Pediatrik Cerrahi Dergisi, 8:15-17, 1994

A survey of 34 childhood germ cell tumors

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Summary

Thirty-four patients with germ cell tumor have been treated by the Pediatric Oncology Group, Istanbul School of Medicine, between January 1981 and April 1991. There were 23 female and 11 male patients with a mean age of three years. The presenting symptoms and signs were abdominal pain, constipation or urinary strain with sacroccocygeal, abdominal or inguinal mass. The tumoral mass was located in the sacral area in 13 patients (38 %), in the ovary in 12 (35 %), in the testes in seven (21 %) and retroperitoneally in the remaining two (6 %).

We did not observe any mediastinal or pineal tumors. Histopathologic study revealed an endodermal sinus tumor (yolk sac tumor) in 15 of the cases (44 %), mature teratoma in 11 (32 %), teratocarcinoma in four (12 %), embryonal carcinoma in two (6 %) and germinoma in two cases. Nine patients were classified to have Stage I, six Stage II, eight Stage III and 11 Stage IV disease.

We observed three hepatic, three pulmonary and six disseminated abdominal metastasis among these patients. All of the patients were operated, total resection was performed in 19 cases where 16 cases underwent subtotal resection. Seven patients underwent a second-look laparotomy following chemotherapy. Patients with mature teratoma received no further therapy.

The patients were treated with VAC (vincristine, actinomycin-D, cyclophosphamide), PEB (cis-platin, bleomycin, Vp-16) or PVB+VAC (vinblastin, bleomycin, cisplatin, vincristine, actinomycin-D, cyclophosphamide) protocols. Five patients are still under treatment, 13 patients died while under therapy and nine patients are lost to follow up. Therapy is terminated in one case and six cases with mature teratoma are doing well after complete resection. The overall survival rate in two years is calculated to be 48 percent.

Key words: *Germ cell tumor, teratoma*

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Introduction

Germ Cell tumors are rare solid tumors of the childhood originating from the primordial germinative cells of the human embryo. During the embryonal stage, germinative cells migrate from the vitellum towards the gonads. Interruption of this migration under any circumstances, may lead to neoplasias at hyphophyseal, mediastinal, retroperitoneal, sacrococcsygeal, ovarial or testicular localization [1].

Germ cells are precursors of male and female gonads and store the potential to differentiate into any embryonal (somatic) and extra-embryonal tissue. Differentation of these germ cells into extra-embryonal tissues may lead to choriocarcinomas or endodermal sinus tumors, where as differentiation into embryonal tissues may lead to teratomas.

Patients with germ cell tumor present with various clinical pictures due to tumor's site of localization. Such a case with an ovarian, retroperitoneal or sacrococcygeal tumor may attend with symptoms of acute abdomen, urinary tract disease or intestinal obstruction. Testicular tumors expose enlargement on the affected side, some mediastinal tumors are seen with chest pain, cough and/or dyspnea [6]. Gynecomastia may be observed due to response to high levels of chorionic gonadotropins. Radiodiagnostic imaging techniques are supplementary in differential diagnosis.

Germ cell tumors are known to excrete Alphafetoprotein (AFP) and human Chorionic Gonadotropins (hCG). These two markers provide valuable information during the follow-up period. Residual tumor or recurrence and the response to therapy is determined by these tumor markers. AFP has a halflife of five days and hCG has a halflife of 30 hours [6].

Materials and Methods

Thirty-four patients with germ cell tumor were treated by the Pediatric Oncology Group, Istanbul School of Medicine, between January 1981 and April 1991. The aim of this study is to evaluate the age and sex distribution, the clinical outlook, laboratory findings, histopathology, staging, therapy and survival rate of these patients.

Results

There were 23 female and 11 male patients, with a mean age of 37 months (range between 2 days - 11 years). A sacrococcygeal mass was the presenting symptom in 30.6 % of the cases, abdominal mass in 30.6 %, abdominal pain in 16.4 %, testicular mass in 14.3 %, strain during defecation in four per cent, constipation, weigth loss and anorexia in two per cent. The site of the primary tumor was the sacral area in 13 patients, ovaries in 12, testes in seven and retroperitoneum in two cases (Table I). None of the cases showed pineal or mediastinal localization. Common histopathologic diagnosis was an endodermal sinus tumor (yolk sac tumor), mature teratoma, teratocarcinoma, embryonal carcinoma, and germinoma respectively (Table II).

Forty per cent of all endodermal sinus tumors originated from the sacral area, 30 % from the testes, 20 % from the ovaries and 10 % from retroperitoneum; 50 % of all teratomas originated from the ovaries, 40 % from the sacral area and 10 % from retroperitoneum; all of the embryonal carcinomas originated from the testes; half of the germinomas originated from the testes, the other half from ovaries. Nine cases were classified as Stage I disease, six as Stage II, eight as Stage III and 11 as Stage IV (Table III). Serum AFP values were over 20 mg/ml (mean 278±21.3) in 17 (74 %) of the 23 determined cases. Serum hCG values were over 8.7 mg/ml (mean 49±5.9) in only five of the 16 determined cases. Sedimentation rate was high in 16 cases (mean 38.4±3.2 mm/hr).

All of the patients were operated. The tumor was resected totally in 19 patients (including all mature teratomas) and partially in 16. We observed three hepatic, three pulmonary and six intraabdominal metastasis. Three cases that had ovarial teratomas attended with acute abdomen. We performed four of the seven second-look operations following chemotherapy (CT), in three cases the tumor rest was totally resected. Patients with mature teratomas received no further therapy. Eleven cases received VAC, four received BEP, eight received BVP+VAC protocols as for chemotherapy. In those cases where VAC protocol failed, we proceeded on with BVP+VAC or Bristol (Vcr, Iphosphamide, Carboplatin, VP-16, Farmarubicin) protocol. Adjuvant radiotherapy was added in six patients who failed to respond to CT protocols. Thirteen cases expired while under therapy, nine were lost to follow up.

Table I. 34 germ cell tumors: Localization

Localization	n	%
Sacrococcygeal	13	38
Ovarial	12	35
Testicular	7	21
Retroperitoneal	2	6

Table II. 34 germ cell tumors: Histopathology

Histopathology	n	%
Endodermal sinus tumor	15	44
Mature teratoma	11	32
Teratocarcinoma	4	12
Embryonal carcinoma	2	6
Germinoma	2	6

Table III. 34 germ cell tumors: Stating & histopathology

	Endodermal sinus tumor	Mature teratoma	Terato-carcinoma	Embryonal carcinoma	Germinoma
Stage I	-	9	-	-	-
Stage II	2	2	-	1	1
Stage III	7	-	-	-	1
Stage IV	6	-	4	1	-
Total	15	11	4	2	2

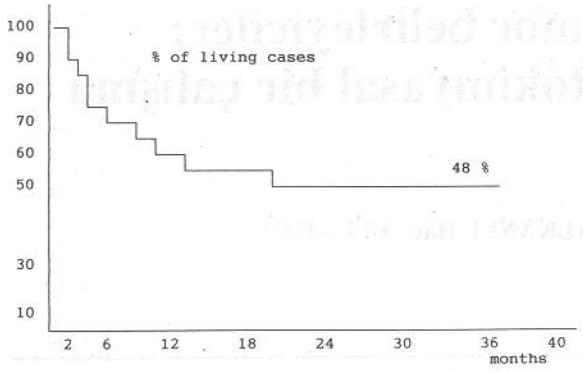

Figure 1. Survival of our patients (Kaplan-Meier estimate).

One patient is considered tumor free and is doing well with the therapy terminated. Five patients are under therapy. The overall two year survival rate is 48 per cent (Figure 1).

Discussion

Germ cell tumors are rare solid tumors of the childhood showing an incidence 2-3 per cent. The male to female ratio is given as 1/1 in the literature, in our series there is a marked female tendency [6]. The reason for this may be that, ovarial (38 %) and sacrococcygeal (35 %) localizations, which are seen more frequently in females, fullfill an important amount in our series [1,6]. The ratio of gonadol localization is also higher (56 %) in our study when compared to the literature [6].

Germinomas and embryonal carcinomas originate mostly from the gonads, whereas teratomas originate from the sacrococcygeal, gonadal presacral and mediastinal region. Endodermal sinus tumors may be localized in the ovaries, testes and the presacral area, where chorio-carcinomas appear mostly in the ovaries, mediastinum and the pineal region [1,5,6]. There is a good correlation between our series and the literature due to tumoral site [1,2].

The overall histopathologic distribution seen in Table II, is also well correlated to the literature [1,3,4,8]. Serum AFP levels were found to be high in 74 % of the observed cases. This implies the use of serum AFP level as a reliable tumor marker during follow-up period.

All patients, excluding those with a mature teratoma, received CT following surgery. Out of the 11 patients who received VAC protocol, five failed to respond to therapy and died, while six others were lost to follow-up. This situation aroused suspicion towards the effectivity of this regimen. The United Kingdom Children's Cancer Study Group (UKCCSG) states that the VAC protocol is ineffective when compared to other CT protocols, with an eight per cent five year survival rate. The survival rate has risen to 65 % with the PVB protocol and 84 % with the BEP protocol [2,6,7]. We reached higher survival rates since we started using these protocols.

Germ cell tumors, although rare could be considered as one of the most difficult tumors of the childhood. With the recent advances in chemotherapy, we hope to speak of better results in the future.

References

1. Ablin A, Isaacs HJ: Germ cell tumors. Pizzo PA, Poplack DG (eds) "Pediatric Oncology", Philadelphia, JB Lippincott, 1989, p.713
2. Cangir A, Smith J, Van Eys J: Improved prognosis in children with ovarian cancer following modified VAC (Vincristine sulfate, D-actinomycin and Cyclophosphamide) chemotherapy. Cancer 42:1234, 1978
3. Flamant F, Schwartz L, Delons E: Nonseminomatous malignant germ cell tumors in children. Cancer 54:1687, 1984
4. Kawai M, Kano T, Furuhashi Y: Prognostic factors in yolk sac tumors of the ovary. Cancer 67:184, 1991
5. Kersh LR, Consdable WC, Hahn SS: Primary malignant extra-gonadal germ cell tumors. Cancer 65:2681, 1990
6. Lanzkowsky P: Germ cell tumors. Lanzkowsky P (ed) "Manual of Pediatric Hematology and Oncology". New York, Churchill Livingstone, 1989, p.387
7. Mann JR, Pearson D, Barrett A: Results of the United Kingdom Children's Cancer Study Groups' malignant germ cell tumor studies. Cancer 63:1657, 1989
8. Vugrin D, Chen A, Feigl P: Embryonal carcinoma of the testis. Cancer 61:2348, 1988