Indian J Pediatr (June 2015) 82(6):549–552
DOI 10.1007/s12098-014-1667-1

ORIGINAL ARTICLE

Testicular Tumors in Undescended Testes in Children Below 5 y of Age

Deepak Mittal · Sandeep Agarwala · D. K. Yadav · D. D. Pramanik · M. C. Sharma · D. Bagga

Received: 1 June 2014 / Accepted: 17 December 2014 / Published online: 11 January 2015

Abstract
Objective To evaluate the presentation, treatment and outcome of testicular tumors in undescended testes (UDT) in boys below 5 y of age.
Methods Case records of boys below 5 y of age, diagnosed to have germ cell tumors (GCT) in the UDT were reviewed.
Results Seven children in the age range of 05–54 mo (mean 26 mo) were included. While five of these 7 (71 %) presented with abdominal mass [one antenatally detected], 2 (29 %) were detected to have a GCT during orchiopexy. In three of these five with abdominal mass, the alpha-fetoprotein (αFP) was markedly elevated. Two of these three with elevated αFP were endodermal sinus tumors while the third was embryonal carcinoma. The 4th patient with an abdominal mass was diagnosed to have an immature teratoma (IMT) while the patient with antenatally diagnosed mass had a mature cystic teratoma (MT). Both the patients with incidentally detected mass during the orchiopexy had mature teratoma (MT). All the seven children are alive and disease free at last follow-up.
Conclusions Though rare, boys with impalpable undescended testes may develop germ cell tumors early in childhood. These can be managed with chemotherapy and resection and have a good disease free outcome.

D. Mittal · S. Agarwala (✉) · D. K. Yadav · D. D. Pramanik
Department of Pediatric Surgery, All India Institute of Medical Sciences, New Delhi 110029, India
e-mail: sandpagr@hotmail.com

M. C. Sharma
Department of Pathology, All India Institute of Medical Sciences, New Delhi, India

D. Bagga
Department of Pediatric Surgery, VMMC and Safdarjung Hospital, New Delhi, India

Keywords Testicular tumors · Undescended testes · Less than 5 y age

Introduction

Undescended testes (UDT) are one of the most common congenital anomalies, occurring in 1–4 % of full-term and 1–45 % of preterm male neonates [1]. Patients having undescended testis are increased risk of developing testicular malignancy [2]. Testicular tumors in uncorrected and undiagnosed UDT occur during third and fourth decades and are usually seminoma [3, 4]. Testicular tumors in UDT in prepubertal patients are rare and differ in histology than tumors in UDT in post-pubertal patients and tumors in normally descended testis. Till date only 35 cases of prepubertal intra-abdominal testicular tumors (IAT) in UDT have been reported (including one of the present series). The authors present the case series of seven patients, all aged below 5 y having testicular malignancy in UDT.

Material and Methods

A retrospective analysis of the case records for cases of germ cell tumors in UDT, in children below 5 y, was done at two institutions from 2008 through 2011. Presentation, investigations, treatment and outcome were reviewed. Benign cases underwent surgery alone while malignant lesions were treated both with surgery and chemotherapy. Chemotherapy used was PEB regimen (cisplatin+etoposide+bleomycin). Total of three cycles were given; two preoperatively and one after surgery. Follow up protocol included measurement of alpha-fetoprotein at 1 mo and then 3 monthly for 2 y, radiological evaluation of abdomen, pelvis and chest was performed at 1 mo and then 3 monthly thereafter for 2 y with alternating ultrasound examination and contrast CT scans.

Table 1 Characteristics of the boys less than 5 y of age having tumors in undescended testes (UDT)

Patients	Age (mo)	Presentation	Laterality	Location	αFP level	Histology
1	24	Right UDT	Right	Palpable	Not done	Mature teratoma
2	54	Right UDT	Right	Palpable	Not done	Mature teratoma
3	24	Inguinal & abdominal mass	Right	Palpable	800 ηg/ml	Embryonal carcinoma
4	30	Abdominal mass	Left	Impalpable	0.5 ηg/ml	Immature teratoma
5	18	Abdominal mass	Right	Impalpable	352,340 ηg/ml	Endodermal sinus tumor
6	27	Abdominal mass	Right	Impalpable	1.98 ηg/ml	Mature teratoma
7[a]	05	Abdominal mass	Left	Impalpable	18,960 ηg/ml	Endodermal sinus tumor

[a] Ref No. 19

Results

Seven boys, less than 5 y of age, were identified to have tumors in UDT. The age ranged from 05 to 54 mo (mean 26 mo). Five patients had right sided and two had left sided UDT. None of these patients had any suspected disorders of sexual development. There were no associated karyotypic or penile abnormalities. There was no history of prior orchidopexy. Four patients had impalpable and three had palpable UDT (Table 1). Palpable UDT may be due to the mass. Among the three with palpable UDT, one patient had testis in inguinal canal, one had peeping testis and one had enlarged testicular mass in the inguinal canal. Five patients had presented with an abdominal mass. Of these five, one had an antenatally diagnosed intra-abdominal mass detected at 27 wk of gestation, while another presented with both inguinal and abdominal masses (Fig. 1). The patient with an antenatal mass had some treatment elsewhere and presented to the authors at age of 5 mo with palpable abdominal mass. Two patients had presented with unilateral palpable UDT and the abdominal masses were detected during orchidopexy (Table 1).

Of the five patients who had presented with intra-abdominal masses, three had malignant germ cell tumors; one each had mature teratoma (antenatally diagnosed) and immature teratoma. Two patients, who had tumors detected during orchidopexy, had mature teratoma (Table 1). Of three malignant germ cell tumors two were endodermal sinus tumors and one was embryonal carcinoma (presented with both inguinal and abdominal mass) (Fig. 1). All three patients having malignant germ cell tumors had elevated alpha-fetoprotein (αFP) levels (Table 1), while in the remaining four with mature or immature teratoma, two had normal αFP and in another two patients αFP was not done pre-operatively. All four mature and immature teratomas underwent successful resection. Partial testicular salvage could not be done as there was no clear dissection plane between tumor and normal testicular tissue. The three patients with malignant germ cell tumors, presenting as large intra-abdominal masses, received two courses of neo-adjuvant chemotherapy (PEB) followed by resection and then one more course of adjuvant chemotherapy. In patients with malignant germ cell tumors αFP levels were normal after completion of treatment and thereafter in follow-up. All three patients were stage 3 disease (large

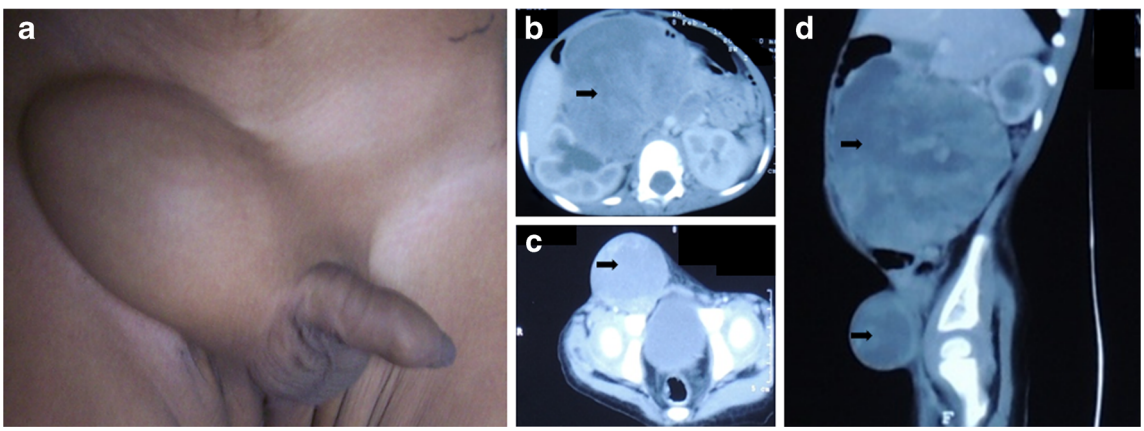

Fig. 1 (**a**) Clinical picture of a boy with right UDT, palpable inguinal mass and an abdominal mass; (**b**) Axial CECT scan showing the large heterogenous retroperitoneal lymph nodal mass and right hydronephrosis in the same boy; (**c**) Axial CECT scan showing the inguinal mass and (**d**) Coronal CECT scan showing both the abdominal and inguinal masses

intra-abdominal mass with adherent lymph nodes). All seven patients are alive and disease free at a follow-up period ranging from 14 to 60 mo. Two patients have subsequently received a testicular prosthesis.

Discussion

The incidence of UDT in the general population is estimated to be between 1 and 4 % [3, 4]. The incidence of UDT is 1–2 % at age of 1 y but the rate of surgery for UDT is approximately double the estimated risk (3–4 %). This suggests that the risk of UDT may vary during childhood depending on linear growth and timing of puberty, retractile testes, ascending testes and missed diagnosis among other things [4–6]. Testicular tumors account for 1–2 % of all pediatric solid tumors, with an annual incidence of 1: 100,000 for boys less than 15 y of age in the United States. The American Academy of Pediatrics, prepubertal testes tumor registry, reported that benign tumors accounted for 38 % of these cases [7]. Although UDT is considered being a major risk factor for developing testicular tumors, there is a lot of confusion related to UDT and testicular cancer because the rates of UDT and testicular cancer are heterogeneous and changing [8]. The relative risk (RR) of developing testicular cancer in cryptorchid or formerly cryptorchid patients ranges from 2.75 to 8 for all patients and 2–3 for patients undergoing prepubertal orchidopexy [9, 10]. Risk factors for development of malignancy in cryptorchidism are; bilateral UDT, abnormal external genitalia, abnormal karyotype, intra-abdominal testis, late correction of UDT and uncorrected UDT [11–13].

Orchidopexy by age of 10 to 12 y results in a 2 to 6-fold RR decrease compared with orchidopexy after age of 12 y or no orchidopexy. The lowest incidence of cancer is reported in children undergoing orchidopexy in the 0 to 6-y age range [2]. An odds ratio (OR) of 0.6 was reported for testicular cancer in patients treated before age of 11 y and an OR of 32 was reported in those treated later [14]. Location of testes affects the subsequent pathological subtype of testicular cancer. Seventy four percent of the malignant tumors developing in uncorrected abdominal or inguinal testes are seminomatous tumors, while the most common (63 %) malignant testicular tumors developing following orchidopexy are non-seminomatous tumors [10].

First intra-abdominal testicular tumor (IAT) was reported more than 60 y ago. Thirty five cases of prepubertal IAT tumors have been reported since that time [15–19]. In these reports the patient's age has ranged from 0 to 15 y (average 2.2 y). Fifty seven percent patients (20/35) were below 1 y and 91 % patients (31/35) were below 5 y of age. The most common histologic type was mature teratoma (28/35) followed by immature teratoma in two, yolk sac tumors in two, embryonal carcinoma in two and seminoma in one. Thus tumors in UDT in children below 5 y differ significantly than tumors in normally descended testis and tumors in uncorrected testis detected at older age.

Out of 35 cases reported [15–19], 4 cases were detected antenatally, four cases missed on initial exploration (no testis found) and these later presented with pain in two and torsion in two. Remaining cases presented with either mass or features of torsion. Two cases presented with undescended testes. In the current series, five patients presented with abdominal mass while two presented with undescended testes and no patient presented with features of torsion. The cause of mature teratoma in UDT in children below 5 y of age may be explained on the basis of germ cell theory as mentioned by Natsumi Tanaka [15], but the cause of malignant tumor in UDT in children below 5 y of age cannot be explained by the postpubertal theory of development of germ cell tumor, which states that all GCTs are thought to arise from a common precursor—the carcinoma in situ (CIS) cell [20, 21]. The cause may be due to unidentified prenatal or perinatal oncogenetic process. If a teratoma develops in a testis prior to its descent, it may itself prevent the descent and present as UDT. The teratoma in these children may undergo malignant transformation and later be diagnosed as malignant teratoma.

Testicular tumors in UDT in boys <5 y of age is rare but should be suspected if a child with UDT presents with an abdominal mass. In prepubertal boys with UDT, the intra-abdominal testicular tumors are usually mature or immature teratoma. However, malignant germ cell tumors are not uncommon and this is in contrast to post-pubertal tumors that are mostly seminomas.

Contributions DM and DDP: Data collection and manuscript writing; DKY: Manuscript writing and editing; SA: Opearting surgeon, oncologist, manuscript editing and guidance for the study; MCS: Pathologist; DB: Opearting pediatric surgeon. SA will act as guarantor for this paper.

Conflict of Interest None.

Source of Funding None.

References

1. Sijstermans K, Hack WW, Meijer RW, van der Voort-Doedens LM. The frequency of undescended testis from birth to adulthood: a review. Int J Androl. 2008;31:1–11.
2. Strader CH, Weiss NS, Daling JR, Karagas MR, McKnight B. Cryptorchism, orchiopexy, and the risk of testicular cancer. Am J Epidemiol. 1988;127:1013–8.
3. Cortes D, Kjellberg EM, Breddam M, Thorup J. The true incidence of cryptorchidism in Denmark. J Urol. 2008;179:314–8.
4. Cryptorchidism: a prospective study of 7500 consecutive male births, 1984–8. John Radcliffe Hospital Cryptorchidism Study Group. Arch Dis Child. 1992;67:892–9.

5. Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA, Holzman IR. Prevalence and natural history of cryptorchidism. Pediatrics. 1993;92:44–9.
6. Dieckmann KP, Pichlmeier U. Clinical epidemiology of testicular germ cell tumors. World J Urol. 2004;22:2–14.
7. Bray F, Ferlay J, Devesa SS, McGlynn KA, Møller H. Interpreting the international trends in testicular seminoma and non seminoma incidence. Nat Clin Pract Urol. 2006;3:532–43.
8. Wood HM, Elder JS. Cryptorchidism and testicular cancer: separating fact from fiction. J Urol. 2009;181:452–61.
9. Ross JH, Rybicki L, Kay R. Clinical behavior and a contemporary management algorithm for prepubertal testis tumors: a summary of the Prepubertal Testis Tumor Registry. J Urol. 2002;168:1675–8.
10. Walsh TJ, Dall'Era MA, Croughan MS, Carroll PR, Turek PJ. Prepubertal orchiopexy for cryptorchidism may be associated with lower risk of testicular cancer. J Urol. 2007;178:1440–6.
11. Cortes D, Thorup J, Petersen BL. Testicular neoplasia in undescended testes of cryptorchid boys—does surgical strategy have an impact on the risk of invasive testicular neoplasia? Turk J Pediatr. 2004;46:S35–42.
12. United Kingdom Testicular Cancer Study Group. Aetiology of testicular cancer: association with congenital abnormalities, age at puberty, infertility, and exercise. BMJ. 1994;308:1393–9.
13. Pettersson A, Richiardi L, Nordenskjold A, Kaijser M, Akre O. Age at surgery for undescended testis and risk of testicular cancer. N Engl J Med. 2007;356:1835–41.
14. Herrinton LJ, Zhoa W, Husson G. Management of cryptorchidism and risk of testicular cancer. Am J Epidemiol. 2003;157:602–5.
15. Tanaka N, Yoneda A, Fukuzawa M. Mature teratoma arising from an intra-abdominal testis in a 2-month-old boy: case report and review of intra-abdominal testicular tumors in children. J Pediatr Surg. 2009;44:E15–8.
16. Hirayama Y, Kubota M, Imamura M, Imai C, Okuyama N, Tsukada M, et al. A 2-year-old boy with a stage III yolk sac tumor occurring in an intra-abdominal retained testis. J Pediatr Surg. 2009;44:2395–8.
17. Deb M, Alexander B, Das K. Embryonal carcinoma in a cryptorchid testis of a 3-year old. Pediatr Surg Int. 2010;26:233–5.
18. Yama B, Georgioua NA, Khullarb P, Coren CV, Katz DS. Radiology-pathology conference: mature teratoma arising from an intra-abdominal undescended testis in a 7-month-old infant. Clin Imag. 2010;34:466–71.
19. Pramanik DD, Bhatnagar V, Subbarao KC, Sharma MC, Agarwala S, Gupta AK. Antenatally detected mature teratoma. Eur J Pediatr Surg. 2011;21:209–10.
20. Hoei-Hansen CE, Rajpert-De Meyts E, Daugaard G, Skakkebaek NE. Carcinoma in situ testis, the progenitor of testicular germ cell tumours: a clinical review. Ann Oncol. 2005;16:863–8.
21. Weir HK, Marrett LD, Kreiger N, Darlington GA, Sugar L. Pre-natal and peri-natal exposures and risk of testicular germ cell cancer. Int J Cancer. 2000;87:438–43.