Intratubular Germ Cell Neoplasia: A Case Report in a 43 Year Old Male

Nerli RB1,2*, Ghagane SC3, Deole S1, Hiremath MB4 and Dixit NS3

1Department of Urology, JN Medical College, KLE Academy of Higher Education & Research, India
2KLES Kidney Foundation, KLES Dr Prabhakar Kore Hospital & MRC, India
3Department of Urology, KLES Kidney Foundation, KLES Dr Prabhakar Kore Hospital & MRC, India
4Department of Biotechnology and Microbiology, Karnatak University, India

Abstract

Intratubular Germ Cell Neoplasia (ITGCN) is the precursor lesion for invasive testicular germ cell tumors of adolescents and young adults. ITGCN is diagnosed by testicular biopsy, and has an appearance similar to that of seminoma. The abnormal germ cells are larger than normal spermatogonia, have large hyper-chromatic nuclei with prominent nucleoli, and contain abundant cytoplasm with conspicuous cell borders. Orchiectomy is the main treatment approach in those with unilateral ITGCN and a contralateral normal testicle; those with an atrophic, poorly functioning testis; and those with oligospermia and ITGCN who are pursuing assisted reproductive techniques. In patients with a solitary testicle, treatment for ITGCN needs to be weighed against the resultant infertility and dependence on exogenous testosterone following orchiectomy. We report a case of a 43 year old male presenting with a right sided testicular swelling, which was diagnosed to be Intratubular germ cell tumor on histopathological examination.

Keywords: Intratubular germ cell neoplasia; Testicular intraepithelial neoplasia

Introduction

Testicular tumors or neoplasms of the testis constitute a diverse group of tumors, of which more than 95% originate from the germ cells and hence called as Germ Cell Tumors (GCTs) [1]. These are further broadly categorized as seminoma and Non-Seminoma Germ Cell Tumors (NSGCT) because of differences in natural history and treatment. Germ cell tumors are rare tumors, accounting for 1% to 2% of cancers among men [1].

There are four well-established risk factors for testis cancer: cryptorchidism, family history of testis cancer, a personal history of testis cancer, and Intratubular Germ Cell Neoplasia (ITGCN) [1]. ITGCN (which is also referred to as carcinoma in situ) is a precursor lesion, and most GCTs arise from them. ITGCN is present in adjacent testicular parenchyma in 80% to 90% of cases of invasive GCT and is associated with a 50% risk of GCT within 5 years and 70% within 7 years [2-4]. 5% to 9% of patients with GCT, have ITGCN within the unaffected contralateral testis [3,5]. ITGCN consists of undifferentiated germ cells that appear similar to seminoma and are located basally within the seminiferous tubules. The tubule usually shows decreased or absent spermatogenesis, and normal constituents are replaced by ITGCN. The presence of ITGCN in an orchiectomy specimen in men with testis cancer does not have any prognostic implications with regard to the risk of relapse [6]. We report a case of a 43 year old male presenting with a right sided testicular swelling, which was diagnosed to be Intra-tubular germ cell tumor on histopathological examination.

Case Presentation

A 43 year old male presented to the Uro-oncological services of the hospital with complaints of painless swelling of the right testis of 4 months duration (Figure 1a). On clinical examination, the right testis was non tender, firm to hard in consistency and enlarged to a size of 5 cm x 4 cm x 4 cm. Serum tumor markers were evaluated and were within normal ranges, Serum alpha fetoprotein 2.49 ng/ml, Beta human chorionic gonadotropin 0.778 mIU/ml and lactic dehydrogenase 167 U/L. Ultrasonography of the scrotum revealed a tumor in the right testes with multiple tiny cystic areas. CT revealed a bulky right testis measuring 5.8 cm x 4.7 cm x 5.0 cm, with an ill-defined heterogeneously enhancing mass within it and dilated vessels along the spermatic cord (Figure 1b).
In view of the history and clinical examination, it was decided to perform a right sided high inguinal radical orchiectomy (Figure 2a and 2b). The testicular specimen was sent for histopathological examination. Gross examination of the testis, revealed an 8 cm testis with 9 cm long spermatic cord. Histopathological examination revealed the tubules filled with small and intermediate sized cells. The tubules showed thickened walls, the stroma in between the tubules contained numerous dilated blood vessels and edematous stroma (Figure 3a-3c). Moreover this patient had normal blood biomarkers and on immunohistochemistry the tumor cells expressed CD117 and immuno-negative to plap.

**Discussion**

Skakkebaek [7,8] was the first to report on the presence of atypical germ cells in the testes of two infertile men and speculated that these cells represented the pre-invasive phase of testicular cancer. ITGCN has been known by several names including carcinoma in situ, seminoma in situ and gonocytoma in situ, and all are considered inappropriate. The right term that is most widely applied now is intratubular germ cell neoplasia, unclassified type (ITGCN-U) [9].

ITGCN-U consists of enlarged cells with clear cytoplasm that are aligned along the basal portion of the seminiferous tubules [9]. The nuclei are round, significantly larger than those of spermatogonia (mean diameter 9.7 mm vs. 6.5 mm, respectively), and are hyperchromatic with prominent nucleoli. The nuclear membranes are thickened and irregular. Mitoses may be frequent and can be atypical but are often not conspicuous [4]. Sertoli cells, but not spermatogonia or more mature spermatogenetic cells, are characteristically intermingled with ITGCN-U but show luminal displacement. Adjacent seminiferous tubules may be completely normal and show intact spermatogenesis [4]. Two or more forms of intratubular germ cell tumors may coexist, usually ITGCN-U with either intratubular seminoma or intratubular embryonal carcinoma [4]. Immunostaining discloses Placental-Like Phosphatase (PLAP) in a high percentage of cases of ITGCN-U. It appears as membranous (predominantly) and cytoplasmic positivity. Non-neoplastic spermatogenic cells are almost always PLAP negative [4].

The population that needs to be screened for ITGCN-U is controversial [10] and includes

1. All patients with a history of unilateral testis cancer,
2. All patients with somato-sexual ambiguity and a Y chromosome,
3. Patients with presumed Extragonadal Germ Cell Tumors (EGCT) and
4. Less strongly, patients with a history of cryptorchidism.

These tumors are usually asymptomatic, unless associated with invasive lesions, and are diagnosed on microscopic examination of a testicular biopsy specimen. Testicular biopsies detect ITGCN with a high rate of sensitivity. A marked cytogenetic anomaly, the isochromosome of the short arm of chromosome 12 [i (12p)], has also been demonstrated in ITGCN lesions adjacent to testicular germ cell tumors [4].

The treatment of ITGCN remains controversial with opinions divided between watchful waiting, chemotherapy, radiation or orchiectomy. With the exception of surveillance, the remaining three treatment modalities put patients at significant risk for infertility, hypogonadism, or both. The decision to proceed with a certain treatment modality has to be individualized based upon specific risk factors as well as patient wishes. Unlike chemotherapy and radiotherapy, orchiectomy is the most definitive treatment with the highest success rate and is the main treatment approach for three patient populations: those with unilateral ITGCN and contralateral normal testis; those with an atrophic testis; and those with infertility and unilateral ITGCN [11].

**Conclusion**

Most, if not all, germ cell tumors of the testis evolve from a common neoplastic precursor lesion i.e. the intratubular germ cell neoplasia. It is defined as the presence of malignant germ cells within the seminiferous tubules. Orchiectomy is the treatment of choice in patients with unilateral ITGCN, and low-dose radiation is efficacious in patients with bilateral ITGCN.

**References**


