



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

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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 × 4 cm × 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 × 4.7 cm × 5.0 cm, with an ill-defined heterogeneously enhancing mass within it and dilated vessels along the spermatic cord (Figure 1b).

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Received Date: 23 Jul 2018

Accepted Date: 20 Aug 2018

Published Date: 24 Aug 2018

Citation:

Nerli RB, Ghagane SC, Deole S, Hiremath MB, Dixit NS. Intratubular Germ Cell Neoplasia: A Case Report in a 43 Year Old Male. *Oncol Case Report J.* 2018; 1(1): 1007.

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Figure 1: 1a) Right sided enlarged testis, 1b) CT scan of the scrotum showing an enlarged Right testis in comparison with the Left Testis.

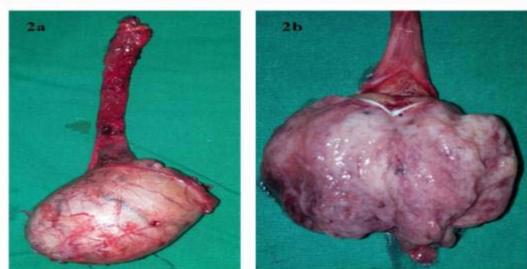


Figure 2: 2a) Gross appearance of the high orchiectomy specimen, 2b) Gross appearance of the Cut section of the testis.

In view of the history and clinical examination, it was decided to perform a right sided high inguinal radical orchidectomy (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 spermatogenic 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

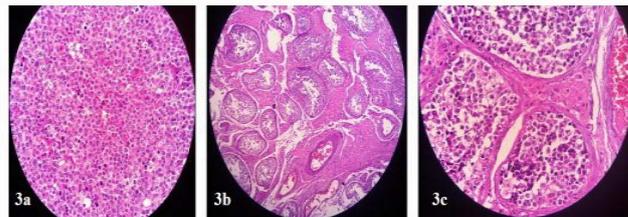


Figure 3: 3a) Sheet like arrangement of neoplastic cells with surrounding lymphocytes (High Power View (40x)), 3b) Neoplastic cells filling up the tubules (Low Power View (10x)), 3c) Neoplastic cells resembling seminoma like germ cells (High Power View (40x)).

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 orchidectomy. 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, orchidectomy 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. Orchidectomy is the treatment of choice in patients with unilateral ITGCN, and low-dose radiation is efficacious in patients with bilateral ITGCN.

References

1. Stephenson AJ, Gilligan TD. Neoplasms of the testis, 11th edition. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh Urology. Philadelphia: Elsevier-Saunders; 2016. p. 784.
2. Skakkebaek NE, Berthelsen JG, Muller J. Carcinoma-in-situ of the

- undescended testis. *Urol Clin North Am.* 1982;9(3):377-85.
3. Dieckmann KP, Skakkebaek NE. Carcinoma in situ of the testis: Review of biological and clinical features. *Int J Cancer.* 1999;83(6):815-22.
 4. Montironi R. Intratubular germ cell neoplasia of the testis: Testicular intraepithelial neoplasia. *Eur Urol.* 2002;41(6):651-4.
 5. Dieckmann KP, Loy V. Prevalence of contralateral testicular intraepithelial neoplasia in patients with testicular germ cell neoplasms. *J Clin Oncol.* 1996;14(12):3126-32.
 6. Von Eyben FE, Jacobsen GK, Rorth M, Von Der Maase H. Microinvasive germ cell tumour (MGCT) adjacent to testicular germ cell tumours. *Histopathology.* 2004;44(6):547-54.
 7. Skakkebaek NE. Possible carcinoma in situ of the testis. *Lancet.* 1992;2(7776):516-17.
 8. Skakkebaek NE. Abnormal morphology of germ cells in two infertile men. *Acta Pathologica Microbiologica Scandinavica Section A pathology-banner.* 1972;80(3):374-8.
 9. Ulbright TM, Amin MB, Young RH. Tumors of the testis, adnexa, spermatic cord and scrotum. In: *Atlas of Tumor Pathology Third Series, Fascicle 25.* Washington DC: AFIP; 1999. p. 41-58.
 10. Rorth M, Rajpert-De Meyts E, Anderson L, Dieckmann KP, Fossa SD, Grigor KM, et al. Carcinoma of the testis. *Scand J Urol Nephrol.* 2000;34(Suppl 205):166-86.
 11. Risk MC, Masterson TA. Intratubular Germ Cell Neoplasms of the Testis and Bilateral Testicular Tumors: Clinical Significance and Management Options. *Indian J Urol.* 2010;26(1):64-71.