PREGNANCY FOLLOWING METHOTREXATE THERAPY FOR CHORIONEPITHELIOMA

(A Case Report)

by

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Hysterectomy is recognised as an optimum basic treatment for choriocarcinoma. However, with the advent of chemotherapy, hysterectomy may be withheld in nulliparous women with chorio adenoma destruens or with invasive mole and in those who may be unfit to withstand surgery.

Thus, there emerges a new group of patients who have been successfully treated for chorionepithelioma with chemotherapy (Kutty and Nalini 1969). There have been several reports of normal pregnancy following the use of methotrexate in the treatment of metastatic chorionic malignancy.

However, in the absence of the uterus or the endometrial scrapings which could be studied histologically the diagnosis necessarily depends upon (1) The clinical behaviour of the disease, (2) the nature of metastases and (3) the pattern of the chorionic gonadotrophin titre.

It is clear that cases which have similar features may have widely different histological pictures if the hysterectomy specimen is examined, varying from a relatively benign metastatic mole to chorio adénoma destruens with metastatic lesions (Mitra and Dutta 1968).

Case Report:

Mrs. P., was admitted into the the Government General Hospital, Kakinada, on 10-5-'69 with the complaint of severe pain in the lower abdomen, vomiting and two months' amenorrhoea.

Previously she was admitted into the hospital on 1-12-'68 for four months amenorrhoea and profuse vaginal bleeding. A vesicular mole was evacuated on the same day. A curettage was performed on 6-12-'68 and the report was, "Organised and infected blood clots. Endometrium in proliferative phase." In February 1969 she had a normal menstrual period. The urine was examined for Frog test and was found to be negative.

Two months later she developed pain in both the lumbar regions, severe pain in the lower abdomen, loss of appetite and loss of weight.

Gynaecological History: Menarche was at the 12th year. Her cycles were previously regular 3-4/30 days, moderate flow, and painless. She had no menstruation after 4-2-69.

Obstetric History: She had three F. T. N. D., last 9 years of age. One abortion of 5 months and the last was a vesicular mole evacuated. Her married life was 16 years.

General Condition: At the time of admission on 10-5-'69 the patient was toxic and grossly anaemic. The tongue was dry and coated. The pulse rate was 100 per minute. The blood pressure was 60/20 mm. of Hg. The temperature was 37° C.

Abdominal Examination: The abdomen distended. Tenderness was present in the left iliac fossa. Peristaltic sounds were heard.

Bimanual Examination: Uterus was anteverted, of normal size, and mobile, fornices were clear.

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On speculum Examination: no secondaries were found in the cervix or in the vagina. She was treated with intravenous fluids, Inj. Streptopenicillin and supportive therapy.

On 11-5-'69 the blood pressure was 120/70. The temperature was 38°C and the pulse rate 120/mm. On 14-5-'69: P. A. View of the chest showed bilateral pulmonary matastases which were massive. (Fig. I).

On 23-5-'69 a bimanual examination revealed a nodule 2 inches in diameter on the anterior aspect of the uterus. The uterus was bulky. The cervix and the vagina revealed no secondaries.

The blood counts were as follows: Red blood cell-3.2 millions/c.mm. Haemoglobin-60% and white blood cell count was 8,650/c.mm.

She had a blood transfusion on 27-5-'69. On the same day she had haemoptysis. On 30-5-'69 her urine was sent for Frog Test and it was positive.

On 31-5-'69—She was started on Methotrexate therapy—about 2.4 milligrams/Kilogram for each course. It was given orally as 2.5 mg. tablets. Two tablets were given thrice a day (15 milligrams/day for 5 days.

Every day, the total white blood cell count, the differential count, the haemoglobin percentage, the red blood cell count, the liver function tests, the bleeding time and the coagulation time were done. The weight of the patient was recorded every day (chart I). She was given two courses of Methotrexate of 75 milligrams each. After each course there was a steep fall of the total white blood cell count as well as of the polymorphonuclear cells and the patient suffered from stomatitis, vomiting, distension of the abdomen and diarrhoea. After each course she was given one to two units of 'O' group blood to bring the blood counts to normal.

After each course of methotrexate there was a rapid thinning of the pulmonary metastases until they disappeared one month after the second course. (Fig. II and III). The Frog test became negative and the nodule on the anterior wall of the uterus was not palpable by the end of the second course.

The urine was tested for Frog test and a check P.A. view of the chest was taken on 26-7-'69. The frog test was negative. (Fig. IV). She was discharged on 25-9-'69 and advised to avoid pregnancy and to come once a month. She was checked up every month with negative results until December '69. (Fig. V). When the lung secondaries also cleared completely.

She attended again in May 1970 with a history of 4 months' amenorrhoea. On examination, the uterus was found to be about 26 weeks size. Diagnosis of twins was suspected and at the seventh month of pregnancy a postero-anterior view of the abdomen was taken. It confirmed the diagnosis of twins. She was advised admission but she refused.

She delivered two live premature female children at the eighth month at home. On 8-9-'70 One died on the ninth day and the other on the twenty-first day. She had continuous slight vaginal bleeding for one month after the delivery.

She attended again on 5-2-'71 for mild salpingitis.

A bimanual examination revealed no abnormality or any evidence of secondaries. A postero-anterior view of the chest revealed no secondaries. The urine was negative for Frog test.

Discussion

Freidman, Morgagnini and Glass in 1962 reported a case of choriocarcinoma successfully treated by Folic acid antagonists with two subsequent normal pregnancies. After the treatment of choriocarcinoma, the patient became pregnant. The pregnancy rise of chorionic gonadotropin titre was mistaken to be due to a recurrence of the growth and two courses of methotrexate, one course of chlorambucil given from the sixteenth week to the 24th week. Subsequently the pregnancy was diagnosed to be one of the twins. She was delivered spontaneously of two premature living infants who were normal. During the subsequent year she was delivered of a normal living female infant.

Hertz, Ross, and Lippsett (1963) reported that full term normal pregnancies occurred in three of 16 patients treated

CHART I

1st Course of Methotrexate

From 1-6-1969 to 5-6-1969

Date	Symptoms	Weight	T. C.	D.C.	Hb%	Bleeding time	Clotting time	Blood Urea	L.F.T.
1/6/69	Chest Pain;	34 Kg.	6.350 cell/c.mm.	P. 22 L. 72 E. 6	45 per cent	1 Min. 5 sec.	2 min. 20 sec.		
2/6	Cough with Haemoptysis streak of blood	—	5750/c.mm.	P. 34 L. 64 E. 2	45 per cent	1 Min. 5 sec.	2 min. 20 sec.		
3/6	Pain in the lower abdomen and Nausea	33 Kg.	5700/c.mm.	P. 40 L. 55 E. 5	45 per cent	1 Min. 5 sec.	2 min. 20 sec.	25 mg.	Vendenbergh negative T.T.t. 3 units Z.S.T. 14 units
4/6	Pain in the lower abdomen, cough Heart, Lung N.A.D.	34 Kg.	—	—	—	—	—	—	
5/6	Cough	34 Kg.	2900/c.mm.	P. 77 L. 19 E. 4	43 per cent	1 Min. 10 sec.	2 min. 25 sec.		
			IInd Course of Methotrexate from 8-7-1969 *to* 13-7-1969						
8/7	No Cough	33 Kg.				2 minutes	3½ minutes		
9/7	—	33 Kg.	7350/c.mm.	—	45 per cent				
10/7		34 Kg.	8200/c.mm.	—	45 per cent				
11/7	Pain in lower abdomen. Nausea	32 Kg.	5620/c.mm.		40 per cent				
12/7	Patient is having dysentery	33 Kg.	6300/c.mm.	P. 58 L. 38 E. 4	40 per cent	45 sec.	3 minutes 10 sec.		
13/7	Dysentery present	31 Kg.	3600/c.mm.						

with methotrexate for non-metastatic trophoblastic disease. These were all evacuated vesicular moles following which the chorionic gonadotrophin titre remained elevated from 1 to 6 months.

Dumoulin and Bakshawe (1963) presented a case report where the patient had been treated after evacuation of a mole with 6 mercaptopurine and six courses of a combination of methotrexate and mercaptopurine. The curettings showed anaplastic trophoblast but villous pattern was visible. An X-ray of the chest was normal but the electrocardiogram showed abnormality suggestive of pulmonary embolism. She conceived after 9 months and was delivered of a healthy male child by an elective caesarean section.

In Bagshawe's series of 12 patients treated by chemotherapy, 4 in addition to the above, became pregnant.

Conclusion

In cases of chorionepithelioma, hysterectomy has the advantage that the source of the tumour emboli is removed and it should be chosen in women who have sufficient number of children and those who are over forty.

Chemotherapy offers an alternative in younger women with the advantage of preserving the child bearing function.

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See Figs. on Art Paper IV-V