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RESEARCH ARTICLE

Clinical and Treatment Characteristics of Pediatric Cranial/Extracranial Germ Cell Tumors and Literature Review

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ABSTRACT

Objective: Germ cell tumors (GCTs) arise from primordial germ cells and vary greatly in clinical behavior, histology, and location. This study reviews the clinical and prognostic features of cranial/extracranial GCTs in the pediatric population through our clinical trial study and literature review.

Materials and Methods: This study is a retrospective analysis of hospital system data on children ages 0–17 with germ cell tumors. A total of 26 patients who were diagnosed and treated for germ cell tumors in the pediatric hematology and oncology department of our university hospital between 2019 and 2023 were included in this study. Patients diagnosed with both intracranial and extracranial germ cell tumors were included. Within the scope of the study, 30 studies were scanned from PubMed and the National Cancer Institute (NCI) data system, and 7 of these were found to be related to the subject and summarized in a table.

Results: The mean age of the 26 patients with GCT was 10.3 years (range: 5 months–17 years). Fifteen patients were girls (58%) and eleven were boys (42%). Three GCTs were located intracranially (3/26, 11%) and 23 extracranially (23/26, 89%). Nineteen patients (73%) received chemotherapy, and 7 patients (26%) had surgery-based treatment with no additional chemotherapy. All 3 patients with intracranial GCTs had chemotherapy plus radiotherapy (11%). In total, 2 patients (7%) died because of chemotherapy-refractory disease.

Conclusion: GCTs are highly responsive to treatment, including surgery and chemotherapy. With new studies, treatment options will be defined with a flow chart, allowing the selection of the best surgery, radiotherapy, and chemotherapy for optimal prognosis.

Keywords: Childhood, clinic, germ cell tumors, treatment, literature

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INTRODUCTION

The majority of GCTs occur in the gonads or along the midline structures of the body.[1] Pediatric GCTs are rare, with an incidence of approximately 11.7 per million for boys and 6.7 per million for girls.[2] Although rare, GCTs account for about 3% of tumors in children under the age of 15 and 14% of tumors in children and young adults between the ages of 15 and 19. Benign mature teratomas (MT) are the most common histology.[3,4]

Although GCTs are histologically similar, classification depends on their location of origin. A germinoma in the brain is histologically identical to a seminoma in the testicle or a dysgerminoma in the ovary.[5] A non-germinomatous germ cell tumor (NGGCT) is typically the same as a non-seminomatous extracranial GCT and includes yolk sac tumor, embryonal carcinoma, choriocarcinoma, or mixed tumors.[2,6]

Another classification depends on the tumor markers they secrete. Elevated alpha-fetoprotein (AFP) is markedly related to yolk sac tumor, dysgerminoma or seminoma, embryonal carcinoma, and immature teratoma.[7] Similarly, elevated human chorionic gonadotropin (β-hCG) is related to tumors such as choriocarcinoma or embryonal carcinoma. Generally, CNS

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GCTs cannot be biopsied, and the diagnosis is based on elevated tumor markers.[8] In the definition of germinoma, serum β-hCG is less than 50 mIU/ml, although germinomas have been reported with β-hCG levels in the range of 50–100 mIU/ml. Alpha-fetoprotein greater than 10 ng/ml is considered above normal and may suggest yolk sac tumor, immature teratoma, or NGGCT.[9,10] In contrast, in extracranial GCTs, immature teratoma is defined as having AFP less than 1000 ng/ml.[11]

GCT survival rates improved dramatically after the introduction of platinum-based chemotherapy in the 1980s. Five-year survival rates of 90% have been reported.[11,12] This study aims to determine the incidence rates, treatment protocols, and outcomes of GCTs in children aged 0–17 years registered in our clinical database system and to review the limited literature.

MATERIALS and METHODS

Patient Selection and Registration

Demographic data, gender, tumor localization, treatment protocol, operation type, AFP, β-hCG, and lactate dehydrogenase (LDH) levels, tumor histology, evidence and localization of metastasis, grade, and prognosis data of patients who were followed up in our pediatric hematology clinic with a diagnosis of GCT between 2019–2023 were evaluated retrospectively. Patients with GCT between 0–17 years old were included in the study. Patients over 18 years and with diagnoses other than GCT were excluded. All data were recorded in patient charts. Verbal and written consent of the patients was obtained during the recording of all data, and the study was designed in accordance with the Helsinki Declaration. Ethical Committee approval was obtained from the Basaksehir Cam and Sakura City University Ethical Committee (KAEK 24.11.2022/2022.10.345).

Review Data

A comprehensive literature search was performed in PubMed using combinations of the keywords: childhood, germ cell tumors, clinic, treatment, literature. The search proceeded by selecting keywords, date range, and all studies related to pediatric germ cell tumors in accordance with the PRISMA guideline. In addition, references of selected papers were retrieved to find relevant studies. After primary selection, 7 of 30 studies were determined to be most relevant to pediatric germ cell tumors.

Statistical Analysis

Data were evaluated using IBM SPSS 21.0 (SPSS Statistics 21.0, Armonk, New York: IBM Corp.). The distribution of variables was examined with the Kolmogorov test. Comparisons between groups with normal distribution were evaluated with the t-test, while groups with non-normal distribution were evaluated with the Mann–Whitney U test. Mean, standard deviation, median, value range, and ratio distribution analysis of variables, K-S Lilliefors test, variance analysis according to distribution (ANOVA/Kruskal–Wallis), chi-square, and Fisher's exact tests for ratios were the methods used in statistical analysis.

RESULTS

The mean age of the 26 patients with GCT was 10.3 years (range: 5 months–17 years). Fifteen patients were girls (58%) and eleven were boys (42%). Three GCTs were located intracranially (3/26, 11%) and 23 extracranially (23/26, 89%). Nineteen patients (73%) received chemotherapy, and 7 patients (27%) had surgery-based treatment with no additional chemotherapy. All 3 patients with intracranial GCTs had chemotherapy plus radiotherapy (11%). In total, 2 patients (7%) died because of chemotherapy-refractory disease. Gonadal and extragonadal distribution according to age groups and gender is displayed in Table 1.

The mean AFP value was 9204 ng/ml (range: 1–121,000 ng/ml). Eight patients had germinomatous histology and nine had non-germinomatous histology. Four patients had teratoma histology, of which 2 were mature and 2 immature. Three patients had mixed histology, all boys with testicular involvement.

Table 1. Gonadal, extragonadal distribution according to age groups and gender

	Gender			
	Boy		Girl	
	n	%	n	%
Age of diagnosis				
0–5 years				
Gonadol	3	11.5	2	7
Extragonadol	0	0	3	11.5
5–10 years				
Gonadol	0	0	1	3.8
Extragonadol	0	0	0	0
10–17 years				
Gonadol	3	11.5	8	30.7
Extragonadol	5	20.2	1	3.8
Total	11	43.2	15	56.8

n: Number of patients

Table 2. Tumors according to location and histology in children aged 0 to 17 years diagnosed with GCTs

Histological type	CNS	Pelvis	Mediastinum	Retroperitoneum	Gonads (overian/testicular)	Other
Yolk sac tumor	-	2	1	-	3(2/1)	
Teratoma	-	-	2	-	2(1/1)	
[a]Germinoma/[b]Dysgerminoma/[c]Seminoma	3(a)	-	-	-	10 (7/3) (2 cases a, 7 case b, 1 case c)	Vaginaa:1 case b
Mixed tumor	-		-	-	3(b)	
Choriocarcinoma	-	-	-	-	-	None
Embryonal carcinoma	-	-	-	-	-	None
Total	3	2	3		18	26

GCTs: Germ cell tumors; CNS: Serebral nervous system; [a]: Germinoma; [b]: Dysgerminoma; [c]: Seminoma.

Human chorionic gonadotropin elevation is seen in tumors such as choriocarcinoma or embryonal carcinoma. Germinoma is defined as having serum β-hCG less than 50 mIU/ml, although germinomas have been reported with β-hCG levels in the 50–100 mIU/ml range. Among extracranial NG-GCT patients, 3 had β-hCG over 50 mIU/ml (mean: 8629 mIU/ml, range: 69.9–18,965 mIU/ml). In laboratory analysis, the mean LDH level was 362 IU/L (range: 151–2000 IU/L).

All GCT patients underwent diagnostic mass biopsy and initial positron emission tomography to confirm the diagnosis, grade, and risk group of the illness. Tumors according to location and histology in children aged 0–17 years diagnosed with GCTs are displayed in Table 2.

Nineteen patients (73%) received chemotherapy, and 7 patients (27%) had surgery-based treatment with no additional chemotherapy. All 3 patients with intracranial GCTs had chemotherapy plus radiotherapy (11%). In total, 2 patients (7%) died because of chemotherapy-refractory disease.

The standard chemotherapy regimen of three drugs—bleomycin, etoposide, and cisplatin (BEP)—was the initial option in 16 extracranial GCT patients (61%). Two patients relapsed and were treated with paclitaxel, ifosfamide, and cisplatin (TIP), commonly used as salvage for pediatric malignant germ cell tumors.

All 3 patients with intracranial GCTs were germinomas and received chemotherapeutic agents including carboplatin, etoposide, and ifosfamide, or cisplatin, vincristine, and cyclophosphamide, combined with reduced-volume or local radiotherapy. One patient had treatment-refractory disease and was switched to an ifosfamide, carboplatin, and etoposide (ICE) salvage regimen.

According to risk classification, the numbers of low-, medium-, and high-risk extracranial GCT patients were 12, 3, and 8, respectively. Additionally, regarding the grading system, the total counts of Grade 1, 2, 3, and 4 extracranial GCT patients were 6, 4, 8, and 5, respectively.

DISCUSSION

Germ cell tumors account for 3% of pediatric cancers. There is a bimodal age distribution, with the first peak at ages 1–3 and the second peak during adolescence. The Turkish Pediatric Oncology Group (TPOG) and Turkish Pediatric Hematology Association (TPHA) established the pediatric cancer registry in 2002. Childhood cancer cases registered between 2002–2024, and the results of this analysis, were presented at the 2025 ASCO (American Society of Clinical Oncology) Annual Meeting. The GCT count was 5.7% of all cancer cases (3042/52,907), with a median age of 9.0 years, and male/female distribution of 1119/1916, along with 4 hermaphrodite and 3 unknown gender cases.[13] The age distribution of our study patients was similar to these data, as the mean age of the 26 patients with GCT was 10.3 years (range: 5 months–17 years). There were 2 patients under 1 year of age (5 and 7 months), 1 patient aged 9 years, 8 patients aged 1–3 years, and 15 adolescent patients (10–19 years).

An extragonadal site of origin is more common in pediatric GCT, with yolk sac tumor being the most common histopathological finding. Origin from pluripotent cells accounts for the wide variety of tumors encountered and their multiple anatomic sites, including gonadal, sacrococcygeal, mediastinal, retroperitoneal, and other para-axial locations. Different histologic types—including endodermal sinus tumor (yolk sac tumor), germinoma (dysgerminoma, germinoma, and sem-

Table 3. Overview of the entities in the new GCT classifcation (WHO classifcation of pediatric germ cell tumors)

Non-invasive germ cell neoplasia	Intratubular germ cell neoplasia (male gonad)
	Gonadoblastoma (mostly in dysgenetic gonad)
Germinoma-family tumours	Germinoma/dysgerminoma/seminoma (GDS)
Non-germinomatous germ cell tumours	Teratoma family
	Mature cystic teratoma
	Extragonadal teratoma
	Fetus in fetu
	Teratomas of the female gonad
	Monodermal teratomas
	Immature teratoma
	Pre-pubertal-type testicular teratoma
	Post-pubertal-type teratoma
	Embryonal carcinoma
	Yolk sac tumor (pre- and post-pubertal type)
	Choriocarcinoma (non-gestational)
	Malignant mixed germ cell tumor

GCTs: Germ cell tumors. Poynter et al.[2]

inoma), embryonal carcinoma, and choriocarcinoma—may coexist in a single tumor, accounting for 25% of GCTs. The 2022 edition of the WHO (World Health Organization) classification of pediatric tumors, introduced in Virchows Archiv, is based on the first organ-independent classification of germ cell tumors, reflecting advances in molecular biology, histopathology, and clinical practice, and is displayed in Table 3.[14]

In our study, the results for GCTs according to location and histology in children aged 0–17 years are displayed in Table 1. In Table 2, the histological diagnoses of our study patients were as follows: 15% cystic teratoma (4/26 cases), 23% yolk sac tumor (6/26 cases), 12% germinoma (3/26 cases), 11% mixed GCT (3/26 cases), 26% dysgerminoma (7/26 cases), and 12% seminoma (3/26 cases).

Figures 1 and 2 show pelvic magnetic resonance images of a patient who presented with a large sacrococcygeal mass in sagittal and axial planes. A trucut biopsy was performed from the patient, who had an 8×6×5 cm mass lesion and a serum AFP level of 49,190 ng/ml at admission. Before pathology results were obtained, the patient developed urinary and stool retention, and the mass had a history of extremely rapid growth. Since the patient's preliminary diagnosis was germ cell tumor, the BEP chemotherapy protocol was started. After the first cycle, the patient's AFP level decreased to 23,100 ng/ml, and after the second cycle it decreased to 2500 ng/ml. The obstructive symptoms caused by the mass disappeared, and the size of the lesion decreased by nearly 80% after 2 cycles of BEP chemotherapy (Figs. 3, 4).

Although literature data indicate dysgerminomas as the most common histological feature, our study was compatible with other histopathological studies, including those by

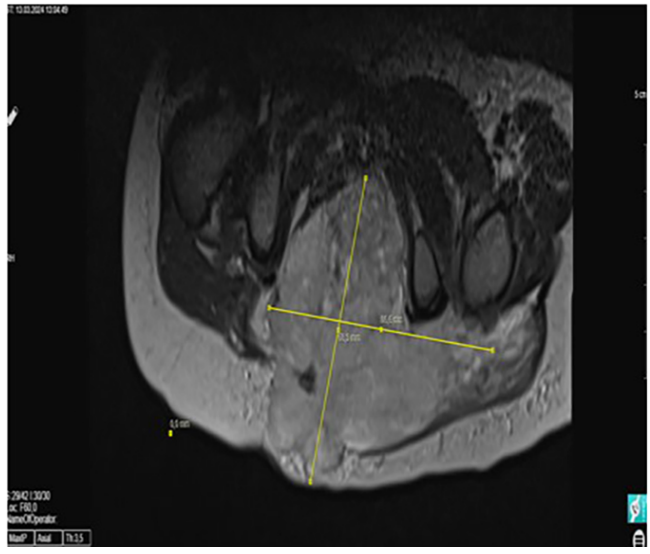

Figure 1. Magnetic resonance imaging of sacrum/coccyx at moment of diagnosis. (Saggital section). A hyperintense mass on T2 sequence, measuring 85×62 mm in axial sections with heterogeneous contrast after vena cava inferior, continuing towards the perirectal region and anal canal level in the distal sacral region. Additionally, 3 lympadenopathy (LAP) were observed in the left parailiac region, the largest of which measured 23×30 mm. An another LAP measuring 21×15 mm was observed in the left inguinal region

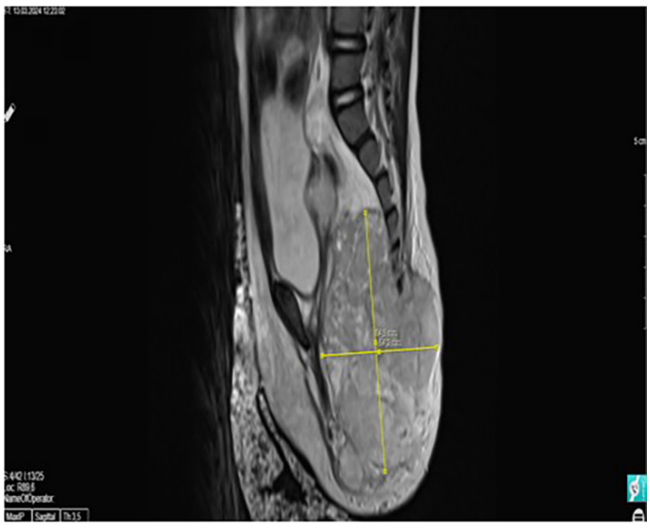

Figure 2. Magnetic resonance imaging of sacrum/coccyx at moment of diagnosis (axial section)

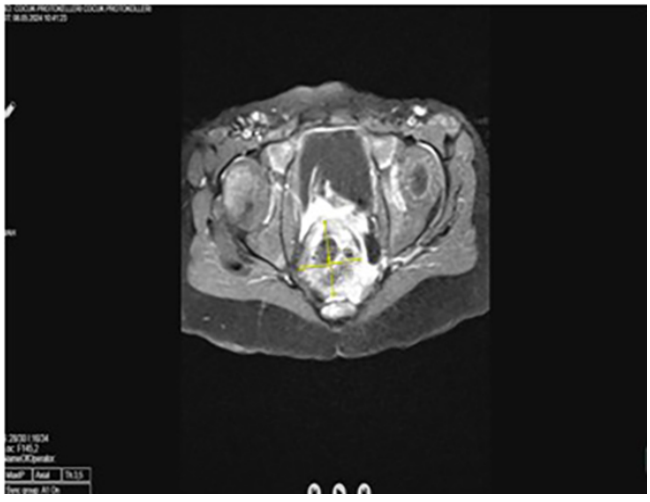

Figure 3. After 2 cycles of BEP chemotherapy, an 80% markeble rate of involution which measn good response to treatment was detected in the lesion (saggital section)

BEP: Bleomycin, etoposide, and cisplatin

Evers et al.[15] and Schneider et al.[16]. No cases of pure embryonal carcinoma or choriocarcinoma were encountered in our study; these histopathological types were observed only as components of mixed GCTs (5/38 cases).

When the locations of the cases are evaluated, ovarian tumors accounted for 10 cases (38%) and testicular tumors for 8 cases (30%). In total, 18 cases (69%) were gonadal and 8 (31%) were extragonadal. These findings are similar to those of Evers et al.[15] and Malogolowkin et al.[17].

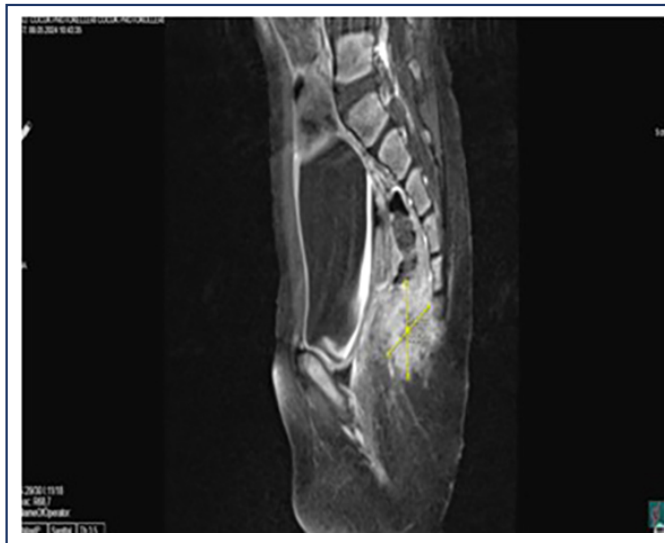

Figure 4. After 2 cycles of BEP chemotherapy, a 24×15mm sized residual lesion with heterogeneous enhancement is observed in the ischiorectal region of the left side of the coccyx (axial section)

In extracranial GCTs, AFP elevation is associated with yolk sac tumor, dysgerminoma or seminoma, embryonal carcinoma, and immature teratoma. AFP is secreted by yolk sac tumors, while β-hCG is secreted by choriocarcinoma. In our study, the mean AFP level was 9204 ng/ml (range: 1–121,000 ng/ml), which is markedly high. Additionally, among extracranial NGGCT patients, 6 had β-hCG levels over 50 mIU/ml (mean: 8629 mIU/ml, range: 69.9–18,965 mIU/ml). Tumor markers are useful both for diagnosis and for monitoring treatment response.

In our study, elevated AFP was found in 46% of patients (12/26), while elevated β-hCG was present in 11% (3/26). In contrast, in the Evers et al.[15] study, only 13% had AFP elevation and 3% had β-hCG elevation. In testicular GCTs in our study, AFP elevation was found in 37% (3/8) and β-hCG elevation in 12% (1/8). In the study by Kutluk et al.,[18] AFP elevation was 88% and β-hCG elevation was 48%. In our gonadal GCT group, AFP elevation was 38% (7/18) and β-hCG elevation was 5.5% (1/18), while in Bartlett et al.[19]'s study, AFP elevation was 22% and β-hCG elevation 3%. Elevated AFP is particularly indicative of yolk sac tumor and embryonal carcinoma, while elevated β-hCG is associated with choriocarcinoma and germinomas.[20,21]

A comprehensive literature search identified 7 of 30 studies as most relevant to the aims of this study. General clinical features of childhood GCTs based on the literature review are displayed in Table 4. In our study, elevated AFP in yolk sac

Table 4. General clinical features of childhood GCTs based on literature review

Study/(reference)	Patient count/age distrbution	Gender		Histopathology	Location of GCT	Overall survival (5 years)
		Girl	Boy			
Evers et al. (Denmark) (1984–2013)/[15]	57 (0–18 years)	71 (%)	29 (%)	1. Yolk Sak Tm (33%) 2. Immature Teratoma (20%) 3. Embryonal Carcinoma (18%)	1. Over(37%) 2. Sacrococcygeal (22%) 3. Testis (18%)	<2 years: 28% >2 years: 48%
Pauniaho et al. (Finland) (1969–2008) (Malignant GCT)/[22]	403 (0–18 years)	37 (%)	63 (%)	1. Mature Cystic Teratoma (69%) 2. Yolk Sak Tm (12%) 3. Immature Teratoma (10%) one	1. Over (46%) 2. Sacrococcygeal (16%) 3. Testis (15%)	97%
Poynter et al. (America) (1975–2006)/[2]	2110 (0–19 years)	54 (%)	36 (%)	- Infant and small child: Teratoma, Yolk Sak tumor - >10 years of age Boys: Teratoma, Embryonal carcinoma, Mixed germ hc tm - >10 years of age Girls: Teratoma, Germinoma	- <4 years of age Boys: Gonadal = Extragonadal - <4 years of age K: Almost all extragonadal - >10 years of age Boys: Testicles come first - >10 years of age Girls: Ovary comes first	94%
Schneider et al. (Germany) (1981–2000)/[16]	1442 (0–18 years)	56 (%)	44 (%)	1. Teratoma (37%) 2. Yolk Sak Tm (27%) 3. Germinoma (18%)	1. Ovarian (29%) 2. CNS (21%) 3. Sacrococcygeal (19%)	Undeclared
Kaatsch et al. (Germany) (1987–2011)/[8]	1366 (0–14 years)	55 (%)	45 (%)	1. Yolk Sak Tm (32%) 2. Teratoma (28%) 3. Germinoma (20%)	- <4 years of age: Pelvis, testicles - 4–14 years of age: CNS, ovarian 85%; lowest)	92% (gonadal:96–98%; highest) (Intracranial:
Malogolowkin et al. (America) (1941–1986)/[17]	188 (0–18 years)	69 (%)	31 (%)	1. Benign Teratoma (56%) 2. Malignant Teratoma (26%) 3. Germinoma (20%)	1. Ovary (39%) 2. Sacrococcygeal (36%) 3. Testis (7%)	81% (Benign teratomas: 96%, Malignant GCT: 46%
Miao et al. (China) (2005–2015)/[32]	127 (0–14 years)	58 (%)	32 (%)	- Girls: 1. Mature Cystic Teratoma (86%) 2. Immature Teratoma (7%) 3. Dysgerminoma (3%), Yolk Sak Tm (3%) - Boys: 1. Mature Cystic Teratoma (58%) 2. Yolk Sak Tm (36%) 3. Immature Teratoma (4%)	- Girls: 55% right 45% left - Boys: 53% right 47% left	Undeclared
Our study	26 (0–17 years)	61 (%)	39 (%)	1. Dysgerminoma (26%) 2. Yolk sac tumor(23%) 3. Cysticteratoma (15%)	1. Ovarian (38%) 2. Testicular (30%) 3. Other (CNS, Sacrococcygeal mediastinal, other extragonadol) (32%)	OS rate of our study (2019–2023) is 87%. The EFS rate was found to be 84.5%.

CNS: Serebral nervous system; OS: Overall survival; EFS: Event free survival

Table 5. The chemothraphy regimens and recommended risk categorization in pediatric extracranial germ cell tumors NHI (National Health Institue) Childhood Extracranial Germ Cell Tumors Treatment (PDQ®) 2024

Risk category	Site of tumor			Surgery and chemotherapy
	Testicular	Ovarian	Extragonadal	
Low-risk	Stage I*	None	None	Surgery alone
Intermediate-risk	Stage II-IV	Stage I-III	Stage I-II	Surgery+PEBx3
High-risk	None	Stage IV	Stage III-IV	Surgery+PEBx4

*: Stage I testicular tumors that do not show fall of αFP as expected or show a rise of αFP after initial decline should be put in intermediate-risk category and receive adjuvant chemotherapy PEB Cisplatin, etoposide, and bleomycin. Evers et al.,[15] NHI (National Health Institue) Childhood Extracranial Germ Cell Tumors Treatment (PDQ®) 2024.[28,29]

tumors and elevated β-hCG in mixed GCTs were consistent findings, with β-hCG elevations related to choriocarcinoma or germinoma components.

According to the Children's Oncology Group (COG) risk classification, the numbers of low-, medium-, and high-risk extracranial GCT patients were 12, 3, and 8, respectively. By grading system, the total numbers of Grade 1, 2, 3, and 4 extracranial GCT patients were 6, 4, 8, and 5, respectively.

In the study by Pauniaho et al.,[22] stage 1 cases were the majority, whereas in our study stage 3 cases predominated. However, low-grade, low-risk testicular tumors were still the majority in our study, similar to Pauniaho's findings. Likewise, in the study by Kutluk et al.[18] on testicular GCTs, stage 1 cases were most common, while in Terenziani et al.[23]'s study on ovarian GCTs, stage 3 cases predominated. Both studies showed outcomes similar to ours.

GCTs most commonly spread via hematogenous and lymphatic pathways, with distant metastases typically occurring in the lungs, liver, and bone. In our study, distant metastases occurred in 3 patients (11.5%, 3/26), all with high-risk Grade 4 yolk sac tumors. Two were ovarian and one was mediastinal.

The first approach in GCT treatment is surgical excision. In our study, surgery was performed in all cases: 12/26 (46%) underwent total excision with oophorectomy (malignant cases), 8/26 (30%) total excision with orchiectomy (malignant cases), and 6/26 (23%) biopsy. Malogolowkin et al.[17] reported 89% total excision and 11% subtotal excision or biopsy. Suita et al.[24] reported 76% total excision and 24% subtotal excision or biopsy. Both studies showed similar rates to ours. For mature cystic teratomas, total surgical excision alone is considered sufficient treatment,[25,26] consistent with our 5 cases, all excised successfully.

Of the 6 non-excisable cases, 3 were intracranial germinomas and 3 mediastinal yolk sac tumors. These tumor types present greater surgical challenges due to their locations, which likely explains their lower excision rates compared with other histopathological types.

Treatment of GCTs typically includes chemotherapy (CT) and/or radiotherapy (RT) after surgical excision. The overall recommendation is 4 cycles of BEP (cisplatin, etoposide, and bleomycin per cycle) for standard-risk patients. An alternative strategy to reduce toxicity in standard-risk patients is carboplatin, a cisplatin analogue with fewer long-term effects. Chemotherapy regimens and recommended risk categories in pediatric extracranial GCTs from the NHI Childhood Extracranial Germ Cell Tumors Treatment (PDQ®) are displayed in Table 5.[27]

In our series, 19 patients (73%) received chemotherapy and 7 (27%) had surgery only. All 3 intracranial GCT patients received chemotherapy plus RT. BEP was the first-line regimen for extracranial GCTs, while 2 relapsed cases were treated with TIP (paclitaxel, ifosfamide, cisplatin). Intracranial germinoma patients received carboplatin+etoposide protocols with RT.[28]

Of the intracranial GCT patients, all received combinations of chemotherapy and RT, with only 1 experiencing refractory disease and requiring TI-ICE. In total, 5 patients died due to chemotherapy-refractory disease.

In our study of 26 pediatric GCT cases, 2 patients (7%) died, 3 (11%) relapsed, and 21 (80%) were cured. The overall survival rate (OS) was 93%. However, this must be interpreted cautiously due to short-term follow-up in the Kaplan–Meier analysis. In Terenziani et al.[23]'s study on ovarian GCTs, the 5-year OS was 98.5% and event-free survival (EFS) was 84.5%.[22] Our OS rates are close, but our EFS rates are lower.

In our intracranial GCT subgroup, the OS was 100% and EFS 83.3%, compared with Voirin et al.,[29] who reported both 100%, and Akyüz et al.,[30] who reported OS of 62.5% and EFS of 37.5%. These discrepancies may be explained by short follow-up duration, small sample size, and differences in chemotherapy protocols, particularly before platinum-based regimens.

Long-term adverse effects in pediatric GCT survivors remain insufficiently studied due to a lack of robust longitudinal data. The Platinum Study, reported in the COG blueprint 2023, has been instrumental in defining late effects in adults with testicular GCTs.[31] Known complications include ototoxicity, peripheral neuropathy, secondary malignancies, and cardiovascular disease. Since children and adolescents receive comparable chemotherapy regimens, it is plausible they experience similar late effects, emphasizing the importance of systematic long-term follow-up.

Limitations

This study has several limitations. The age range (0–17 years) excludes older adolescents and young adults (up to 25 years), which may limit generalizability. In our country, the national health insurance system does not support patients aged 18–25 as pediatric cases, so they cannot be treated by pediatric oncologists. Future studies should include this group to provide more representative data.

Another limitation is the short follow-up, which affects OS and EFS rates in the Kaplan–Meier analysis. A larger, multicenter design would help overcome sample size limitations and provide stronger evidence for pediatric GCT outcomes.

CONCLUSION

Proper surgical resection and staging techniques are critical to achieving the best outcomes and ensuring that patients receive appropriate treatment without unnecessary overtreatment or inadequate therapy. Collaborations with international centers and new studies will help reduce treatment-related toxicities and late effects while improving outcomes for high-risk patients. Future multicenter trials and international collaborations to standardize treatment protocols are strongly needed.

Disclosures

Ethics Committee Approval: The study was approved by the Basaksehir Cam and Sakura City University Clinical Research Ethics Committee (No: 2022.10.345, Date: 24/11/2022).

Informed Consent: Obtained from patients' parents. Written informed consent was provided for publication of clinical details and identifying images.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: Concept – H.A.S., D.Ö.Y., A.A., S.A.T.; Design – H.A.S., D.Ö.Y.; Supervision – H.A.S., D.Ö.Y., A.A., S.A.T.; Funding – H.A.S.; Materials – H.A.S., D.Ö.Y., A.A., S.A.T.; Data collection and/or processing – H.A.S., D.Ö.Y.; Data analysis and/or interpretation – H.A.S., D.Ö.Y., A.A., S.A.T.; Literature search – H.A.S., D.Ö.Y.; Writing – H.A.S.; Critical review – H.A.S., D.Ö.Y., A.A., S.A.T.

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