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Pediatric Germ Cell Tumor: A Single Centre Experience

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Abstract

The germ cell tumors (GCT) of childhood are heterogeneous group of tumors. GCT are classified as malignant or benign. These are uncommon and comprise only 4% of childhood cancer. Yolk sac tumors (YST) are the most prevalent malignant gonadal and extragonadal tumors. A retrospective study was designed to analyze pediatric germ cell tumor treated at tertiary care center from western India. All patients with the pathological diagnosis of GCT treated at Gujarat Cancer Research Institute during January 2015 to December 2017 were studied. Demographic, clinical, treatment and response data were gathered and analyzed.

Forty-six patients were evaluated. Male to female ratio was 1:1.56. The median age was 3.5 years (range: 6 months -14 years). The most common pathological type was YST 17 (36.95%). Gonadal tumors were common 25(54.34%), of which 17(68%) patients had ovarian and 8(32%) testicular involvement. Commonest ovarian and testicular pathology was teratoma 7(41.11%) and YST 6(75%) respectively. Presenting symptom was abdominal mass (30.43%) followed by gluteal mass (28.26%). Of 21(45.66%) extragonadal tumors, sacrococcygeal 15(71.42%) were frequent. At presentation advanced stage tumors were 26(59.09%) and early stage 18(40.91%). Six (14.63%) were treated with surgery alone and 17(41.46%) with combined (surgery plus chemotherapy).

All 6 treated with surgery attained complete remission (CR). Thirty-five patients received optimal treatment and 4 were lost to follow up on treatment, 5 did not seek any treatment and 2 died. Of these, 27(77.14%) had CR, 6(17.14%) progressive disease, 2(5.71%) relapsed after short DFS. CR rate in yolk sac histology was 62.5% and that of non-yolk sac histology was 68% (p=0.75). 94.5% patients of early stage attained CR as compared to 30.43% of advanced stage (p=<0.0001). Gonadal tumors had more CR rate than extragonadal (88% vs 31.25%, p=0.0004). The median OS was 17.5 months. GCT had female preponderance. Gonadal tumors were most common. Most common histology was YST and most of the patients presented in advanced stage. Histology didn't affect the response, while stage and site of presentation had significant impact on response.

Key words: *Germ cell tumor, yolk sac tumor, pediatric germ cell tumor, dysgerminoma.*

Introduction

The germ cell tumors (GCT) of childhood are heterogeneous group of tumors. GCT are classified as malignant or benign. (1) These are uncommon and comprise only 4% of childhood cancer. Yolk sac tumors (YST) are the most prevalent malignant gonadal and extragonadal tumors. A retrospective study was designed to analyze pediatric germ cell tumor treated at tertiary care center from western India.

Material and Methods

All patients with the pathological diagnosis of GCT treated at Gujarat Cancer Research Institute during January 2015 to December 2017 were retrospectively studied. Demographic, clinical, treatment and response data were gathered and analyzed.

Results

Forty-six patients were evaluated. Male to female ratio was 1:1.56. The median age was 3.5 years (range: 6 months -14 years). The most common pathological type was YST 16(36.95%). [Fig 1] Gonadal tumors were common 25(54.34%), of which 17(68%) patients had ovarian and 8(32%) testicular involvement. Commonest ovarian and testicular pathology was teratoma 7(41.11%) and YST 6(75%) respectively. Presenting symptom was abdominal mass (30.43%) followed by gluteal mass (28.26%). Of 21(45.66%) extragonadal tumors, sacrococcygeal 15(71.42%) were frequent. At presentation advanced stage were 26(59.09%) and early stage 18(40.91%). Thirty-five patients received optimal treatment and 4 were lost to follow up on treatment, 5 did not seek any treatment and 2 died. Among evaluable patients, 29(82.85%) had CR, 6(17.14%) progressive disease, 2(5.71%) relapsed after short DFS. CR rate in yolk sac histology was 75% and that of non-yolk sac histology was 89.47% (p=0.38). 100% patients of early stage were in CR as compared to advanced stage (p=0.0445). Gonadal tumors had more CR rate than extragonadal (91.67% vs 63.63%, p=0.063) [Table 2] The median OS was 17.5 months.

Discussion

GCTs are a rare and diverse group of heterogeneous tumors that include both benign and malignant histologies (6). Since they are rare, conducting retrospective research seemed the best policy for gathering information on these tumors in our country and paving the way for future studies.

In present study there were a total of 46 patients, and the most common pathologic type was yolk sac tumor (36.95%), in contrast to study published by Ahmad Khaleghnejad-Tabari et.al, (2) and Zachary Horton et al (3) teratomas were most prevalent type of tumors. In a study by Billmire and colleagues (4), most common histology was reported to be ovarian teratoma. The most frequent ovarian GCT found in present study was mature teratoma (41.11%). The most frequent presentation was with abdominal mass (30.43%) followed by gluteal mass and abdominal pain, as against study done by Xiaokun Lin (5), of gonadal germ cell tumor, most common presenting symptom was abdominal pain and distention. In present study, 25(54.35%) cases were of gonadal and 21(45.65%) cases of extragonadal involvement as compared to the observation made by Ahmad Khaleghnejad-Tabari et al (2), 32 cases were extragonadal and 12 cases were of gonadal type. In Marina et al (6), study of 73 patients with extra cranial immature teratomas, there were 51 gonadal involvements and 22 extra gonadal cases. In Brodeur GM et al (7) study with the total number of 57 patients, gonadal involvement was seen in 30 cases and extragonadal involvement in 27 cases.

Mann et al (8) evaluated 126 patients aged 0 to younger than 16 years with malignant GCT, serum AFP measured in 123 patients was elevated in 115 patients, whereas HCG was high in 19 of 77 cases. In our study, 29 patients had elevated AFP, of which 15(51.72%) cases were of yolk sac tumor. In 6 patients beta HCG was elevated. (Table 1). Two patients whose AFP was very high died. In a study published by Ahmad Khaleghnejad-Tabari et al, 14 cases of yolk sac tumor and one patient of immature teratoma, AFP was elevated, and also beta HCG was increased in one case of choriocarcinoma.

As stated in the International Germ Cell Consensus Classification (9) the degree of elevation of alpha-fetoprotein, human gonadotropin, and lactic dehydrogenase in adults is a risk factor for poor prognosis but this is not true in pediatric GCTs and only degree of elevation of AFP is associated with a poor prognosis in the pediatric population.

Advanced stage accounts for (stage III and IV) 59.1% of patients. In a study published by Ahmad Khaleghnejad-Tabari et al (2), the most common stage was stage I (53%). Amongst 46 patients, 35 patients received optimal treatment and 4 were lost to follow up on treatment, 5 did not seek any treatment and 2 died. Of these 35 patients who were evaluable for response, 29(82.85%) had CR, 6(17.14%) progressive disease, 2(5.71%) relapsed after short DFS. As against Ahmad Khaleghnejad-Tabari et al, (2) demonstrated complete remission in 31(77.5%), patients and 9 (22.5%) patients died. The response rate was found significantly associated with stage of presentation and there was trend towards the complete response according to site. The median OS in this study was 17.5 months (Range 8- 43months). 1 year and 2-year overall survival in present study was 82.05% and 30.76% respectively. (Fig. 1)

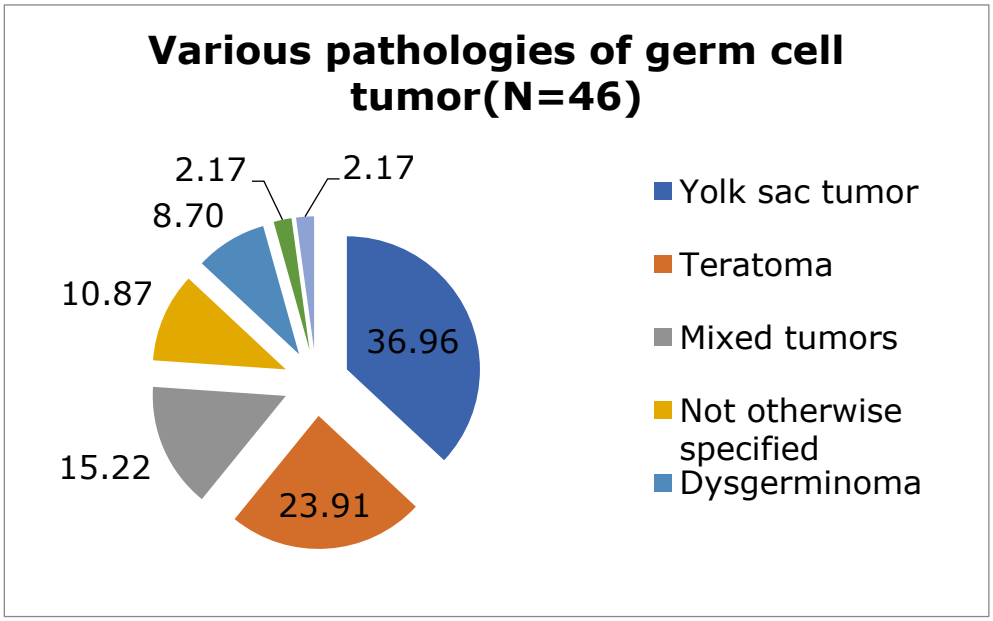

Fig 1: Pathologies of germ cell tumor.

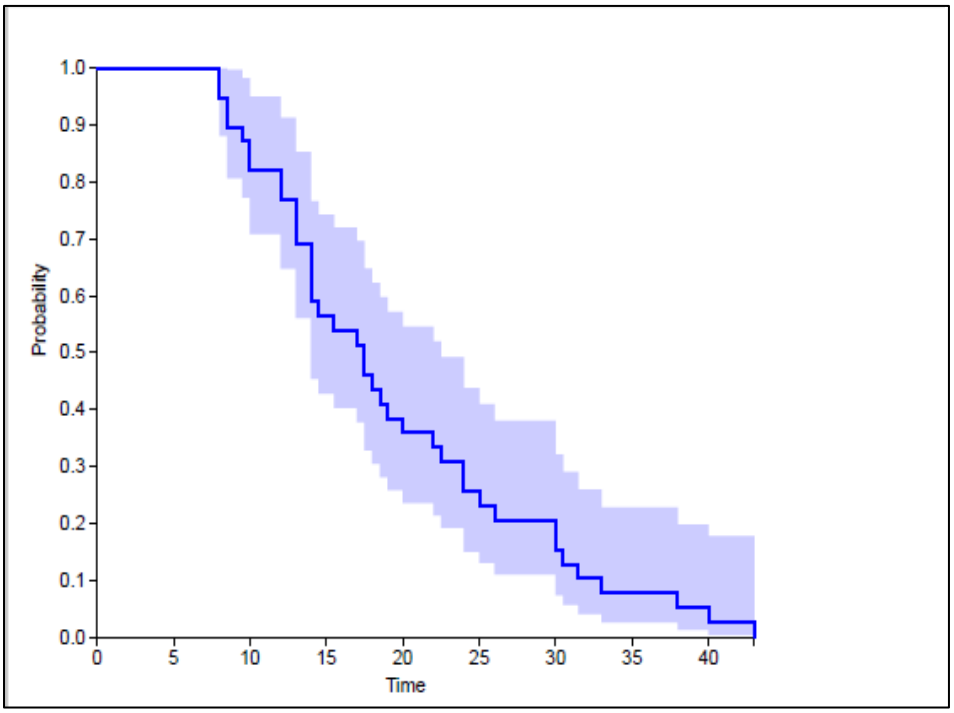

Fig 2: Kaplan -Meier survival graph.

Histology	AFP	LDH	Beta HCG
Yolk Sac	15	14	1
Mixed histology	6	2	2
NOS	3	2	1
Dysgerminoma	0	4	1
Teratoma with focal yolk sac	2	2	0
Immature teratoma	2	4	1
Embryonal	1	1	0

Table 1: Tumor markers elevated according to histology.

Clinical response according to Histology				
	Yolk sac	NYST	Total(N=35)	P Value
CR	12	17	29	
No CR	4	2	6	p=0.38
Clinical response according to Stage				
	Early	Advanced	Total(N=34)	
CR	17	12	29	
No CR	0	5	5	p=0.0445
Excluding brain GCT				
Clinical response according to Site				
	Gonadal	Extragonadal	Total(N=35)	
CR	22	7	29	
NO CR	2	4	6	p=0.063

Table 2: Clinical response according to Histology, Stage and Site.

Conclusion

GCT had female preponderance. Gonadal tumors were most common. Most common histology was YST. Majority of the patients presented in advanced stage. Histology didn't affect the response, while stage and site of presentation had significant impact on response. Early stage and gonadal GCT had more CR rates.

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