Original Article

Survival of Children with Germ Cell Tumors in Ali Asghar Hospital since 1990 to 2003

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ABSTRACT

Background and Objective: **Germ cell tumor (GCT) accounts for approximately 2-3% of all malignancies in children. In this respect, about 20% of patients with GCT are still resistant to therapy.**

Materials and Methods: **The cross-sectional strategy of this survey was undertaken on 57 patients with germ cell tumor who admitted to Ali Asghar Children hospital during the years 1990-2003. In this study, information regarding sex, age, pathological findings, clinical signs, treatment, and survival (event-free survival) were gathered in order to have better treatment and follow-up. The obtained data were analyzed using SPSS software.**

Results: **The findings showed that the mean age of patients was 4.9 ± 0.1 years (1 months-14 years). Meanwhile, 54% and 46% of patients were male and female respectively with a ratio of 1.1. Regarding site of involvement, 57.8% and 42% of patients had sacrococcygeal and gonadal tumors respectively. In addition, regarding their pathological typing, 61.4%, 12.2%, 14%, and 10.5% of them had yolk sac tumor, dysgerminoma, malignant teratoma, and embryonal carcinoma respectively. The most common clinical signs were buttock mass, testicular mass, an abdominal mass, and abdominal pain in 31.5%, 28%, 17.5%, and 10.5% of patients respectively. All of the patients were treated with chemotherapy (bleomycin, vinblastin, cisplat). Mean duration of follow-up was 48.4 months. In this regard, 31.5% of the patients were alive, no information was available for 15.7% of them, and 52.6% of cases were expired. Meanwhile, 70% of the patients had tumor relapse. In this regard, event-free survival (EFS) for patients was 42%.**

Conclusion: **The analysis of the treated patients showed that extragonadal location of primary tumor (especially sacrococcygeal), level of AFP above 10 ng/ml in patients, an age equal to or greater than 6 months, and metastatic disease were the most unfavorable factors for overall survival .**

Key words: Germ cell tumor, Pediatric age group, Survival

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Introduction

Germ cell tumors (GCT) account for approximately 2-3% of all malignancies in children (1,2). Almost all of the tumors in this age group arise from totipotential germ cells which have migrated from the extra-embryonic yolk sac endoderm to the gonads or to other sites (2,3). They may be benign (mature teratoma) or malignant (germinoma, malignant teratoma, embryonic carcinoma, yolk sac tumor, and/or choriocarcinoma), or may contain several of these elements. About half of germ cell tumors arise in the gonads and the remainder in intra-cranial and intra-spinal or other non-gonadal sites (2). Gonadal carcinoma is extremely rare in children. Sex and age distribution reflects the heterogeneity of these tumors. Boys reach a peak of occurrence, infants and girls reach a peak of occurrence around age 13 years, but the pattern varies widely according to the histology of the subgroup and the site of the tumor (2). A marked cytogenetic anomaly, the isochromosome of the short arm of chromosome i(12p) has been demonstrated in over 80% of all histological varieties of testicular germ cell tumors. In the remaining group of i(12p)-negative, an over representation of chromosome 12p sequence has been found (4). The serum alpha fetoprotein and HCG level is elevated in most cases with yolk sac tumor (3, 5,6).

Therefore, we studied 57 patients with germ cell tumor who were admitted to Ali Asghar children hospital to evaluate the effect of main factors on survival.

Materials and Methods

This study was undertaken on 57 patients with germ cell tumor who were admitted to Ali Asghar children hospital during the years 1990-2003. This study was cross-sectional and data were analyzed using SPSS software. During this study, information about demographic variables including sex, age, clinical signs, type of pathology, site of tumor, treatment, and event-free survival, and tumor markers were gathered.

Results

The findings showed that mean age of patients is 4.9 ± 0.1 years with a range of 1 month- 14 years). In addition, 43.8% of patients had an age under 2 years, 22.8% of them had an age between 2 and 4 years, and 19.2% were above 8 years. In addition, 46% and 54% of cases were female and male respectively with a ratio of 1.1.

Clinical signs in patients included buttock mass (31.5%), abdominal mass (17.5%), testis (27%), abdominal pain (10.5%), constipation (7%), and secondary amenorrhea (1.7%) (Table 1). Regarding anatomical site, 57.8%, 12.2%, 3.5%, 13.7%, and 10.5% of cases had a sacrococcygeal, right ovary, left ovary, left testis, and right testis origin respectively (Table 2).

Table 1. Distribution of clinical signs in germ cell tumor

Clinical findings	Count	Prevalence (%)
Buttock mass Abdominal mass	18 10	31.57 17.54
Left testicular enlargment	9	15.7
Right testicular enlargement	7	12.28
Abdominal pain	6	10.5
Constipation	4	7.01
Fever	2	3..5
Secondary amenorrhea	1	1.75
Total	57	100

Table 2. Distribution of tumor location

Site of tumor	count	%
Sacrococcygeal	33	57.8
Left testis	9	15.7
Right testis	6	10.5
Right ovary	7	12.2
Left ovary	2	3.5
Total	57	100

Pathologically, yolk sac involvement, dysgerminoma, malignant teratoma, and embryonal carcinoma included 61.4%, 12.2%, 14%, and 10.5% of cases respectively (Table 3). With respect to tumor markers, the mean of alpha feto protein was 4589 mg/dl (1.8-36800 mg/dl). Regarding staging, stage IV included 20 cases, stage

III were 5 cases, and 37 of them had stage II. All of the patients were treated with surgery and chemotherapy. Protocol of treatment was CVB (cisplat, vinblastin, and bleomycin).

Table 3. Distribution of tumors according to histological subtypes

Histological type	count	%
Yolk sac tumor	35	61/4
Dysgerminoma	7	12/2
Malignant teratoma	8	14
Embryonal carcinoma	6	10/5
Teratoma	1	1/9
Total	57	100

The duration of follow-up was 84 months. In this respect, 17 patients were alive and no information was available for 15.7% of cases, 52.6% of cases were expired, and 70% of cases had relapse. In this study, EFS (event-free survival) was 42%.

Discussion

Germ cell tumor has some histological subtypes, dependent on presenting clinical characteristics. Sacrococcygeal teratoma is the most common germ cell tumor in children, accounting for 40% of all the germ cell tumors and up to 78% of extragonadal germ cell tumors (7). Approximately, 75% of patients are females and 80% of cases are diagnosed within the first month of life. Approximately 17% of sacrocogcygeal teratoma exhibit malignant features (7). Most of patients are at stage IV. The most common malignant elements identified within the sacrococcygeal lesions are yolk sac tumor and embryonal carcinoma. More than 90% of cases have elevated levels of AFP in yolk sac tumor, suggesting that follow-up should be included using AFP measurements, radiography, and abdominal sonography (6-9).

The pediatric oncology group reviewed 892 patients with germ cell tumor during the years 1971-1984. They showed an improved survival for each 5-years period regardless of tumor site, no statistically significant difference between yolk sac and embryonal carcinoma in children, and a better than reported prognosis for sacrococcygeal tumors occurring after neonatal period, particularly poor prognosis for neonatal and benign saccrococcygeal teratoma resected (8). Another study registered 210 patients in University of Dusseldorf. In this regard, 76 cases with sacrococcygeal primaries presented either with pure yolk sac tumor or mixed, 41 patients had metastases, and 35 children presented with extension into bone. Meanwhile, 22 cases had an AFP elevation less than 10 ng/ml, median observation time was 54 months after diagnosis, and 5-years survival rate was 76% (10). In a study conducted in Italy, 95 patients were studied. Their age at the time of diagnosis ranged from 1 month to 15 years and the median of follow-up was 33 months. The site of the primary tumor was gonadal in 59 patients (63%) and extragonadal in 38% of cases. Overall survival was 82.7% and EFS (event-free survival) was 71.4% (10). The analysis of the patients treated showed that extragonadal location of primary tumor (especially sacrococcygeal), level of AFP above 10 ng/ml in patients equal to or greater than 6 months, and metastatic disease were the most unfavorable factors for overall survival (10).

In conclusion, in our study like other studies, sacrococcygeal mass and yolk sac tumor were primarily presented. Event-free survival was 42% that is less than other studies.

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