The Incidence and Management of Malignant Ovarian Tumors In Girls Upto 20 Years of Age

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OBJECTIVE – To find out the incidence of and suitable treatment for malignant ovarian tumors in girls upto 20 years of age. **METHOD –** A prospective study of malignant ovarian tumors in girls upto 20 years of age was undertaken over a seven year period from 1995 to 2001. Laparotomy, with surgical staging was done. Fertility sparing surgery was followed by chemotherapy with bleomycine, etoposide and cisplatin. **RESULTS –** 13.91% of ovarian tumors occurred in girls below 20 and 35.7% of them were malignant. Eighty eight percent of malignant tumors were of germ cell variety, dysgerminoma being the commonest. Ninety percent of dysgerminoma and 80% of immature teratoma cases came in stage I and were salvaged. Endodermal sinus tumor and mixed tumors had dismal outcome as 85% of them presented in stage III or IV and could not survive. The overall survival rate was 68%. **CONCLUSION –** Early detection, prompt treatment and monitoring by tumor markers can reduce mortality.

Key words : germ cell tumors of ovary, dysgerminoma, endodermal sinus tumor, immature teratoma

Introduction

Ovarian tumors in children and adolescent girls constitute an important part of gynecological oncology. Detection of these tumors at such a young age creates much anxiety to the parents and throws a great challenge to the doctors in charge as the question of operative safety, chance of malignancy and prospects of future child bearing are all associated with the treatment

It is well known that germ cell tumors (GCT) are the commonest ovarian neoplasm in the young age group. In the first two decades of life, approximately two thirds of ovarian tumors are of germ cell origin, of which about one third are malignant accounting for two-thirds of ovarian malignancy in this age group[1]. Norris and Jensen[2] found that 1% of epithelial carcinoma occurs before 21 years of age.

Sex cord stromal tumors are rare tumors accounting for 5-8% of all ovarian malignancy[3]. Granulosa cell tumors are found in prepubertal girls in 5% of cases.

In general, the prospect of malignant ovarian germ cell tumors is gloomy due to a high degree of mortality. In the past two decades major development has taken place in the area of treatment of these malignant tumors making the outlook better. Practice of fertility sparing surgery, replacement of radiotherapy by chemotherapy and arrival of newer chemotherapeutic drugs has made the prognosis much better today.

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Aims and Objects

Today, management of malignant tumors of the ovary in young girls is not satisfactory due to our inadequate experience and their varied nature. In this prospective study, we wanted to find out the incidence of malignant ovarian tumors in girls aged upto 20 years to know the magnitude of the problem and to study the clinical presentation, histological type and the result of treatment so that these relatively uncommon but lethal tumors can be treated in a better way in future.

Material and Methods

All girls upto 20 years of age admitted with ovarian tumors in S.S.K.M. Hospital, Kolkata from 1995 to 2001 were included in the study. Other causes of adnexal tumors were excluded from the study. Careful history taking and physical examination were done regarding the symptoms and their duration, general condition, size and consistency of the mass and any other important features. Routine investigations, LFT, chest X-Ray and USG were done in all, and tumor markers like serum AFP, HCG, LDH and CA-125 were estimated in suspected malignancies. Karyotyping was advised in prepubertal girls but not done due to high costs involved. Laparotomy and surgical staging were done in all cases. In stage I unilateral tumor, ovarian cystectomy or unilateral salpingo – oophorectomy was done. Biopsy

from contralateral ovary used to be taken previously but this step is now omitted to prevent tubal adhesion. In bilateral solid ovarian tumors we did total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy followed by radiotherapy in dysgerminoma. In unilateral stage three and four tumors with extensive intraperitoneal metastases, we did unilateral salpingo-oophorectomy with debulking as much as possible with omentectomy keeping uterus and other ovary intact unless they were involved by metastasis. Surgery was followed by chemotherapy with BEP (bleomycin, etoposide and cisplatin). Recurrent cases were treated with BEP or PVB (cisplatin, vinblastin and bleomycin) regime.

Doses employed were bleomycin : 20 U/m^2/week, etoposide : 100 mg/m^2/d for 5 days every 3 weeks, cisplatin : 20 mg/m^2/d for 5 days every 3 weeks. (Cycles were repeated every three weeks).

Results

Out of a total of 503 women admitted with ovarian tumors, 70 (13.91%) were at or below 20 years, and in them the incidence of malignancy was as high as 35.7% (Table I).

Table II shows that germ cell tumors (GCT) were the most common ovarian tumor in young girls. Fifty seven (including 35 dermoid cysts) out of 70 cases i.e. (81.4%), belonged to germ cell variety. Among 25 malignant tumors, 22 (88.00%) were GCT. Dysgerminoma was the commonest malignant GCT (45.4%).

Table III gives signs and symptoms of the patients. Acute pain in abdomen was present in six girls due to torsion, intracystic hemorrhage, and necrosis. Jaundice was present in two girls, chest symptoms were present in five cases and convulsion occurred in one case of stage IV tumor. Precocious puberty with breast development (stage II) with vaginal bleeding was found in a baby of two years with GCT. Hirsutism was present in a girl aged 18 years with Sertoli and Leydig cell tumor. As the germ cell tumors are very rapidly growing tumors, most of the patients give short history and develop a moderate to huge lump in the abdomen in three to six months. Majority of our patients came from very low socioeconomic conditions.

Table IV depicts the results of investigations. USG showed huge lump in six cases. Chest x-ray showed metastatic lesion in six cases. Serum AFP was raised in all endodermal sinus tumors (EST), in mixed tumors with EST component, and some immature teratoma. Serum HCG was high in chorio-carcinoma containing mixed tumors. LDH was raised in the presence of dysgerminomas or its component. Serum testosterone and androstenedione were high in a Sertoli and Leydig cell tumor and CA-125 was elevated in immature teratoma and in epithelial carcinoma.

Table V depicts details of management. There were 10 cases of dysgerminomas between 6 to 20 years of age. Nine (90%) belonged to stage I. Two girls had bilateral tumors, where TAH+BSO was followed by radiotherapy. Unilateral salpino-oophorectomy with or without contralateral ovarian biopsy was done in seven cases followed by four cycles of BEP. All of them are doing well. The only girl with stage IV tumor, had RSO done three years back for dysgerminoma with no follow up. This time she had left sided dysgerminoma with brain and lung metastases having convulsion and coma. USO with TAH and omentectomy was done on her. She expired on the sixth day of operation without chemotherapy (CT) or radiotherapy (RT).

Mixed GCT and endodermal sinus tumors were very disappointing. Among three cases of mixed GCT, two had EST and chorio-carcinoma, and one had EST and dysgerminoma. Six among seven cases (85.7%) belonged to stage III and IV with widespread metastases. USO + debulking + omentectomy was done in them. Three cases were prepubertal, youngest being of only three years who developed liver metastasis and died. CT with BEP or cisplatin, vinblastine and bleomycin (PVB) was given, but most of the patients took only one or two courses and became so ill that further courses were delayed. Four patients developed rapid recurrences. All six cases expired in this series. The only case with stage Ia EST survived after USO and four courses of BEP.

Among four cases of immature teratomas, one was in stage IV with extensive lung metastases and ascitis. She underwent TAH+BSO+ omentectomy and received three courses of chemotherapy but expired. Other four cases (80%) with stage Ia grade two or three tumors, survived following USO with BEP.

There were three other cases of malignant nongerm cell tumors. One was a two years old girl, the youngest of our series having a granulosa cell tumor with breast development, Tanner's-stage 2 and vaginal bleeding. USO was done with no CT. The second case was of serous cystadenocarcinoma stage Ia treated with USO and biopsy of contralateral ovary and received four cycles of VAC. Third case had a huge Sertoli-Leydig cell tumor on one side and a benign cystic teratoma on the other side. USO with other sided ovarian cystectomy was done.

The overall survival among young girls with

malignant ovarian tumors was 68%. All girls with stage IV disease died.

Discussion

Ovarian tumors in children and young girls are not infrequent. Oumachigui et al[4] found the incidence to be 6% of all ovarian tumors. Sawai and Sirsat[5] recorded the incidence as 11.2% In our study, 13.91% of all ovarian tumors occurred in girls, aged less than 20 years. Bren and Maxon[6] reported that 35% of all ovarian neoplasms in childhood and adolescent were malignant. We also found this incidence as 35.7% (Table I).

Ehren et al[7] found that 60-85% of ovarian neoplasms of pediatric and young adolescent patients were of germ cell origin. In our series, 57 (81.4%) ovarian tumors in young girls were of germ cell variety (Table II). Among malignant tumors 22 (88%) were GCT. Dysgerminoma was the commonest malignant GCT (45.4%). The commonest mode of presentation of these malignant GCT was abdominal mass, acute or sub acute pain, anorexia, loss of weight and fever.

Solid or heterogeneous mass on USG is generally indicative of malignancy. Chest x-ray can detect lung metastases. Tumor markers are elevated in different varieties of germ cell malignancies and are helpful in diagnosis and followup.

Ninety percent of of dysgerminoma cases came in stage I. Gordon et al[8], showed that 75% of dysgerminomas are stage I, and 10-15% are bilateral. We got 3 (30%) bilateral tumors. In one patient who expired, the tumor had appeared in other ovary three years later. TAH with BSO was done in two bilateral cases. Conservative fertility sparing surgeries were done in seven cases followed by chemotherapy. Today, chemotherapy has replaced radiotherapy in most cases. A combination of bleomycin, etoposide and cisplatin has been evolved as the gold standard of chemotherapeutic regimen in the field of malignant GCT[9], with a overall disease free survival rate of more than 95%. An alternative regimen is PVB.

85.7% of our cases of EST and mixed GCT came in at a very late stage with wide spread intraperitoneal and distant metastases with very poor general condition. Bilaterality was not seen in these lesions and additional hysterectomy and contralateral oophprectomy does not improve the outcome. All gross metastatic lesions should be removed. In incompletely resected tumor, PVB is more effective. But our patients came at such advanced stages with severe malnutrition and pallor that, most of them could not be given full four cycles of chemotherapy due to the occurence of severe myelodepression and rapid recurrences.

Even in immature teratoma, the only cases with stage IV disease died, but other cases with stage Ia, grade 2 or 3 survived following only salpingo-oophorectomy and BEP for four courses. In these tumors, apart from staging, grading is also an important factor for prognosis. Maximal tumor resection is the goal of surgery.

Two cases of sex cord stromal tumor and one of epithelial carcinoma were found in our series. All are well till now.

Table – I : Incidence of Malignant Ovarian Tumors in Adult and Young Girls.

Year	Adult		Age below 20 years	
	Total	Malignant	Total	Malignant
1995	60	14	7	4
1996	77	10	13	3
1997	63	12	11	4
1988	60	14	6	2
1999	56	12	11	3
2000	60	10	13	5
2001	57	10	9	4
Total	433	82 (19%)	70	25(35.7%)

Table – II : Distribution of Histological Types of Ovarian Tumors in Girls at or below 20 years of age (n=70)

Benign tumors	**45**
Mature teratoma (dermoid cyst)	35 (Bilateral in 7)
Simple serous cyst	7
Follicular cyst	2
Corpus luteal cyst	1
Malignant tumors	**25**
Germ cell tumors	22 (88%)
Dysgerminoma	10 (45.4%)
Endodermal sinus tumor	4
Mixed germ cell tumor	3
Immature teratoma	5
Granulosa cell tumor	1
Sertoli – Leydig cell tumor	1
Serous cystadenocarcinoma	1

Table – III : Modes of Presentation of Malignant Tumors in Girls at or Below 20 years of age (n=25)

Symptoms and Signs	
Abdominal mass, pain	25
Acute pain in abdomen	6
Anorexia	12
Loss of weight	10
Fever	10
Cough, hemoptysis	5
Jaundice	2
Convulsion	1
Marked pallor	7
Precocious puberty	1
Hirsutism	1

Table – IV : Special Investigations

Investigation	No. of Patients
a) USG	
Size of the mass	
5-10 cm.	4
10-15 cm.	15
15-20 cm.	6
Bilaterality	22
Unilateral	
Bilateral	3
b) Tumor Marker :	
Serum AFP raised	10
HCG raised	2
LDH raised	11
CA 125 raised	3
Testosterone and Androstenedione raised	1
c) Chest X-Ray	
Metastases	6
No metastsis	19

Table – V : Details of Treatment of Malignant Ovarian tumors in Girls at or below 20 years of age

Type of tumors	Stage	Operation	CT/RT	Result
Dysgerminoma (10 cases)	Ia – 7 Ib-2 IV-I	USO-7 TAH & BSO 2 TAH & USO 1	BEP-7 RT-2 No CT-1	Expired -I
EST-4 Mixed GCT-3 (7 cases)	Ia-I III-1 IV-5	USO-1 USO & Debulking-6	BEP-2 BEP & PVB-3. No therapy 1	Expired-6
Immature Teratoma (5 cases)	Ia-4 IV-1	USO-4 TAH & BSO-1	BEP-4 BEP & PBB 1	Expired-1
Nongerm cell Tumors	Ia-3	USO-2 USO & Biopsy of other ovary – 1	VAC-1	Nil

USO – Unilateral Salpingo Oophorectomy
BSO – Bilateral Salpingo Oohorectomy
TAH – Total Abdominal Hysterectomy
CT - Chemotherapy
RT – Radiotherpay
EST – Endodermal Sinus Tumor

Thus overall 17 of 25 (68%) girls below 20 years of age with malignant GCT survived, all belonging to stage I, while all patients in stage IV expired. The patients who survived are carefully followed clinically, by USG and by tumor marker.

Conclusion

The incidence of malignant ovarian tumors in young girls is significantly high, most being germ cell tumors and mortality is still very high as a considerable number of cases come in a very late stage in a poor general condition when they tolerate surgery or chemotherapy very poorly. Detection of these cases in stage I with prompt surgery and effective chemotherapy and proper follow up can reduce the mortality.

References

1. Scully RE, Young RH, Clement PB. Germ cell tumors: Tumors of the ovary maldeveloped gonads, fallopian tube and broad ligament. Washington DC: *Armed Forces Institute of Pathology, 1998; 239-66.*
2. Norris HJ, Jensen RD. Relative frequency of ovarian neoplasm in children and adolescents. *Cancer 1972; 30: 713-9.*
3. Berek JS, Hacker NF. Ovary and Fallopian tubes. In Haskell CM ed. Cancer treatment 4th ed. Philadelphia. *WB Saunders, 1995; 628-61.*
4. Oumachigui A, Narasimhan KL, Reddy KS et al. A clinicopathological study of ovarian tumors in children . *J Obstet Gynecol Ind 1991; 140: 441-5.*
5. Sawai MM, Sirsat MV. Ovarian neoplasm in children and adolescents. *Ind J Cancer 1973; 10: 302-11.*
6. Bren JL, Maxon WS. Ovarian tumors in children and adolescents. *Clin Obstet Gynecol 1977; 20: 607-23.*
7. Ehren IM, Mahour GH, Issacs H Jr. Benign and malignant ovarian tumors in children and adolescents : A review of 63 cases. *Am J Surg 1984; 147: 339-44.*
8. Gordon A, Lipton D, Woodruff JD. Dysgerminoma : a review of 58 cases from the Emil Novak Ovarian tumor Registry. *Obstet Gynecol 1981; 58: 497-504.*
9. Gershenson DM. Update on malignant ovarian germ cell tumor. *Cancer 1993; 71:1581-90.*