumors. Reports[6] indicate that nearly 90% of yolk sac tumor cases have increased serum AFP level, in addition, yolk sac cancer is the most common tumor among all the pediatric testicular germ cell tumors.

For children with normal AFP level, we can not exclude the possibility of benign testicular tumor; however all testicular tumors should be treated as malignant in their early treatment, in order to avoid serious consequences such as local recurrence, metastasis, etc. To ensure treatment effects and to retain function as much as possible in suspected benign pediatric testicular tumor cases, we first block the spermatic cord through inguinal region, and then take biopsy; in the case of benign tumor we will perform tumor resection without removal of the testis.[7] Multiple centers report that testicle-sparing operations for testicular benign tumors are safe and reliable. There are reports of no complications (such as recurrence, testicular atrophy, etc.,) after more than ten years follow-up.[1]

For the clinical stage I pediatric testicular yolk sac tumor confirmed after radical orchiectomy, recent literature suggests that radical orchiectomy alone can achieve good therapeutic result.[8,9] Whether to perform retroperitoneal lymph node dissection or

adjuvant chemotherapy is still under debate. Some studies show that[10] testicular yolk sac tumor mainly transfer through the blood stream and the most common metastasis happens in the lung, while retroperitoneal metastasis is relatively rare. Data from Fudan University Children's Hospital (formerly the Pediatric Hospital of Shanghai Medical University) demonstrate that.[11] there is no need to perform retroperitoneal lymph node dissection in pediatric testicular yolk sac tumor after radical orchiectomy since retroperitoneal lymph node metastasis is rare. They believe that retroperitoneal lymph node dissection does not improve the prognosis and may cause ejaculation obstacles and serious perioperative complications including death. There are also reports that suggest that adjuvant chemotherapy for clinical stage I pediatric testicular yolk sac tumor is safe and effective.[12,13]

With the advance of medical imaging technology and knowing the correlation between serum AFP level and the recurrence and metastasis of yolk sac tumor, close follow-up can find recurrence and metastasis in their very early stage. The current trend is to perform radical inguinal orchiectomy alone, to give chemotherapy to patients with lung metastasis, and to do retroperitoneal lymph node dissection on patients with retroperitoneal metastasis. In this group of ten stage I pediatric testicular yolk sac tumor patients, eight cases received only radical inguinal orchiectomy with good results, so far no recurrence has been identified during follow-up. One case of patient with vascular invasion received two courses of BEP regimen with no recurrence or metastasis. One case of bilateral testicular yolk sac tumor received EP regimen for three courses as adjuvant chemotherapy treatment, and metastasis was found in peritoneum and lung after 23 months of follow-up. This patient was then given PEB regimen salvage chemotherapy and achieved a complete remission, no recurrence or progression was found after another 25 months follow-up.

We believe that in clinical stage I pediatric yolk sac tumor, radical inguinal orchiectomy alone can achieve good results, so there is no need for retroperitoneal lymph node dissection. For cases with high risk of recurrence or progression (vascular invasion), standard BEP adjuvant chemotherapy regimen should be included in their treatment for 2–3 courses. For cases with retroperitoneal or lung metastasis, chemotherapy can achieve good results.

References

[1] Oottamasathien S, Thomas JC, Adams MC, et al. Testicular tumors in children: a single-institutional experience. BJU Int, 2007,99(5):1123-1126.

[2] Agarwal PK, Palmer JS. Testicular and paratesticular neoplasms in prepubertal males. J Urol, 2006,176(3):875-881.

[3] Wei GH, Li XL, Gong YB, et al. Clinical features of pediatric painless scrotal mass—A report of 81 cases. Chin J Urol, 2001,22(8):506-507. [in Chinese]

[4] Walsh TJ, Grady RW, Porter MP, et al. Incidence of testicular germ cell cancers in U.S. children: SEER program experience 1973 to 2000. Urology, 2006,68(2):402-405.

[5] Stang A, Rusner C, Eisinger B, et al. Subtype-specific incidence of testicular cancer in Germany: a pooled analysis of nine population-based cancer registries. Int J Androl, 2007,30(1):1-11.

[6] Wen J J, Du C Q, Wen J G, et al. Clinical significance of monitoring serum AFP of infants and children with solid tumors[J]. Journal of Zhengzhou University[Medical Sciences],2002,37(1):65-67. [in Chinese]

[7] Wang Z, Liu GL, Wang Y, et al. Effects of testis-sparing surgery for benign testicular tumors in children. J Applied Clin Pediat, 2003,l8(l0):833-834. [in Chinese]

[8] Zeng XY, Qin GQ, Liu SQ, et al. The pediatric testicular yolk sac tumors at stage I. J Clin Urol, 2004,19(1):13-14. [in Chinese]

[9] Terenziani M, Piva L, Spreafico F, et a1. Clinical stage I nonseminomatous germ cell tumors of the testis in childhood and adolescence:an ana1ysis of 31 cases. J Pediatr Hematol Oncol, 2002,24(6):454-458.

[10] Grady RW, Ross JH, Kay R. Patterns of metastatic spread in prepubertal yolk sac tumor of the testis. J Urol, 1995,153(4):1259-1261.

[11] Hu CG, Jin BX. Effects of retroperitoneum lymph node dissection for pediatric testicular yolk sac tumors. Chin J Pediat Sur, 1993,l4(4):213-214. [in Chinese]

[12] Lu L, Ma JH, Li CL. Endodermal sinus tumor of testis (report of six cases). Chin J Med, 2005,40(10):36-38. [in Chinese]

[13] Sun XF, Yang QY, Zeng ZJ, et al. Treatment outcomes of children and adolescents with germ cell tumor after combined therapy-A report of 44 cases. Aizheng, 2006,25(12):1529-1532. [in Chinese]