A Clinical study of endodermal sinus tumour of the ovary.

A.C. Kataki • G.G. Ahmed
Dr. B. Borooah Cancer Institute, Gopinath Nagar, Guwahati-781016, Assam.

Summary: **Seven cases of endodermal sinus tumour of the ovary were seen at Dr. B. Borooah Cancer Institute, Guwahati from November, 1988 to July 1997. The age group varied from 8 to 20 years. All the patients had elevated serum AFP. One patient had mixed tumour with dysgerminomatous element. One patient who did not receive adjuvant chemotherapy recurred after 15 months. Six patients treated with BEP regimen were all free from disease (5,8,28,50,58 and 108 months) and are still undergoing follow-up. Menstrual functions returned to all 5 patients treated with chemotherapy with intact uterus.**

Introduction

Germ Cell tumours of ovary are rare, accounting for 2% to 3% of all ovarian cancers. Before modern combination chemotherapy, malignant embryonal carcinoma, endodermal sinus tumours, and malignant teratomas had extremely poor prognosis with surgery alone, and long term survival was achieved by only a small percentage of patients even with stage I disease (Woodruff et al 1968).

Endodermal sinus tumours are unusual and aggressive tumours of germ cell origin. They reproduce the extraembryonic structures of early embryo. The tumour is rarely bilateral. Before the use of combination chemotherapy, the tumour was almost invariably fatal.

Materials and Methods

This study was carried out at Dr. B. Borooah Cancer Institute, Guwahati from November, 1988 to July 1997. During this period, seven cases of endodermal sinus tumour of the ovary were recorded. Four cases had initial surgery outside and accurate staging was not known. In all the cases, serum alpha fetoprotein levels were estimated. Ultrasonography of whole abdomen and pelvis was done. Complete haematological and biochemical tests including liver and renal function tests were carried out. The patients were put on adjuvant chemotherapy with BEP (Bleomycin, Etoposide, Cisplatin) regimen. The dosage schedule was as follows: Bleomycin 15mg. I.V. on day 2,9 and 16. Etoposide (VP-16) 100 mg. per sq. mt. in dextrose-saline over 30 minutes daily for five days. Cisplatin 20 mg per sq.mt. of body surface in 200 cc of normal saline over 30 to 60 minutes daily for five days with adequate pre-treatment hydration and post treatment diuresis. The regimen was repeated at four weeks interval and continued for 2 more cycles after serum tumour marker levels returned to normal. Before each course of chemotherapy, patients underwent a complete blood count, platelet count, haemoglobin estimation and renal function tests along with tumour marker. Pulmonary functions were closely monitored in all patients and chest radiographs were obtained as indicated.

Patients were considered to be clinically assessable for response if, before chemotherapy began, they had a tumour mass detectable by physical examination or radiographic studies. A complete response was defined as complete disappearance of all palpable or radiographic evidence of disease for atleast one month.

After completion of chemotherapy, patients were evaluated at monthly interval for the 1st year and at gradually increasing intervals thereafter. At each visit, patients had a physical examination and serum tumour marker estimation and radiographic studies when appropriate.

Results and Observation

Out of 7 cases, presented to us, one patient with stage Ia disease did not take any form of adjuvant treatment due to financial difficulties, and reported back with intraabdominal recurrence and abdominal scar metastasis after 15 months of initial surgery at our institute.

In 3 cases where exact staging was known, 2 patients had stage Ia disease and 1 patient had stage IIIa disease. In all the cases, AFP (Alpha fetoprotein) levels were elevated. In 3 patients AFP returned to normal value after 2 courses of chemotherapy, in 2 patients after one course and in 1 patient after 4 courses of chemotherapy. All the 6 patients who completed treatment, achieved complete response varying from 5 months to 9 years (5,8,28,50,58,108 months). All the patients are still undergoing follow-up and are free from disease. Menstrual function returned to all the 5 patients with intact uterus who had completed treatment. One patient who achieved 9 years disease free survival obtained graduation and got married 6 years after completion of treatment.

Table I
Characteristics of the Patients

Characteristic	No. of Patients
All patients	7
Age (years)	
Median	12
Range	8-12
Type of surgery	
USO	3
USO + OT	3
TAH + BSo	1
Residual disease	
0	3
< 2cm	1
> 2 cm	3
No of courses of chemotherapy	
0	1
3	2
4	3
6	1

Abbreviations: USO/BSO - uni/bi/lateral salpingo-oophrectomy TAH, Total abdominal hysterectomy, OT, Omentectomy

Toxicities associated with the BEP regimen are very tolerable and were similar to other reports. Alopecia was universal.

Likewise, all patients experienced some degree of nausea and vomiting although these were considered severe (>48 hours duration) in only one patient. No significant Ototoxicity, neurotoxicity or nephrotoxicity occured in this small group of young patient population.

Discussion

Endodermal sinus tumour of the ovary is the 2nd most common ovarian malignant germ cell tumour in girls and young women (Norris & Jensen 1972). It represents 1% of all ovarian malignancies. The age range of patients is from 14 months to 45 years, but very few cases are reported in persons over 40 years. The median age is 19 years (Kurman & Norris 1976) or younger in some series. In our present small series the median age was 12 years with a range varying from 8 to 20 years.

The clinical presentation is frequently acute. Three fourth of patients have abdominal pain and nearly all have a large abdominal or pelvic mass. Symptoms are produced mainly by rupture, torsion or haemorrhage. AFP is the characteristic marker for endodermal sinus tumour, either primary or recurrent.

The tumour tends to be solid and large, ranging in size from 7 to 28cm (median - 15 cm) in the Gynecologic Oncology Group series (Slayton 1984, Creasman & Soper 1985, Gershenson et al 1986). The tumour is usually unilateral, large, solid, very soft, contains large and small cysts all throughout. Fourteen percent of endodermal sinus tumours co-exist with benign cystic teratoma in the same ovary, and 5% with it in the opposite ovary. One fifth of the endodermal sinus tumours contain admixtures

with one or more malignant germ cell elements, usually dysgerminoma. In our series, one patient had dysgerminomatous elements in the same tumour.

The Ovarian Tumour Registry of American Gynaecological Society reported that 31 of 34 patients with endodermal sinus tumours were dead of disease after surgery alone, and the 3 survivors had stage Ia disease (Jimerson & Woodneft 1977). Gallion et al (1979) reviewed the literature on 150 cases of endodermal sinus tumours. Before the use of chemotherapy, the overall 2 year survival rate for patients with stage I disease was 27%. Surgery alone was ineffective, producing a 16% 2 year survival rate.

After the introduction of VAC regimen (Vincristine, Actinomycin-D, Cyclophosphamide), the survival rate has improved to 60% to 70% (Rothenberg 1993, Cangir et al 1978). VBP (Vinblastine, Bleomycin, cisplatin) is a more effective regimen in the treatment of endodermal sinus tumour (EST), particularly in the treatment of measurable or incompletely resected tumour (Slayton et al 1985). A combination of Bleomycin, Etoposide, Cisplatin (BEP) by the Royal Marsden group (Smales & Pekhan 1987) has achieved encouraging results. Although no randomized trial exists comparing VAC with VBP or BEP, it is likely that the latter two regimens are preferred therapy for endodermal sinus tumours.

Charing Cross Hospital in London have developed the POMB-ACE regimen for high risk germ cell tumours (Newlands 1989) with a maximum of 9 years follow-up. This Charing Cross Group has seen no long term side effects in patients treated with POMB-ACE.

The optimal number of treatment cycles has not been established. The Gynaecologic Oncology Group (GOG) protocols have used 3 to 4 treatment cycles given every 4 weeks (Williams et al 1991, Williams et al 1989).

The policy followed at UCLA School of Medicine, Los Angeles is to give 3 cycles for patients with stage 1 and completely resected disease and two further cycles after negative tumour marker status for patients with macroscopic residual disease prior to chemotherapy.

Conclusion

Endodermal sinus tumour is a rare germ cell tumour of the ovary. Once a universally fatal tumour, can be cured completely with cisplatin based combination chemotherapy irrespective of the stage and residual disease status at the end of primary surgery and even recurrent disease.

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