ORIGINAL ARTICLE

The Histopathological Spectrum of Extracranial Germ Cell Tumors in a Tertiary Care Center of Western India

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ABSTRACT

Introduction: Germ cell tumors (GCTs) arise from the malignant transformation of primordial germ cells. GCTs can be benign or malignant. GCTs are mostly gonadal but can be extragonadal. This study comprised of a histological spectrum of extracranial GCTs and their correlation with clinical findings such as age, sex, and site with the histological type of GCT to know the overall incidence of GCT in our institute. **Methods:** A 3-year retrospective study was carried out in the department of pathology. Of 16,436 surgical specimens, 56 cases were of GCTs. The detailed clinical history including age, sex, and anatomic site was taken into account. Routine hematoxylin and eosin staining was used. All the data were tabulated, and a clinicopathological correlation was attempted and percentages calculated for different variables. **Results:** Of 56 cases of GCTs, 33 (59%) were females and 23 (41%) were males. GCT was commonly seen in children and adolescents (32 cases). Maximum (65.35%) cases were seen below the age of 20 years. The most common sites for GCTs were ovary, eye, and adnexa (19.64%) followed by sacrococcyx (12.5%). Dermoid cyst (64.28%) was the most common GCT, followed by mature teratoma (23.21%) and immature teratoma (7.14%). **Conclusion:** GCTs can be gonadal or extragonadal. Extracranial GCTs are rare. Childhood extragonadal GCTs are more common than adult gonadal GCTs. In children, sacrococcyx, and in the adult, ovary were the most common site of GCT. Overall, dermoid cyst was the most common tumor involving face and ovary.

Key words: Extracranial, germ cell tumors, gonads, histopathology

INTRODUCTION

Germ cell tumors (GCTs) arise from malignant transformation of primordial germ cells[1,2] and can be benign or malignant. Germ cell tumors are mostly gonadal (ovary and testis) but can be seen at extragonadal sites.[1,2] Extragonadal GCTs occur in the midline of the human body. The anterior mediastinum, sacrococcygeal region, pineal gland, and neurohypophysis are the common sites. Extragonadal GCTs are made of tissue that is histologically identical to that in gonadal GCTs.[2] Extragonadal GCTs were thought to be isolated metastases from an undetected primary tumor in a gonad, but it is now known that many GCTs are congenital and originate outside the gonads from migrated primordial germ cells.[2,3] GCTs are rare in children younger than 15 years, accounting for approximately 3% of cancers in this age group.[4,5] GCTs are classified by their histology regardless of location in the body.[6] GCTs are broadly divided into two classes. They can be seminomas or nonseminomatous. Nonseminomatous GCTs consist of embryonal cell carcinomas, choriocarcinomas, yolk sac tumors, or teratomas. The nonseminomatous GCTs include all other GCTs, pure and mixed type.[7,8]

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MATERIALS AND METHODS

This is a retrospective study conducted over a period of 3 years. Of 16,436 surgical specimens received, 56 cases (0.3%) which were clinically suspected and histopathologically diagnosed as GCTs were selected [Table 1]. The detailed clinical history including age, sex, and anatomic site was taken into account. The specimens received in the pathology laboratory were grossed and sections were stained with routine stain hematoxylin and eosin stain. PAS and reticulin stain were also done wherever needed. Percentages calculated for different variables. All the data were carefully tabulated, and a clinicopathological correlation was attempted.

RESULTS

This is a 3-year study carried out in the department of pathology. A total of 16,436 specimens were received during this period; of these, 56 were GCTs (0.3%) [Table 1]. There was a female predominance with 33 (59%) and 23 (41%) males [Table 2]. The male:female ratio was 0.7:1. GCTs were more common in children of the age range of 0–15 years (57.14%) [Table 3]. Extragonadal extracranial GCTs (41 cases) were more common than gonadal GCT (15 cases). Gonadal GCTs were more common in the age group of 16–30 years (15 cases) and not seen in children below 15 years of age [Table 4]. Ovarian GCT (11 cases) was more common than testicular GCTs (4 cases). Extragonadal extracranial GCTs were more common in children (30 cases) than adults (11 cases). Overall, the most common site of GCTs was ovary (19.7%) along with eye and adnexa (19.7%), postauricular (14.27%), and sacrococcygeal region (12.5%). The most common sites of GCT in pediatric age group were sacrococcyx (7 cases), postauricular area (7 cases), and eye and its adnexa (6 cases) [Table 5]. However, in neonates (<1 year), most common GCTs were immature teratoma (2 cases), both were retroperitoneal. Overall, the most common type of GCT was dermoid cyst (36 cases, 64.29%) followed by mature teratoma (13 cases, 23.21%) [Table 6]. The most common GCTs in children and adolescents were also dermoid cyst (20 cases), mature teratoma (8 cases), and immature teratoma (4 cases). Mixed GCTs were not seen in children and adolescents below 15 years of age. In

Table 1: Incidence of GCT

Total specimens received in three years of study period	Total number of germ cell tumors
16436	56
100%	0.3%

Table 2: Age-wise distribution of GCTs

Age group	0–15 years	Above 16 (16–70) years
Total cases	32 (11 male and 21 female)	24 (10 male and 14 female)
Percentage	57.14	42.86

GCT: Germ cell tumor

Table 3: Gender-wise distribution of Germ cell tumors

Gender	Number of cases	Percentage (%)
Males	23	41
Females	33	59
Total	56	100

Table 4: Distribution of GCT based on locations

Type of GCT	Age in years (0-15)	Age in years (16-70)
Gonadal GCT (15 cases)	0	15
Extragonadal GCT (41 cases)	30	11

GCT: Germ cell tumor

Table 5: Site-wise distribution of GCTs

Site	Number of cases (%)
Ovary	11 (19.7)
Eye and adnexa	11 (19.64)
Posterior auricular	8 (14.27)
Sacrococcyx	7 (12.5)
Scalp	6 (10.71)
Testis	4 (7.14)
Retroperitoneum	3 (5.35)
Mediastinum	1 (1.78)
Adrenal	1 (1.78)
Angle of mouth	1 (1.78)
Gastric	1 (1.78)
Fetiform	1 (1.78)
Submental	1 (1.78)
Total	56 (100)

GCT: Germ cell tumor

Table 6: Histopathological subtypes of GCTs

Histopathological diagnosis	Total number (%)
Dermoid cyst	36 (64.29)
Mature teratoma	13 (23.21)
Immature teratoma	4 (7.14)
Mixed GCT	3 (5.36)

GCT: Germ cell tumor

case of adults above 16 years, the most common GCT was also dermoid cyst (16 cases), followed by mature teratoma (5 cases) and mixed GCT (3 cases). Immature teratoma was not seen in adults. The most common ovarian GCT was dermoid cyst (six cases) in 16–30 years followed by mature cystic teratoma (4 cases). In males, testicular GCTs were more common in the young age group (16–45 years), and mixed GCTs (embryonal carcinoma with mature teratoma) (3 cases) were more common than pure GCTs.

DISCUSSION

Germ cells are the cells that develop in the embryo (fetus or unborn baby) and become the cells that make up the reproductive system in males and females.[1] These germ cells follow a midline path through the body after development and descend into the pelvis as ovarian cells or into the scrotal sac as testicular cells. The ovaries and testes are called gonads. Most ovarian tumors and testicular tumors are of germ cell origin. Tumor sites outside the gonad are called extragonadal sites.[1,2] The tumors also occur along the midline path and can be found in the central nervous system, chest, retroperitoneal, and sacrococcygeal area.[2,5] GCTs are a heterogeneous group with respect to patient age, histologic features, and primary tumor location.[2,8] Pediatric GCTs are neoplasms derived from primordial germ cells[9] and may be gonadal or extragonadal.

Overall, the incidence of GCTs was bimodal, with a peak in the 1–10 years and 20–50 years in the present study. Germ cell cancer is the most common malignancy in men aged 15–35 years.[10] Gonadal GCTs (15 cases) and extragonadal GCTs (10 cases) in adults were more commonly seen in the 16–30 years of age group. Pediatric gonadal GCTs are rare.[11,12] A larger percentage of tumors were diagnosed in children before the age of 10 years (26 cases) than in children diagnosed after age 10 years, similar to the study of Poynter *et al*.[5] This difference is may be due to the differences in the maturity of the germ cells that give rise to the tumors in these age groups.[9] GCTs were also seen in neonates <1 year old (5 cases).

In children and adolescent age group (0–15 years), GCTs were also more common in female (17 cases) than males (13 cases), and in adults also, female GCT (16 cases) was more common which was similar to the study of Poynter *et al*.,[5] also Kaatsch *et al*.[11] found that GCTs in childhood were more common in females (54.5%) than in males (45.5%), with M: F ratio of 0.8:1.

The age distribution of GCTs varied according to the tumor location, type, and gender, indicating heterogeneity of the GCTs.[11] In pediatric and adolescents, extragonadal GCT was more common, arising in the midline location,[5,8] and in adults, gonadal GCTs were more common.[5] In the present study, all cases between the age 0 and 15 years were extragonadal, and in 16 onward age group, of 24 cases, 15 (62.5%) cases were gonadal. GCTs in early childhood and older children were histologically distinct and occurred at different sites.[11] In children (<5 years), the most common site of extragonadal extracranial GCTs is sacrococcygeal.[8,11,13] However, in older children, facial dermoid cyst was more common. The most common sacrococcygeal GCTs were mature teratomas which mostly behave as benign tumors and less commonly, as malignant ones, of these, 50–70% are found in the first few days of life[14] which was similar to our study where the sacrococcygeal region and mature teratoma were common in the pediatric and adolescent age group. Teratomas are among the more common tumors of childhood with an incidence of 1:4000 live births.[13] The most common GCT in <1 year old was teratoma (4 cases), of which 2 cases were immature teratoma, both were located retroperitoneally similar to the study of Kumar *et al*.[15] who stated that the incidence of retroperitoneal teratoma is bimodal with peaks in the first 6 months of life and in early adulthood. Three cases of neonatal retroperitoneal teratoma were reported by Lack *et al.,*[16] of these two were immature. In adults, the most common location of extragonadal and extracranial GCTs was around eyes (eyelids, eyebrows, and lateral canthus) (5 cases) and all cases of extragonadal GCTs except mediastinal GCTs were dermoid cysts in the present study. Dermoid cysts were most frequently midline cysts, resulting possibly from the inclusion of skin at the time of embryonic closure. Craniofacial dermoid cysts comprise approximately 7% of all dermoids and 60% of all facial cysts.[17] Shinagare *et al*.[8] and Schmoll[10] found that the most common extragonadal GCT locations were mediastinum and retroperitoneal in adults. In the present study, only one case of mediastinal mature teratoma in adult was seen and three retroperitoneal immature teratomas were seen; all were present in a child <5 years old.

Gonadal GCT is more common in females, i.e. ovarian GCT which is more common than testicular GCT. In ovarian GCT, the most common is dermoid cyst followed by mature teratoma. Testicular GCTs usually occur in adolescents and young adults (16–40 years),[2,18,19] and mixed GCT is more common in a study done by Ueno *et al*.[2] similar to our study. However, seminomatous testicular GCTs were more common than nonseminomatous.[18-20] Dermoid cyst is extremely rare in testis, and teratoma mostly occurs as a component of mixed GCTs in the testis. The most common component of mixed GCTs was teratoma and embryonal carcinoma. All cases were reported in testicular GCTs[20] similar to the present study. The most common mediastinal GCT was mature teratoma[2,8] similar to our study in which one mediastinal GCT was reported and which was mature teratoma. Primary gastrointestinal GCT has been rarely reported in the literature.[21] In our study, only one case of gastric GCT and immature teratoma was reported in a 2-year-old child.

CONCLUSION

GCTs are a heterogeneous group with respect to patient age, histologic features, and primary tumor location. GCTs can be cranial or extracranial. Extracranial GCTs are rare. Childhood extragonadal GCTs are more common than adult gonadal GCTs. In children, the sacrococcyx, and in the adult, the ovary were the most common site of GCT. Overall, the dermoid cyst was the most common tumor involving face and ovary.

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