CHORIO CARCINOMA

By

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SUMMARY

The gestational trophoblastic neoplasia is a rare disease. This has a crude incidence of 0.4/100,000 population and a frequency of 0.08% at the institute. We have treated 49 female patients (age range 17-45 years M 26) in the department of medical oncology, Cancer Institute, Madras over a period from 1970 to 1985. Eighty per cent patients were under 30 years of age. Antecedent history of vesicular mole, abortion, ectopic and full term pregnancy was present in 65.3%, 14.3%, 10.2% and 10.2% respectively. 'New England trophoblastic disease centre' staging revealed: stage O in 4.2%, I (16.3%), II (24.5%), III (34.7%) and IV in 20.4% cases. All patients received chemotherapy with either methotrexate alone or methotrexate and actinomycin D combination. Overall 65.3% patients achieved complete remission: Stage O 2/2 (100%) I 8/8 (100%), II 12/12 (100%), III 8/18 (44.4%) and stage IV in 2/9 (22.2%). We emphasize that all patients with vesicular more should be followed up with ßHCG estimation so that those with progressive disease can be treated early, failing which prognosis is poor.

Gestational trophoblastic neoplasia is a rare complication of conception occurring approximately 1 : 50,000 term pregnancies and 1 : 30 molar pregnancies (Bagshawe, 1969). The outlook for patient with gestational trophoblastic tumours has greatly improved over last two decades as a result of the introduction effective cytotoxic chemotherapeutic drugs (Newland, 1972), identification of high risk groups (Begent, 1982), sensitive HCG (Human Chorionic Gonadotropins) assay methods (Goldstein, 1978) and multi-modal approach in the management of this disease. After the initial demonstration of the effectiveness of methotrexate (Li *et al*, 1956) a number of drugs have been identified e.g. D-actinomycin, Chlorambucil, daunomycin, cisplatinum, etoposide (VP-16) and hydroxyurea etc. (Newland, 1982). With our present knowledge all the early stage cases can be cured of their disease while the majority (upto 80%) can be salvaged even with advanced disease (Stage III and IV) (Newland, 1982; Begent and Bagshawe, 1982). In this retrospective study we describe the results of treatment in patients treated between 1970-1985 at the Cancer Institute (WIA), Madras, India. This disease has a crude

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incidence of 0.4/10,000 population and a frequency of 0.08% at the institute.

Material and Methods

Forty nine patients with histologically proven gestational trophoblastic neoplasia (GTN) were treated in the Dept. of Medical Oncology between 1970 tc 1985. Initial valuation of each patient included—a history, detailed physical examination, haemogram, urine, renal and liver function tests and radiogram of chest. Serum and urine HCG were done periodically. Ultrasound pelvis and abdomen, computerised axial tomography of brain and CSF examination were done as and when necessary. 25 patients had pulmonary metastasis on presentation, bilateral and multiple in 21, and unilateral (1-3) in 4 patients. Radiologically these were defined as either coin shaped or snow storm appearance and miliary pattern. Liver metastasis seen in 7 patients were evidenced by enlarged tender liver, raise alkaline phosphatase, radionuclide or ultrasound scan. Metastases to CNS (3) and bone (2) were also seen.

Schedules of chemotherapy used were

I — Inj. Methotrexate 25 mg I V day 1-4 q 2 weeks.

II — Inj. Methotrexate 25 mg I V day 1-4.
Inj. Actinomycin — D 500 μg I V day 1-4 q 2 weeks.

Assessment

During the treatment blood counts were done daily and liver, renal function tests were measured twice a week. Serum and urine HCG were done either weekly or prior to each course.

Complete response was defined as complete disappearance of the lesion clinically and radiologically with return of the Beta-HCG values to normal. Chemotherapy was continued till 3 consecutive normal values of Beta HCG were achieved. Whenever there was evidence of relapse/resistance as suggested by plateau or progressive increase in the values of ß-HCG, patients were put on the combination CT (Schedule II) or alternative chemotherapy.

Results

Eighty per cent patients were under the age of 30 years (age range 17-45, median 26). Majority (65.3%) were multigravidas. Antecedent history of vesicular mole, abortion, full term, and ectopic pregnancy was present in 65.3% 14.3%, 10.2% and 10.2% cases respectively (Table I). Histological subtypes and staging (Goldstein and Berkowitz, 1976) are shown in Table II and III. Overall (65.3%) patients achieved complete remission—Stage 0 2/2 (100%), I 8/8 (100%), II 12/12 (100%), III 8/18 (44.4%) and stage IV 2/9 (22.2%).

TABLE I
Risk Factors

	No. of patients	%
Vesicular Mole	32	65.3
Abortion	7	14.28
Ectopic pregnancy	5	10.20
Full term pregnancy	5	10.20

TABLE II
Histology Subtypes

Histology	No. of patients	%
Choriocarcinoma	38	77.55
Chorioadenoma destruens	9	18.36
Vesicular mole	2	4.08
	49	100.00

TABLE III
New England Trophoblastic Disease Centre Staging

Stage	No. of patients	%
0 Molar pregnancy		
(a) Low risk	0	
(b) High risk	2	4.08
I	8	16.32
II	12	24.48
III	18	34.69
IV	9	20.40

TABLE IV
Results of Treatment

Stage	No. of patients	N.E.D. %
0	2	2/2 (100)
I	8	8/8 (100)
II	12	12/12 (100)
III	18	8/18 (44.4)
IV	9	2/9 (22.20)
	49	32 (65.30)

N.E.D.—No evidence of disease (3-18 years follow up).

Patients were followed up with monthly clinical examination, urine and serum HCG and chest X-ray during first year thereafter every three months. Contraception was advised during the first year. Three patients cured of their disease, had conceived normal children.

Toxicitiy

The most common toxicities encountered were: mucositis with methotrexate alone; nausea, vomiting and oral mucositis with methotrexate and 4 actinomycine combination. Mild to moderate myelosuppression was seen in 13 (27.1%) patients receiving combination CT. One patient developed bilateral pulmonary miliary tuberculosis while on CT. She recovered completely wih anti tubercular treatment.

Discussion

Gestational trophoblastic neoplasia represents a broad biological spectrum ranging from benign vesicular mole to locally aggressive choriocarcinoma destruens and to a highly malignant choriocarcinoma. Upto 26% of vesicular moles may develop into secondary trophoblastic disease (Morrow *et al*, 1977). This figure is more relevant in a country like India where incidence of vesicular mole is high (1 : 160-1 : 400) as compared to western countries (1 : 2500) (Pai, 1967). Antecedent history of vesicular mole in 2/3rd of our cases confirms above fact. Further choriocarcinoma affects young females (below 30 years) as seen in this study (80%). Multigravidity and multiparity in these probably reflects high fertility rate in our Population.

In our experience lung, liver and brain remain the most frequent sites of metastases occurring in 51%, 14.2% and 8.1% cases respectively. Presence of bilateral lung metastases in all four patients with CNS involvement possibly reflects high risk of CNS disease in patients with bilateral, multiple pulmonary metastasis.

Overall 32 (65.3%) patients achieved complete remission with chemotherapy: 20 of these (62.5%) had undergone surgery earlier in the form of hysterectomy (2) elsewhere prior to admission to this hospital. Chemotherapy was advised either due to presence of metastatic disease or high risk factors (2).

All the patients in early stage (0, I, II) achieved complete response and are cured. Therefore all the patients with vesicular mole should be followed up with serial HCG estimations (Morrow *et al*,

1977; Lurian *et al*, 1983) and with earliest evidence of progressive disease, should be treated when tumour volume is minimal and the probability of cure is high and risk of drug resistance is minimal.

Poor response 44% and 22% in advanced stage reflects increased tumour bulk, decreased chemosensitivity and possibly presence of drug resistance. This reiterates the need for an aggressive approach with multidrug chemotherapy protocols to improve outlook in such cases. Once CNS is involved, prognosis is generally poor (0/4). The need for CNS prophylaxis in such high risk group (Bilateral multiple-pulmonary metastases) with cranial irradiation and intrathecal methotrexate (Athanassiou *et al*, 1983) has to be considered.

Three of our patients have conceived normal children. There is ample evidence now to show that there is no increase in congenital anomalies in pregnancies following methotrexate treatment. However, contraception should be advised for a period of one year (Ross, 1976).

Choriocarcinoma is an excellent solid tumour model depicting curative potential of chemotherapy but the reasons for this unique responsiveness are not clear. Unravelling this unique feature of choriocarcinoma will provide insights into understanding the response or resistance of these tumours to chemotherapy.

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