Familial testicular tumour in two brothers—a case report

Gupta MK, Seam RK, Gurung DS, Kanika S
Department of Radiotherapy & Oncology, Regional Cancer Centre, IGMC, Shimla, India.

Correspondence to: M. K. Gupta, E-mail: mkgupta62@yahoo.co.in

Abstract

Testicular tumors account for 1% of all cancers in men and it occurs in 1 in 500 men. Incidence of familial testicular tumours is rare. Total number of cases till the year 1992 in identical twins is 21, in brothers 82 and father–son both affected in 31 pairs. We report a case of two brothers presenting simultaneously with testicular tumours. Both were subjected to retrograde orchidectomy. Histopathologic examination of one revealed embryonal cell carcinoma and other mature teratoma of the testis. Patient with embryonal carcinoma was given adjuvant chemotherapy based on Bleomycin, Etoposide and cisplatinum and one with mature teratoma was put on a follow up.

Key Words: Testicular germ cell tumor, Familial testicular cancer; Testicular intraepithelial neoplasia, Chromosome Xq27

Familial testicular tumor is a rare entity. Two percent of testicular germ cell tumour (TGCT) cases report another affected family member. Epidemiological studies have shown that there is an eightfold to tenfold increase in relative risk of TGCT to brothers of patients and a fourfold increased risk to fathers and sons. This relative risk is considerably higher than for most other common cancers, which rarely exceeds four and strongly suggests that genes may play an important role in TGCT. However, the search by genetic linkage analysis for familial TGCT susceptibility genes has been confounded by the limited numbers of large multiple case families. We report the case, as it was first of its kind presenting in our department.

Case history

Two brothers aged 23 years and 35 years presented in outpatient department with complaints of scrotal swelling since 1 year and 3 months, respectively. They had no complaints of any pain or redness in swelling; there was no history suggestive of trauma, mumps or cryptorchidism in the past. They were initially managed conservatively in local hospital; on suspicion of malignancy retrograde orchidectomy was performed in both patients. The histopathological examination (HPE) revealed embryonal cell carcinoma in 35-year-old patient and mature teratoma of testis in 23-year-old patient. On presentation their general condition was good and there was no obvious abnormality on clinical examination. In 35-year-old patient serum alpha feto protein (AFP) and β human chorionic gonadotrophin (HCG) levels were slightly raised (AFP levels–10 ng/ml and β HCG levels–9.5 MIU/ml). In 23-year-old patient serum AFP and beta HCG levels were in normal range (AFP level–2 ng/ml and β HCG level–2.25 MIU/ml). Computed tomography scan abdomen in 35-year-old patient revealed enhancing para aortic and paracaval group of lymph nodes. In view of raised serum markers, embryonal cell carcinoma on HPE and evidence of secondary metastatic disease in lymph nodes 35-year-old patient was treated with chemotherapy based on cisplatin, etoposide, bleomycin (BEP regimen) for four cycles. The 23-year-old patient was kept on close follow up in view of normal serum markers, no evidence of secondary metastatic disease and HPE of mature teratoma of testis.
Discussion

Testicular tumors account for 1% of all cancers in men and it occurs in 1 in 500 men.[1] Incidence of testicular tumors is increasing and mortality related to testicular tumors is decreasing.[2] In USA in year 2003 about 7500 new cases of testicular tumors have been reported and 400 deaths have been attributed to this tumor.[3] The highest incidence is in Denmark followed by Switzerland and Norway. Patients usually present at younger age. The usual age of presentation is 15–35 years. Various risk factors have been identified in testicular tumours. Race and ethnicity have some role as White Americans are affected more than Blacks.[4] Cryptorchidism has been considered a risk factor for testicular tumours. Incidence of cryptorchidism is 3% in general population and there is an increased risk of testicular tumour by 3–17 folds. About 14% of patients with testicular germ cell tumour give history of cryptorchidism. Abdominal testis is involved more than inguinal tests. About 25% of patients develop testicular germ cell tumour (TGCT) in normally descended testis. Orchiopexy may reduce risk if done before 10 years of age, but risk is still higher. Trauma has also been implicated as risk factor but mostly it draws attention to the underlying disease. Testicular intraepithelial neoplasia (TIN) is an important high risk factor and is present in 0.2% of the general population. It is seen in 0.5% cases of impaired fertility and 2–5% cases of cryptorchidism.[5] Ultrasonography in TIN reveals microcalcification. Progression to TGCT occurs in 50–100% of the cases diagnosis of TIN is usually incidental and is present in 5% of contralateral testis in patients of TGCT.[6] Infertility with low sperm concentration and defective sperm motility has been observed in testicular tumour patients.[7] This was attributed to the damage to the key testicular cells by environmental factors such as nutrition, alcohol consumption, smoking and drug use. Conditions leading to increased oestrogen exposure like obesity also predisposes to testicular tumours. In patients with history of prior TGCT the cumulative risk of developing testicular tumour in contralateral testis is 5% at 25 years.[8] Nonseminomatous tumours occur more than seminomatous tumours in these cases. Other risk factors include occupation such as miners, oil and gas workers, leather workers, and fire workers. Presence of multiple atypical naevi, previous injury, HIV infection, and other infections such as mumps may also act as risk factors. Body size has also been studied as risk factor Sweden study indicates increased risk in tall and slim men. Vasectomy is also considered as risk factor for testicular tumors. Maternal hormones such as consumption of diethyl stilbister during pregnancy or increased oestrogen levels during pregnancy as in twin pregnancy, obesity, etc., is also risk factor. Exercise especially strenuous exercise during teen years has also been implicated as risk factors. Reasons are thought to be increased hormonal levels and repeated trauma as in cycling and horse riding. Miscellaneous factors identified as risk factors include gonadal dysgenesis, Klienfelters syndrome, inguinal hernia, low birth weight and sedentary life style.[9]

Familial testicular tumours is the term given when more than two family members are affected. Its incidence is low and about 2% of patients with TGCT give history of similar complaint in other family members. Pattern of familial TGCT inheritance is different as compared to other familial malignancies. Many family members spread over many generations is a rare finding and majority are two cases in a family, which may be father–son, twins, or brothers. Familial testicular tumours occur at earlier age than nonfamilial and are often bilateral. Total number of cases till the year 1992 in identical twins–21 pairs, brothers–82 pairs, and father–son both affected–31 pairs. The risk of familial testicular tumour is overall sixfold, in brothers it is eight to tenfold if one brother is affected, in father–son group risk is fourfold, and risk rises to 40-fold in identical twins.

In testicular germ cell tumour the commonest chromosomal abnormality seen is isochromosome for the short arm of chromosome 12, i.e., 12p. In familial testicular cancers autosomal recessive or X–linked recessive mode of inheritance is being considered as mode of transmission of testicular tumors. The international testicular cancer linkage consortium (ITCLC) which was formed to study the genetic inheritance of familial testicular tumors assembled a series of 300 families with multiple cases which are now being used for gene mapping and cloning studies. In this study group the study of first 134 families led to the conclusion that these families had a pattern of inheritance compatible with X-linked cancer susceptibility disorder. They further identified a candidate locus on the long arm of female X chromosome band q27.[10] This is very close to fragile X gene and this locus accounts for most of the family clusters. It was named TGCT1 gene. This is one of the 300 genes on the long arm of X chromosome. The gene is yet to be isolated. When the mutant gene is present on the X chromosome, the likelihood of woman getting affected is exceedingly small. Since men carry only one X chromosome, they are more likely to express manifestations. However, there is an exception father to son transmission is not possible with X linked inheritance. This led to the belief that other genes may also be responsible for familial testicular cancer, which needs further investigation.
References


