PREGNANCIES FOLLOWING METHOTREXATE TREATED CHORIOCARCINOMA

(A Case Report)

by

INDU TANDON,* M.D., D.G.O.

and

V. L. BHRGAVA,** M.B.,B.S., M.D.

Introduction

The use of chemotherapy in the treatment of gestational trophoblastic tumour since 1956 has resulted in an increased number of long term survivors. As these chemotherapeutic agents leave the reproductive organs intact and functional, cases of pregnancy following treatment of cheriocarcinoma have appeared in the literature. One such young patient is reported here who had 3 pregnancies following treatment of choriocarcinoma with methotrexate.

CASE REPORT

Veena, 15 years old, P° + 1 was first seen at the Gynaecology Out Patients' Department of the A.I.I.M.S. Hospital, New Delhi on 13th January 1973. She gave history of irregular bleeditng per vaginum since her abortion on 26th November 1972. Prior to this, her last normal menstrual period was on 18th August 1972. After three months ammenorrhoea, she started bleeding per vaginum and a curettage was done by a private practitioner at Bombay. No record was available regarding the nature of the abortus. Fifteen days later, she started bleeding again. She came to Delhi and a repeat curettage was done at another Delhi Hospital on 18th December 1972. Bleeding recurred after three weeks. She again reported to the same hospital where she was given the histopathological report and advised to attend the A.I.I.M.S. Hospital for further management. The report read "Hypertrophic Chorionic Villi with markedly proliferative sheets of ? hypertrophic tissue."

Menstrual History: Menarche 12 years, Cycles 4-5/28-30 days, flow moderate.

Examination: General physical and systemic examinations were essentially normal. Speculum examination showed a healthy vagina with a small erosion on the posterior lip of the cervix. Vaginal examination revealed cervix pointing forwards, uterus retroverted and normal in size. Left ovary was palpable 3 cm x 2 cm. Slight pinkish discharge was present on examining finger.

Investigations: Haemogram, urine, blood urea and sugar and x-ray chest were normal. Endometrial aspirate was reported unsatisfactory. She was put on haematinics and observed for a few days. Curettage was done under general anaesthesia on 20th January 1973. Uterine cavity was 3" long and smooth. Currettings were profuse. Histopathological report was "The tissue submitted shows gestation pedicle with trophoblastic cells which appear anaplastic. No chorionic villi seen. Chorionic carcinoma cannot be excluded." In view of the previous and the later histopathological reports at an interval of 5 weeks where the hypertrophic chorionic villi had changed into anaplastic cells a diagnosis of choriocarcinoma was made. It was decided to treat her with methotrexate.

Treatment: She was given five courses of methotrexate as shown in Table I. Blood counts renal and hepatic functions were closely ob-

*Ex-Senior Resident.

**Assistant Professor.

Department of Obstetrics and Gynaecology.

All India Institute of Medical Sciences, New Delhi-110016.

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TABLE I

	Methotrexate			Pregnancy Test		HCG Level	
Course	Date	Dose	Total	Date	Result	Date	Result
1.	3-2-73 to 8-2-73	5 mg. QID x 5	100 mg.	31-1-13 to 4-2-73	—ve —ve	—	—
2.	24-2.73 to 28-2-73	5 mg. QID x 5	100 mg.	24-2-73 to 12-3-73	+ve +ve	—	—
3.	24-3-73 to 29-3-73	5 mg. QID x 6	125 mg.	23-3-73	+ve	—	—
4.	22-10-73 to 26-10-73	15 mg. I.V. O.D. x 5	75 mg.	—	—	28-9-73	3000 I.U.
5.	8-11-73 to 15-11-73	15 ng. I.V. x 5	75 mg.	—	—	31-11-73 10-2-74	—ve —ve

served. She was admitted to the hospital for administration of each course. Pregnancy tests or serum HCG by immunoassay (whichever available) were done before and after each course.

The side effects of methotrexate were stomatitis and pain in the eyeball. These were treated symptomatically. She resumed normal periods soon after. Repeat currettage was done under general anaesthesia on 28th August 1973 and only small amount of normal looking currettings were obtained. X-ray chest were done periodically and were normal. She was put on oral contraceptive after the HCG levels had become negative.

Successive Pregnancies: In April 1975, she reported with 10 weeks amenorrhoea and pregnancy was confirmed. Pregnancy was uneventful and she had a full term normal delivery in December 1975. The male baby was healthy with no congenital anomalies. He has had normal milestones and is growing normally.

In March 1976, she attended the hospital with one and a half months amenorrhoea and was found to be pregnant. She developed hypertension at the end of first trimester and had spontaneous abortion followed by evacuation in the hospital. The expelled products did not show any vesicular degeneration.

She conceived again in March 1977 but reported to the hospital only at 32 weeks gestation with history of antepartum haemorrhage. On examination there was no sign of toxaemia and pregnancy was normal. She delivered normally in November 1977. This child is also growing normally so far.

Discussion

Though choriocarcinoma can occur at any age it is uncommon to find it in women under 20 years of age. Radha et al (1974) in a statistical analysis of choriocarcinoma found only 4% of cases occurring in women below 19 years of age. Although the treatment of choriocarcinoma with chemotherapeutic agents is well established now, its early diagnosis still remains a problem. Ultimate prognosis of the patients depend also on the time interval between onset of symptoms and advent of therapy (Hertz, 1967; Baggish, 1974). In this respect this patient also posed a problem but the clinical picture alongwith histopathological findings helped in the diagnosis and early treatment with methotrexate could be instituted. HCG titre is the most valuable guide in the therapy, but short of it one has to depend on the traditional pregnancy test eventhough it is less reliable.

More interesting however are the next

pregnancies. The interval between treatment and successive pregnancy is very important and essential. Early pregnancy may pose problem in differentiating it from a recurrence. An interesting case is reported by Freedman *et al* (1962) where a twin pregnancy was mistaken for recurrence of choriocarcinoma because of high HCG titres and treated with chemotherapy. There is increasing evidence from animal studies that methotrexate has deleterious effect on developing ova and chromosomal aberrations can be induced by it (Rohrborn and Hansmann, 1971). Therefore, enforced period of contraception can also ensure wastage of these defective ova and prevent birth of malformed child. Other safeguard against producing such malformations would be preimplantation egg loss and early abortions. Ross *et al* (1967) also found a high incidence of early abortion and stillbirths in a group of women treated with chemotherapy for choriocarcinoma. Walden and Bagshawe (1976) in a study on reproductive performance of women having gestational trophoblastic tumour found that their obstetrical history tends to be poor, though not significantly worsened by treatment. They found a live-birth rate of 70% in the treated group as compared with 87.5% in the control group. They also reported a higher incidence of malformations, P.E.T., placenta praevia, PPH and LSCS. Malformations included various neural tube defects and umbilical hernia. There was also a case of desquamating fibrosis alveolitis in an infant born to a mother who had conceived within six months of therapy. Vanthiel *et al* (1970) on the other hand found no increase in foetal wastage and malformations and suggested that these drugs do not damage the human cocyte in the doses used. He did not exclude the possibility that recessive mutations may occur and remain undetected. Long-term follow up of the offsprings of women treated with chemotherapy would be required to settle the issue finally.

Other important question that may arise in the mind of the patient as well as the obstetrician is whether the disease can recur during or following next pregnancies. Though hydatidiform mole is known to recur in successive pregnancies (Endress, 1961), there are no such reports with choriocarcinoma so far.

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