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Experience of management of germ cell tumors in paediatric population at a tertiary care institute.

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Abstract

Background: Germ Cell Tumor (GCT) is a rare malignancy in paediatric age group. It accounts for 2%-3% of all pediatric tumors. It can be found both gonads and extra gonadal sites such as sacrococcygeal region, mediastinum, and retro-peritoneum.

Method: The clinical presentation and management of all cases of GCT admitted in the department of pediatrics and pediatric oncology were analysed. The post-operative treatment, pathological features, relapses and survival outcome were evaluated retrospectively and results were drawn.

Results: The study period was between 2015 and 2021. A total of 72 patients (39 male and 33 female) were included in this study. The vast majority 42% of patients presented with a combination of symptoms and signs including abdominal pain/distention, pelvic mass, sacrococcygeal mass and precocious puberty. The most common age group was between 11-16 months/years. Thirty seven percent had gonadal tumors, 15% ovarian testicular, 22% had ovarian tumors. Histologically teratoma was the most common type (27.77% mature, 13.88% immature). Yolk sac tumors, embroyonal cell, dysgerminoma and seminoma constituted about 22.22%, 8.33%, 11.11%, 55% respectively. The overall five years survival was 86.9%. The relapse free survival rate was 83.6%. The mean follow-up was 56 months.

Conclusion: Sacrococcygeal Teratoma (SCT) constituted the most common extragonadal site of the GCT in children. A peculiar feature of our findings was the late presentation of both benign and malignant GCT. The overall survival rate found in benign GCT in our study was almost similar to that reported by other authors. Early diagnosis and management (surgical and medical) are of paramount importance in the management of this disease.

Keywords: Germ Cell Tumors (GCT), Sacrococcygeal Teratoma (SCT), Seminoma, Teratoma, surgery.

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Introduction

GCT is rare tumors in pediatric age group, occurring at a rate of 2.4 cases/million children. They constitute about 1% of all pediatrics tumors [1]. The relative incidence of yolk sac tumor among toddler is decreasing [2]. The incidence of seminoma and dysgerminoma increases with the onset of puberty. In general, girls have a higher overall incidence of GCT. GCT arises from totipotent primordial germ cells which are capable of embryonic or extra embryonic differentiation. The histological features of each sub type are independent of presenting clinical characteristics, tumor biology and clinical behavior varies with site of origin, stage and age of patient [3].

The treatment of pediatric GCT is based on multimodal strategy that includes surgery, chemo and radio therapy. Tumor resection is considered complete if it is performed as an unblock resection of tumor including adjacent organ of origin. Ovarian tumors are resected along with ovarian tissue and the fallopian tube. In testicular tumors a high inguinal orchidectomy is compulsory. In SCT a complete resection of tumor along with the resection of coccyx is essential [4]. Adjuvant treatment depends on the stage of the tumor and site of the tumor. Teratoma is considered a distinct histological entity having variable grades of immaturity.

Mature teratoma represents the benign nature of the disease. The recurrent GCT tumors are managed initially by a second look surgery with a hope for complete resection of the lesion.

The cure rates of children with GCT in India are improving particularly after the advent of platinum based chemotherapeutical agents, akin to the western world. However reports from several institutions in India suggest that outcome is inferior to that achieved in the west. Hence a need to assess survival data and identify risk factors in our set of patients. Although there are multiple studies performed across the world, there is paucity of literature available on the risk factors, pattern/histology of disease and outcome of children with GCT in India.

There are variations between different geographical regions with respect to demographic profiles and outcome of GCT. In particular data from Asian countries especially from India are very limited. Thus the aim of our study is to fulfill the huge data gap that exists. Hence, we plan to conduct this study. This study was conducted to look for epidemiological characteristics like clinical spectrum, management and outcome of GCT over a period of 6 years.

Materials and Methods

Seventy two children admitted and treated in the department of paediatric oncology and paediatric surgery were include in this study from 2015 to 2021. The clinical characteristics including age, sex, site histology and stage of the lesion was noted down. The operative findings were recorded in detail. The method of adjuvant treatment was also evaluated. The follow up including any relapse and survival were retrospectively evaluated.

This study was approved by hospital ethical committee of our hospital No; EC-SKIMS/340/21. An informed consent was obtained from the guardian/parents of all the patients. The quantitative variables were described using median and range. Qualitative variables were described using frequency and percentage chi-square was used to examine the relationship between comparable variables. Kaplan Meier survival analysis and free survival has P-value equal to 0.05 was considered statically significant.

Results

During the study 72 patients were admitted and treated in the department of pediatric surgery and pediatric oncology. There were 39 males and 33 female patient (M:F). Fifteen (21%) patients belonged to urban and 57 (79%) to rural area. Most common presenting symptoms were mass palpable from the site of origin. The ovarian GCT typically presented with abdomen–pelvic mass. Acute or chronic pain Abdomen was reported in 5.5% of patients. Abdominal distention was noted in 25% of patients. Other symptoms included organ specific signs and symptoms like testicular mass in 27.77% cases.

Sacrococcygeal mass in SCT, gastrointestinal symptoms, urinary symptoms and precocious puberty. The duration of symptoms ranged from 7 days to 9 months with an average symptom duration of 3.36+2.7 month. Age ranged from 1 month to 21 years with average age of 12 ± 3.1 years. We observed a bimodal age distribution of GCT in our study. First peak was at an average of 6 years. The 2nd peak was noticed in 14 years irrespective of gender. Overall GCT was more frequently found in girls. The reason of more female predominance was related to high number of ovarian tumors 25%-34% ovarian *vs.* 20 (27%) testicular. 50% children has gonadal GCT, (20.83% testicular, 30.55% ovarian), 10 (3.38%) had sacrococcygeal tumors. Seven (9.72%) had retroperitoneal and 4 (5.5%) tumors in the neck region. Among gonadal tumors the ovarian GCT was more common in age group of 6 to 12 yrs.

Testicular tumor was more frequently found between 1 to 6 years of age. Most common site for extragonadal GCT was SCT and retroperitoneal region. Sixty five percent of extragonadal tumors were diagnosed during first year of life. Magnetic resonance imaging was performed in 81% of the patients. Ultrasonography was the first and most common investigation performed in all the patients. Computed tomography was performed in 19% of patients with GCT. A high level of AFP levels was found in 29 of 72 patients with malignant GCT. B-HCG was high in 09 of 72 patients. Normal AFP level was found in 47.72% of malignant GCT patients. In mature teratoma AFP and B-HCG was normal for age in all cases. Most frequent histology found was teratoma (20 (27.77%) mature and 10 (13.88%) immature). Yolk sac, mixed call and embroyonal histology was found in 16 (22%), 8 (11%), and 6 (8%) of cases respectively. Seminoma and dysgerminomas was found in 4 (5.55%) and 8 (11.11%) each respectively (Tables 1 and 2).

Age group	No	Percentage
1-5 years	15	20.83
6-10 years	6	8.33
11-15 years	16	22.22
16-21 years	35	48.61
Gender	No	Percentage
Male	33	45.83
Female	39	54.16
Total	72	100
Region	No	Percentage
Urban	15	20.83
Rural	57	79.16
Total	72	100
Presenting symptoms/ signs	No	percentage
Abdominal distension	18	25
Abdominal pain	4	5.55
Sacrococcygeal mass	8	11.11
testicular mass/pain	20	27.77
Incidental USG finding	10	13.88
Others	12	16.66

Total	72	100
Organ involved	No	Percentage
ovarian	22	30.55
Mediastinal	7	8.33
Scrococcygeal	10	13.88
Testicular	15	20.83
Retroperitoneum	7	9.72
Neck	4	5.55
Total	72	100
Tumor markers	NO	Percentage
Increased AFP	29	40
Increased B-HCG	9	12
Normal AFP and B-HCG	34	47.22
Total	72	100

Table 1. Summary of clinical features, baseline, stage of disease and follow-up investigations for patients of germ cell tumors.

Management	**No.**	**Percentage**
Surgery	36	50
Surgery with chemo		
(BEP)	28	38.88
(VAC)	8	11.11
Surgery , Chemo, RT	8	11.11
Post-operative complications	No	Percentage
Wound infection	4	5.55
Ileus	2	2.7
atelectasis	2	2.7
Sepsis	1	1.3
Out come	No. of pts	Percentage
Alive	49	68.05
Lost to f/u	10	13.88
Died	4	5.55
Total	72	100

Table 2. Management, post-operative complications and outcome.

We observed dysgerminoma and teratoma was common histological subtype during adolescence. The common age for yolk sac histology was 6 years (range 3-15 yrs). Out of all the GCT, 52% were benign and 48% were malignant tumors. 22.32% had stage I, 15 (20.83%) had stage II, 34 (47.22%) had stage III and 7 (9.72) had stage IV disease. Surgery alone was performed in 36 (50%) cases having mature and immature teratoma. In coccygeal tumors the complete enblock resection was possible in 80% of the cases. Adjuvant chemo therapy was administered 6 cycles of (bleomycin, etoposide, cisplatin). 50% tumors had recurrence; surgery was considered the only treatment in 50%. 50% required chemo therapy in addition to surgery 8 (11.11%) patients required surgery+chemotherapy +radiotherapy.

72% patients were disease free at a median follow-up of 56 months 10 patients had relapse of the disease at 20 months to 6 yrs. The median time for tumor recurrence was 23 months. 10% recurrences were local and 8% were symptomatic. Median follow-up was 56 months. Two patients died. Five years overall survival was 86.9% and relapse free survival 83.6% mean follow up time was 56 months.

Discussion

GCT is rare in children with an overall incidence of 0.9/100000 [5]. These occur due to normal differentiation of germ cells and include heterogeneous group of neoplasm with remarkable variability concerning histology and site of presentation. We observed that GCT localization and histological sub type vary according to gender and age group. The mean age group in our series was 84 months (0-252 months), which was slightly higher than other studies. In a large population based cohort study from Germany, including 1442 cases up to 15 yrs of age. In this study with bimodal age distribution, the first peak was observed at 2 yrs of life in both sexes, while as the second peak was observed at 7 years in girls and 10 years in boys respectively [6]. In our study the incidence of GCT was higher in girls in age group of birth to 1-6 years, while as incidence was almost similar in both boys and girls between 6-21 years of age. The first and second peak was observed at 6 years and 14 yrs respectively. This difference could because of better referral of female patients to over centers.

The most common presentation in our patients was abdominal mass followed by testicular mass and SC mass. In a study by Ablin et al., the patients presented with a combination of symptoms and signs including acute and chronic abdominal pain, abdominal mass and distention [7] We believe that the cause of abdominal mass in abdominal/pelvic lesions is primarily due to late presentation of the children in our services and the relative shallow pelvis in pediatric age group. The presentation of GCT primarily depends on the site involvement. As noted in our results a good proportion of cases may also present with associated nonspecific GI and urinary symptoms. At time precious puberty may be a catching sign in GCT especially if malignant.

The duration of symptoms was long in our patients before referral to our center. The average duration in our patients was 3.36 yrs ± 2.7 months. In a study by Ablin et al., the duration of symptoms ranged from 1 day to 6 months [7]. The most common site of origin of GCT in our study was the testis 20.83%. In a study by Buyukpamukcu et al., 57% patients had gonadal tumors (34 ovarian and 24 testicular) and 43% were extra gonadal in origin [8]. Our findings of site of origin are

almost similar to that report by other authors. The ovarian tumor was more frequent in age group of 10-15 yrs. This was in contradiction to that reported by Mann et al., where the ovarian GCT was frequent in age group of 5 to 10 yrs [9]. The incidence of yolk sac tumor in our study was 16 (22.22%). In a study by Polynter et al., the percentage age of yolk sac tumor was 35% which was higher than reported by our series [10].

In our study most common histology was teratoma, 43.65% of cases, which was 40% reported by Buyukpamukcu et al., Dysgerminoma was found in patients after the age of 5 years in our study. In a study by Feltbower et al., Dysgerminoma was the predominant histological subtype found in Adolescence [11]. The histological evaluation of GCT is difficult because of heterogeneous appearance of tumors and because of conflicting terminology. GCT arises from the primordial germ cells which are capable of embryonic and extra embryonic differences [12,13].

AFP, B-HCG are secreted by the Gobel tumors depending on their histological differentiation. AFP levels are excessively raised in neonates and infants. We found AFP and B-HCG levels in 117 patients with malignant GCT. In a study by Harms et al., and Heifetz et al., High levels of AFP were detected in 43 of 75 patients with malignant GCT [14,15]. The patients presenting at stage III and IV disease were proportionally higher than found in the literature. We have 41% of stage IV and III cases, which was higher than reported in the study by Gobel and Schneider et al., [16].

Conclusion

GCT in children are rare tumors, this malignancy can have both gonadal as well as extra gonadal presentation. In pediatric age group extra gonadal tumors are more frequent. GCT in paediatric age group occurs more frequently in sacrococcygeal area. In our study ovarian GCT was more common than testicular GCT. Teratoma was the most common histology found in this study. This difference could be because of late presentation and time wasted by pediatric physicians in the periphery.

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