Original Article

Indian Journal of Cancer Education and Research
Volume 6 Number 2, July - December 2018
DOI: http://dx.doi.org/10.21088/ijcer.2321.9815.6218.1

Testicular Tumors in Undescended Testes

R.B. Nerli[1], Shridhar C. Ghagane[2], Vishal Kadeli[3], Neeraj S. Dixit[4], Murigendra B. Hiremath[5]

Author's Affiliation: [1]Professor and Head, Department of Urology, JN Medical College, KLE Academy of Higher Education & Research, JNMC Campus, Nehru Nagar, Belagavi-590010, Karnataka, India. and KLES Kidney Foundation, KLES Dr. Prabhakar Kore Hospital & M.R.C, Belagavi-590010, India. [2]Research Associate [4]Resident Department of Urology, KLES Kidney Foundation, KLES Dr. Prabhakar Kore Hospital & M.R.C, Nehru Nagar, Belagavi-590010, India. [3]Resident, Department of Urology, JN Medical College, KLE Academy of Higher Education & Research, JNMC Campus, Nehru Nagar, Belagavi-590010, Karnataka, India. [5]Professor, Department of Biotechnology and Microbiology, Karnatak University, Dharwad, Karnataka 580003, India.

Corresponding Author: R.B. Nerli, Professor and Head, Department of Urology, JN Medical College, KLE Academy of Higher Education & Research (KLE University), KLES Kidney Foundation, KLES Dr. Prabhakar Kore Hospital & M.R.C, Belagavi-590010, Karnataka, India.

Email: rbnerli@gmail.com

Received on 29.05.2018, **Accepted on** 22.06.2018

Abstract

Introduction: The failure of testicular descent or cryptorchidism is the most common defect in newborn boys. Cryptorchidism is an established risk factor for infertility and testicular germ cell tumors (TGCT). About 10% of all cases of testicular germ cell tumors (TGCT) occur in men with a history of cryptorchidism. The common type of TGCT in cryptorchid testes is seminoma, believed to be derived from pluripotent prenatal germ cells. We report our series of patients with cryptorchidism presenting with TGCT in this study. *Materials & Methods:* We retrospectively reviewed our hospital medical records for patients presenting with testicular tumor in an undescended testis. The age, presenting symptoms, examination findings, blood biochemistry reports, imaging records were examined, and noted. The histo-pathology reports were reviewed. Treatment records, including operative notes were examined in detail and analyzed. *Results:* During the study period Jan 2001 to Dec 2015 a total of five patients presented with testicular tumor in an undescended testis. Mean age of patients at presentation was 38.33±0.95 years (29-47 range). The most common presenting symptom was a painless mass in the groin or lower abdomen. *Conclusions:* Very little is known about mechanisms of TGCT tumourigenesis. Painless enlargement of a mass in the groin, or an abdominal mass is the most common mode of presentation in these patients. Pain in the region of the mass remains the second most common symptom. Most of the patients present with a locally advanced or metastatic disease and need to be treated with multi-modal treatment options.

Keywords: Undescended testes; testicular tumors; seminoma; orchidopexy; intra-abdominal testis.

Introduction

Males with a history of cryptorchidism are known to be at increased risk of testicular germ cell tumors (TGCT) and this has been known for many years [1, 2]. About 10% of all cases of testicular germ cell tumors (TGCT) occur in men with a history of cryptorchidism [3]. Cryptorchidism is an accepted risk factor with a relative risk of 3.7–7.5 times higher than the scrotal testis population [4]. It is also well known that there is an increased cancer risk in bilateral as opposed to unilateral cryptorchidism. Some studies have also indicated that there is a direct correlation between how long the testis was subjected to a cryptorchid position and incidence of TGCT. Data on surgical correction of cryptorchidism has shown a reduction of the risk of testicular cancer. Batata et al reported that 13 out of 14 uncorrected cryptorchid patients between 1934 and 1975 developed TGCT in their abdominal testes [5]. A Swedish group studied almost 17,000 men treated for cryptorchidism between 1964 and 1999 with the average age of surgery being 8.6 years. In this group, 56 individuals developed testicular cancer. Individuals who had corrective surgery before the age of 13 had an incidence rate of

2.23%, whereas those who were treated after 13 had an incidence rate of 5.4% [6]. Based on this and similar other data,the recommended age of surgical correction for undescended testes has been reduced and the surgery is usually performed before the age of 2 years [6]. Even after early surgical correction the risk of TGCT is somewhat higher in patients with cryptorchidism.

Other factors that appear to play a role in TGCT incidence include the relative position of the cryptorchidtestes, and hence the degree of environment insults on the gonads, such as heat. It has been shown that an abdominal testis presents a greater risk for TGCT than an inguinal testis [7]. Although the corrective surgery is known to reduce the risk from fivefold to twofold,yet in some cases the formerly cryptorchid testis becomes cancerous, indicative of permanent epigenetic change in the cryptorchid testes [8]. Indeed, differences in promoter methylations and corresponding gene expression of several genes have been reported in TGCT. Apart from cell transformation such changes might be a result of environmental insults in the cryptorchid testis. The other aspect that has been extensively studied is the risk of TGCT in the normally descended contralateral testes in men with unilateral cryptorchidism. Recent meta-analysis of such data indicated that the TGCT risk factor is much higher in the affected testes than in scrotal one (6.33 vs. 1.74) [9].

The TGCT most commonly associated with cryptorchidism is the seminoma. It is generally believed that the classical seminomas develop from a precursor lesion, intratubular germ cell neoplasia (or carcinoma *in situ*, CIS). CIS is believed to develop *in utero* from precursor germ cells or early gonocytes [10]. In this study we report our series of patients with cryptorchidism presenting with TGST.

Materials & Methods:

We retrospectively reviewed our hospital medical records for patients presenting with testicular tumor in an undescended testis. This study wasconducted on permission obtained from the Institutional review/ethical board. The age, presenting symptoms, examination findings, blood biochemistry reports, imaging records were examined, and noted. The histo-pathology reports were reviewed. Treatment records, including operative notes were examined in detail and analyzed.

Results

During the study period Jan 2001 to Dec 2015 a total of five patients presented with testicular tumor in an undescended testis. The mean age of the patients at presentation to our hospital was 38.33±0.95 years. The most common presenting symptom was a painless mass in the groin or lower abdomen, progressively growing in size. The other symptoms included pain in the swelling, loss of appetite, loss of weight and mild fever. The size of the mass ranged from 9–14 cm at the maximum diameter. The ipsilateral testis was not palpable in the scrotum. Three of the patients had normal values of Fetoprotein and β HCG. Two patients had elevated levels of β HCG and alkaline phosphatase.

On ultrasonographic imaging of whole abdomen, the mass appeared as a large complex soft tissue mass with a hypoechoic oval area at the centre (suggestive of testicular growth). Computed tomography (Figure 1 a & b) confirmed the huge mass in all the patients. All patients underwent exploration of the mass (through a groin incision), radical orchidectomy (Figure 2) including of vas deferens upto its disappearance into the prostate. Histopathological report revealed a seminoma in all the patients with tumour cells having clear to granular cytoplasm,arranged in lobular pattern and separated by a thick band of fibro-collagenous septa infiltrated by lymphocytes and plasma cells.

All patients underwent staging Computed Tomography of the abdomen, chest x-ray and

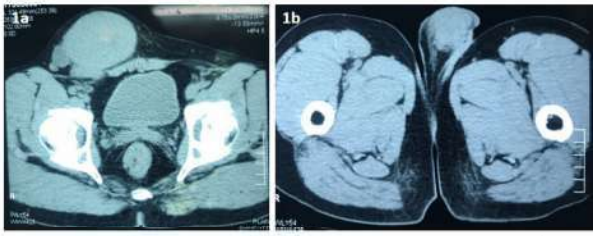

Fig. 1 a & b: Computed tomography shows a mass in the region of Rt. groin of the size 11cm X 9cm.

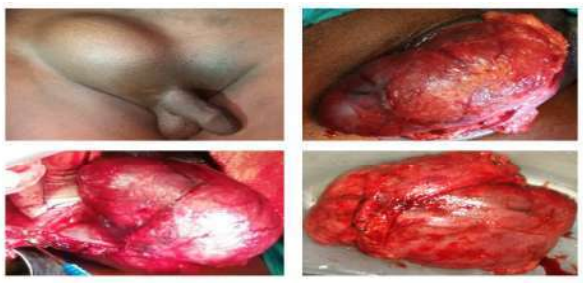

Fig. 2: Shows the mass in the region of the Rt. groin. Operative steps show an inguinal incision, dissection of the mass and the excised specimen.

complete blood counts. The patients were referred to Oncologists for further management. Two of these patients had chest metastases and were treated with chemotherapy and the remaining three were treated with a combination of radiotherapy and chemotherapy. All patients are alive with a mean follow-up of 47.09±0.12months (25 to 53 months).

Discussion

Undescended testis, or cryptorchidism, is one of the most common congenital abnormalities and occurs in 2 to 5% of boys born at term [11]. Cryptorchidism is associated with impaired fertility and is also a risk factor for testicular cancer. The risk of cancer is increased two to eight times, among men who have had undescended testisand 5 to 10% of all men with testicular cancer have a history of cryptorchidism [3,11]. It is not known whether cryptorchidism and testicular cancer have a common cause, or whether cryptorchidism is in itself a cause of testicular cancer.

Several factors seem to play a role in the occurrence of TGCT apart from the relative position of the cryptorchidtestes. Environmental insults such as heat also plays a role in the occurrence of TGCT. An abdominal testis presents a greater risk for TGCT than an inguinal one [7]. It should be noted, that in many epidemiologic association studies the relative position of testes, age of surgical or spontaneous correction, presence of additional developmental abnormalities, or even variable definitions of cryptorchidism were not always taken into account. However, a large majority of data indicates that age of surgery and the relative position of the cryptorchid testis are contributing factors to a greater risk of TGCT [12].

Most children have fully descended testes at birth, and those testes that are undescended at birth may descend spontaneously during early life, but seldom thereafter. By 12 months of age, only about 1% of all boys have cryptorchidism [11, 13]. There is evidence that postnatal germ-cell development deteriorates in the undescended testis after the first year, and perhaps for this reason, the risk of infertility increases with age [11]. The recommended age for orchiopexy is now recommended for patients younger than 2 years old and even as young as 6 months old [14]. A few studieshave suggested thatorchiopexyperformed at an early age decreases the risk of testicular cancer. Pettersson et al. [6] investigated the risk of testicular cancer according to the age at orchiopexy in a cohort of almost 17,000 Swedish men who were surgically treated for cryptorchidism between 1964 and 1999. They identified 56 cases of testicular cancer during follow-up. The relative risk of testicular cancer among those who underwent orchiopexy before reaching 13 years of age was 2.23 (95% confidence interval [CI], 1.58 to 3.06), as compared with the Swedish general population; for those treated at 13 years of age or older, the relative risk was 5.40 (95% CI, 3.20 to 8.53). The authors concluded that treatment for undescended testis before puberty decreased the risk of testicular cancer.

Very little is known about mechanisms of TGCT tumorigenesis and at present there is no animal model that develops testicular cancer as a result of an undescended testis phenotype. Gene expression studies on cryptorchid patients and animal models have indicated that growth factors known to be important for the balance of self-renewal and the proliferation of germ cells are deregulated [12]. The aberrant testicular environment also has a detrimental effect on Sertoli and Leydig cells that may lead to an inability to support the stem cell population. Accumulation of mutations in the somatic cells may lead to mis-expression of important growth factors and morphological breakdown. Consequently, in the cryptorchidtestis, an alternative differentiation pathway for spermatogonial stem cells (SSCs) is proposed which can result in the formation of TGCT. Identification of new markers specific for fetal germ cells and SSCs in human patients will help to delineate the origin of TGCT [12].

Conclusion

It is rare to see an adult patient with undescended testes as this condition is well recognized and the patients would have been treated in childhood. However poverty, poor socio-economic status and ignorance may still be the reasons for not undergoing elective orchiopexy. Painless enlargement of the testis, or an abdominal mass are the commonest modes of presentation in a patient with undescended testicular malignancy. Rarely, these tumors can cause acute abdomen, pain or hematuria due to infiltration of adjacent viscera. The treatment of testicular tumors in an undescended testis is based on the stage of the disease. A combination of effective diagnostic techniques, tumor markers, early surgery, multi-drug chemotherapy and radiotherapy in the past few years has led to dramatic improvements in survival in these patients.

References

1. Barthold JS and Hagerty JA. Etiology, Diagnosis and Management of the undescendedtestis. In Campbell 2016.p.3430.
2. Hutson JM, Balic A, Nation T, and Southwell B. Cryptorchidism. Semin. Pediatr. Surg. 2010; 19:215–24.
3. Mannuel HD, Mitikiri N, Khan M, and Hussain A. Testicular germ cell tumors: biology and clinical update. Curr. Opin. Oncol. 2012;24:266–71.
4. Thorup, J., Mclachlan, R., Cortes, D., Nation, T. R., Balic, A., Southwell, B. R., et al. What is new in cryptorchidism and hypospadias – a critical review on the testicular dysgenesis hypothesis. J. Pediatr. Surg. 2010;45:2074–86.
5. Batata, M. A., Whitmore, W. F. Jr., Chu, F. C., Hilaris, B. S., Loh, J., Grabstald, H., et al. Cryptorchidism and testicular cancer. J. Urol. 1980;124:382–87.
6. Pettersson, A., Richiardi, L., Nordenskjold, A., Kaijser, M., and Akre, O. Age at surgery for undescended testis and risk of testicular cancer. N. Engl. J. Med. 2007;356:1835–41.
7. Cortes D., Thorup J.M., and Visfeldt J. Cryptorchidism: aspects of fertility and neoplasms. A study including data of 1,335 consecutive boys who underwent testicular biopsy simultaneously with surgery for cryptorchidism. Horm. Res. 2001; 55:21–27.
8. Hutson J. M, Balic, A., Nation, T., and Southwell, B. Cryptorchidism. Semin. Pediatr. Surg. 2010; 19:215–24.
9. Akre O., Pettersson, A., and Richiardi, L. Risk of contralateral testicular cancer among men with unilaterally undescended testis: a meta-analysis. Int. J. Cancer 2009;124:687–89.
10. Skakkebaek N. E., Berthelsen, J. G., Giwercman, A., and Muller, J. Carcinoma-in-situ of the testis: possible origin from gonocytes and precursor of all types of germ cell tumours except spermatocytoma. Int. J. Androl. 1987;10:19–28.
11. Toppari J, Kaleva M. Maldescendus testis. Horm Res 1999; 51:261-69.
12. Ferguson L and Agoulnik AI. Testicular cancer and cryptorchidism. Frontiers in Endicrinol 2013; 4:1-9.
13. Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA, Holzman IR. Prevalence and natural history of cryptorchidism. Pediatrics 1993; 92:44-49.
14. Idem. Testicular descent and cryptorchidism: the state of the art in 2004. J PediatrSurg 2005; 40:297-302.