Case Report

Familial germ cell tumor

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Familial testicular germ cell tumors are well known in literature. Only few cases are reported where both brother and sister of the same family suffered from germ cell malignancies. We present a family where the proband is a survivor of ovarian dysgerminoma stage IA. Her elder male sibling became acutely ill and was detected to have disseminated testicular malignancy with grossly elevated markers and vegetations in the mitral valve leaflets. Despite all measures he could not be saved. Presence of germ cell malignancies in the siblings of different sex in the same family points toward a genetic susceptibility. Literature review revealed only six similar cases. A discussion regarding the rare occurrence of familial germ cell malignancies with the affected family members may be worthwhile.

Key words: Familial, genetics, germ cell tumor

Introduction

Testicular cancer is the most common solid tumor in young adult males.[1] Ovarian germ cell tumors are rare malignancies. Familial clustering of testicular malignancies is well documented in literature. Children or siblings of affected family members are at higher risk for testicular germ cell tumors. A definite genetic mechanism cannot be attributed to this. A testicular cancer susceptibility gene has been located on Xq27.[2] Familial ovarian germ cell tumors are rare, may be due to the rarity of the cancer itself.[3] Trentini and Palmieri first reported a family where both brother and sister developed germ cell malignancies.[4] Since then, around six families were found to be affected in a similar fashion. We present a family where the sister was diagnosed initially to have dysgerminoma and then the elder brother developed a disseminated testicular malignancy.

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Case Reports

Case 1

A 16-year-old postmenarchal girl presented to us with 3 months history of amenorrhoea. She was asymptomatic otherwise. She had undergone repair of atrial septal defect of osteum secundum type when she was 3 years old. Clinically, she had a large abdominopelvic mass measuring 10 cm above the symphysis pubis. She did not have any ascites or palpable peripheral lymph nodes. Computed tomogram (CT) of the abdomen revealed a large abdominopelvic mass probably of ovarian origin. Her serum tumor markers were asked. HCG levels were mildly elevated (28 mIU/ml) and AFP was normal (1 ng/ml). A laparotomy was performed which demonstrated large left ovarian tumor measuring 20 × 15 cm with no peritoneal or liver deposits. Contralateral ovary and uterus were normal. Left ovariectomy and pelvic nodal dissection were performed with sampling of peritoneum and para-aortic lymph nodes. Postoperative ovarian histopathology was suggestive of dysgerminoma. Other sampled sites were free of tumor. Hence, she was diagnosed as dysgerminoma and has completed 5 years of follow-up and is disease free.

Case 2

A 24-year-old gentleman, elder brother of Case 1,

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presented with abrupt onset of vomiting and loss of consciousness. Later, he noticed weakness of the left side of the body. CT scan of the brain showed a large infarct in the left middle cranial artery territory. He was also noticed to have a large scrotal swelling. Chest X-ray showed multiple cannon ball shadows. Serum HCG was 1567 mIU/ml. Alfa fetoprotein (AFP) also was elevated (8663 ng/ml). Ultrasound of the scrotum revealed multiple hypoechoic areas in the left testes. Ultrasound of abdomen revealed multiple retroperitoneal lymph nodes. ECHO cardiogram showed large vegetations on the mitral valve leaflets. Chemotherapy could not be given in view of the very poor general condition. Histological confirmation could not be attempted. However, his general condition deteriorated and could not be revived despite all supportive treatment given.

Discussion

Testicular cancer is the most common solid tumor in men between the ages 18–35. Familial testicular germ cell tumors are well described in literature especially among siblings.[1] The precise genetic basis for this is unknown. Rapley *et al.,* proposed TGCT1 on Xq27 as the testicular susceptibility gene and suggested 8–10 times increased risk of testicular cancer among siblings.[2] Ovarian germ cell tumors are rare compared to testicular tumors. Stettner *et al.,* reported seven families with more than one relative was affected with malignant ovarian germ cell tumors.[3]

Male and female germ cell tumors in the same family are rather rare. Trentini and Palmieri first described the rare occurrence of dysgerminoma of the ovary and embryonal carcinoma of the testes in siblings of one family in 1974.[4] A possible genetic transmission was suggested. Kingsbury *et al.*, elaborated on a family with 46XY gonadal dysgenesis syndrome where two phenotypically female siblings and one phenotypically male sibling developed malignant germ cell tumors. They proposed removal of dysgenetic gonads as a prophylactic measure even in phenotypical male members which may be justified.[5] Akyuz *et al.*, reported a family where siblings had germ cell tumors. The elder sister was a survivor of dysgerminoma of the ovary when the brother was diagnosed to have mediastinal nonseminimatous germ cell tumor. A karyotyping was done which was reported normal for both the patients.[6] Hartley *et al.*, reported six germ cell tumors in in relatives of children with bone or soft tissue sarcomas and raised the doubt that germ cell tumors may be part of Li Fraumeni syndrome.[7] Galani *et al.*, presented a family with three affected members; two had ovarian tumors (teratoma and bilateral dysgerminoma) and the male sibling had mixed germ cell tumor.[8]

Bruce *et al.*, demonstrated BRCA 1 mutation in a patient with ovarian dysgerminoma. There was a strong family history of ovarian cancer and BRCA 1 was positive in all of them. The significance of this observation is unknown as malignant germ cell tumors are not there in the spectrum of BRCA-associated cancers.[9] Giambartolomei *et al.*, summarized the literature to date regarding familial germ cell tumors.[10] Six families were identified with both ovarian or testicular germ cell tumors. Dysgerminoma predominated in females whereas seminoma was the most common histology in males.

A definite genetic abnormality has not been identified for the familial incidence of germ cell tumors. However, the increasing reports of the same give a wakeup call for further research on this subject. Screening of family members may be debatable, but a discussion regarding these reports with the affected family may be worthwhile.

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