Malignant Germ Cell Ovarian Tumours-Six Years Experience At GCRI.

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Summary: 36 patients of malignant ovarian germ cell tumours were encountered for treatment at Gujarat Cancer & Research Institute from 1989 to 1994. Many patients were referred after primary surgery from outside or when recurrence developed. 29 patients were given chemotherapy. 10 patients underwent primary surgery at G.C.R.I. Fertility preservation was done in 4 cases.

Introduction

Germ cell ovarian tumours constitute about 15 to 20 percent of all primary ovarian neoplasms and are second only to epithelial tumours in frequency of occurrence. These tumours are highly virulent and rapidly growing. The younger the patient, the more common is the diagnosis of germ cell tumour and the greater the likelihood of malignancy. Because of recent improvement in chemotherapy, the outlook has changed.

The evolution of modern chemotherapy management for the treatment of ovarian germ cell malignancies has resulted in changing these most virulent malignancies into highly curable malignancies. In 1980's combination chemotherapy was given for non-dysgerminomatous tumours, but in 1990's we have started using combined chemotherapy, instead of radiotherapy in dysgerminomas as they are found to be very sensitive to chemotherapy and radiation castration is avoided.

Fertility preserving surgery is now an accepted mode of treatment for all young patients desirous of childbearing regardless of stage, unless of course the contralateral ovary and uterus is involved. This article reviews the overall experience of patients treated at Gujarat Cancer and Research Institute, Ahmedabad.

Material and Methods

From 1989 to 1994, 36 women with ovarian germ cell malignancies were encountered for treatment at GCRI. Most of the patients were referred after primary surgery at other hospital or after manifestation of recurrence and so the staging of the disease was not known in these cases.

The protocol of chemotherapy used was vinblastin, actimomycin, cyclophosphamide (VAC) in 5 cases, cisplatin, vinblastin, bleocin (PVB) in 5 cases, cisplatin, etoposide, bleomycin (PEB) in 14 cases and others in 5 cases (Table I). Radiotherapy was given in 2 cases. Tumours markers were estimated serially in most of the patients.

Table I

Chemotherapy Protocol	
Chemotherapy	No. Pt.
VAC	5
PVB	5
PEB	14
Others	5
Total	29

VAC = VINBLASTINE
A = ACTINOMYCIN
C = CYCLOPHOSPHAMIDE
P = CISPLATIN
B = BLEOMYCIN
E = ETOPOSIDE

Observations

12/36 patients were referred after primary surgery and 13 patients were referred for recurrence of the disease. After complete preoperative assessment, 10 patients had

undergone primary surgery at GCRI. The age distribution was from 9 years to 60 years. 25/36 patients were less than 25 years of age. 23 patients were menstruating normally before taking any treatment. 6 young girls were yet to start menarche. 2 patients were menopausal. 12 patients had completed their childbearing. The histopathology reports of the entire series are presented in Table II.

Table II

Histology	No	%
Endodermal Sinus Tmour	12	33.33
Dysgerminoma	13	36.11
Mixed Germ Cell Tumour	4	11.11
Immature Teratoma	6	16.66
Choriocarcinoma	1	2.77
Total	36	

12/36 cases, (33.3%) had endodermal sinus tumour. 13 (36.12%) had dysgerminoma. Mixed germ cell tumour in 4 cases (11.1%), Immature teratoma in 6 cases (16.6%), Choriocarcinoma in 1 case (2.7%). After complete preoperative assessment, 10 patients underwent primary surgery at GCRI. After generous vertical incision, methodical exploration and staging was done in 10 patients. All the abdominal organs, peritoneal surfaces and retroperitoneal nodal areas were inspected and palpated. Ascitic fluid or peritoneal washings for cytology were taken. Random biopsy from high risk and suspicious areas were taken. Once the staging procedures were completed and the tumour removed and if the patient had finished child bearing, complete surgery was done. Unilateral salpingo oophorectomy with omentectomy and lymph node dissection was done in 3 patients. Wedge biopsy of contralateral ovary was taken in 3 cases of opposite normal ovary in cases of dysgerminoma. In 6 patients total abdominal hysterectomy with bilateral salpingooophorectomy was done in cases where childbearing was completed.

Combination chemotherapy is the main modality of adjuvant therapy in most of our cases. 29 patients were given chemotherapy. The recently used CT protocol is BEP. Etoposide is used instead of vinblastine as peripheral neurotoxicity is very common with vinblastine and 'now a days etoposide is freely available. Approximately 4-6 courses are given. We prefer to give 1 to 2 courses after tumour markers turn negative. Serial measurements of tumour markers help in diagnosis, monitoring of treatment response and detection of subclinical recurrence. Serum alpha feto protein (AFP) is a very sensitive tumour marker for endodermal sinus tumour. (Fig. 1) (Fig. 2) All the 12 cases of EST were monitored with AFP. Serum βHCG was helpful in a case of choriocarcinoma. Serum Lacto Dehydrogenase (SLDH) is nowadays considered a sensitive tumour marker for dysgerminoma. We have also found it to be helpful in some cases. (Table III). Second look surgery has not been

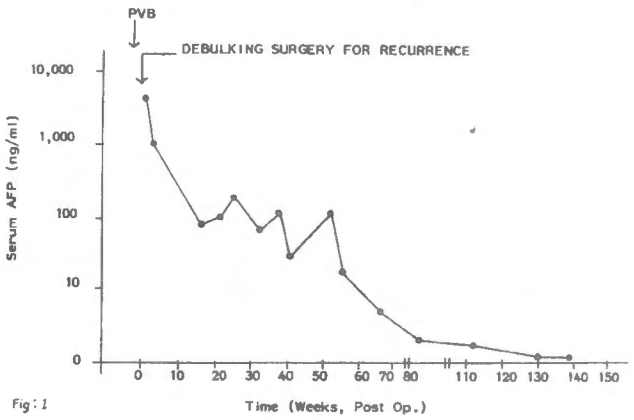

Fig: 1

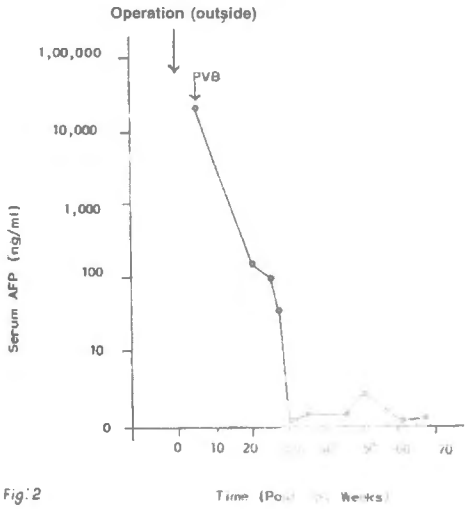

Fig: 2

routinely recommended since 1984. Patients who were clinically free of disease at completion of their planned program of chemotherapy, were followed with serum tumour markers assay and clinical examination.

Table III

Tumour markers	No of patients
AFP	12
β.HCG	1
S.LDH	6

Discussion

The malignant germ cell tumours of ovary are rapidly growing tumours and occur commonly in young girls. There are widely accepted criteria for preservation of fertility in malignant ovarian GCT.

Bakri & Giveri (1984) reported a case of normal pregnancy following conservative surgery for an endodermal sinus tumour & emphasized that this type of surgery should be confined to cases of stage IA disease only. Berek (1989) suggested that a unilateral salpingo-oophorectomy should be performed in a young patient whose lesion appears confined to a single ovary. According to the results of conservative surgery in the present series, fertility preservation was done in 4 patients treated at GCRI and all are menstruating regularly after taking treatment and one had full term delivery followed by completion of surgery. After thorough staging, cytoreductive surgery including omentectomy and RPLND is done to maximise effectiveness of adjuvant CT. Second look surgery was done in only 2 cases. One patient was found to be free of disease. One had viable growth.

Chemotherapy is the main modality of adjuvant therapy in most of the cases. 29 patients were given chemotherapy. The VAC regimen was initially given to treat endodermal sinus tumour, the most virulent germ cell ovarian tumour. The duration of VAC therapy was 6-12 months. VAC therapy was quite effective for all stage I germ cell malignancies. But due to initial VAC treatment failures and due to long duration of therapy, the CT protocol was changed to PVB and then to BEP therapy for all early and advanced malignant germ cell tumours.

Wiltshaw et al (1982) treated 8 patients with PVB and achieved CR in 7 patients. Gershanson et al (1985) achieved sustained CR in 7 out of 8 patients. 18/29 patients were given CT as adjuvant treatment after primary surgery and 11 for recurrence. Upto 1997, 15 patients are in sustained remission. Of these 15 cases, 6 patients had EST, 8 had dysgerminoma and 1 had a mixed germ cell type histology. (Table IV). 15 patients were lost to follow up. 6 patients died during treatment. 3 deaths were due to intercurrent disease, 2 were due to septicemia and 1 due to multiple lung secondaries.

Table IV

Histological type and outcome	
Sustained remission	15
Endodermal sinus tumour	6/12
Immature teratoma	0/6
Dysgerminoma	8/13
Mixed type	1 /4

Malignant ovarian germ cell tumours should be managed on the basis of tumour histology and the FIGO stage. But it was very difficult for us to know the proper stage of the patients as most of the patients are referred from outside after primary surgery, or when recurrence developed, so the staging was unknown in many patients.

Side effects of chemotherapy were acceptable. Common side effects were anaemia, vomiting, leucopenia, thrombocytopenia, nausea, fever, mucositis, alopecia and impaired renal functions. Alopecia was total almost in all cases. Other toxicities were grade I or II only. The currently available data shows that substituting Carboplatin for Cisplatin and Etoposide for Vinblastine reduces toxicity. Some centres use Cisplatin and Etoposide regimen and eliminate bleocin to reduce pulmonary toxicity. We did not see clinical or radiological

evidence of bleomycin toxicity in present study however routine pulmonary function studies were not done.

Approximately 3 to 4 courses were given in our study. We prefer to give 1 to 2 courses after negative tumour marker. Gershanson et al (1986) have used 4 to 6 cycles of PVB. In GOG study 4 cycles of PVB were given. Taylor et al (1985) used 3 to 4 cycles of PVB in 14 patients with achievement of CR in 13 patients (3 cycles in 6, 4 cycles in 6, 2 cycles in 1 patient.).

Upto June 1997, 15 patients with sustained remission have been followed up regularly. 15 patients were lost to follow up. 6 patients died during treatment. 4 deaths were due to intercurrent disease, 2 were due to septicemia and 1 due to multiple lung secondaries.

Gershenson et al (1986) reported a sustained remission rate of 70% in 66 patients, with malignant ovarian GCT treated primarily with the VAC protocol. In their series, 56% of patients had stage I disease and 30.3% had stage III disease. Pektasides et al (1987) reported for the first time a series of 21 cases of ovarian GCT with special reference to fertility after chemo treatment. Out of which 14 patients had regular menstruation & 5 became pregnant.

Pao chen wu et al (1991) reported a study of fertility preservation in 28 young pts. with malignant GCT. The protocol of chemotherapy treatment used was VAC in 10 cases, PVB in 3 and other regimes in the remaining cases. Persistent remission was achieved in 22 cases. The late effects of cytotoxic agents on babies born to mothers after CT have raised deep concern. A long term follow up study of the babies for any abnormalities in growth & development is yet to be carried out.

Conclusion

Fertility preserving surgery and combination chemotherapy is now the accepted mode of treatment regardless of stage. Availability of modern chemotherapy and tumour markers had changed the bleak outlook in these highly virulent tumours of young girls. Exploratory laparotomy with proper staging and debulking, followed by prompt aggressive chemotherapy gives the girls the best chance for cure when they are best treated at specialised centres.

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