CHEMOTHERAPY IN TROPHOBLASTIC TUMOURS

Reviewed by

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EXPERIENCES WITH CHEMOTHERAPY IN TROPHOBLASTIC TUMOURS—REPORT OF TWO CASES OF PREGNANCY FOLLOWING CHORIOCARCINOMA

by

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The treatment of Choriocarcinoma hitherto has been hysterectomy. Advent of chemotherapy has modified the prognosis and treatment of this disease.

Dr. Mukherjee reported two cases treated by chemotherapy and in whom subsequent successful pregnancy was achieved.

Case report

Case 1. K. N. 18: Primigravida was admitted at General Hospital, Pondicherry, on 9/2/65 with bleeding for 3 days following evacuation of a molar pregnancy seven weeks ago. Her menstrual history was regular. Her last menstrual period was 7/10/64 and molar pregnancy was evacuated about the middle of December 1964.

She was a well nourished woman and was not anaemic. Pelvic examination revealed an anteverted, bulky uterus. Fornices were clear. Speculum examination revealed a haemorrhagic friable growth from anterior lip of the cervix. Biopsy of this growth came as choriocarcinoma. Her haemoglobin was 10.0 gm%. Male toad test of urine was positive 1 in 200. X-ray chest showed no secondaries. A week later dilatation and curettage was done. Uterus was moderately and bulky. The report was proliferative endometrium. The growth from the cervix was excised at the same time. The report was choriocarcinoma.

Patient had 3 courses of Methotrexate orally. The dose was 5 mg 4 hourly for 5 days. Subsequent courses were repeated after an interval of 10 days. She had mild toxic symptoms. The frog test was positive for three weeks after the commencement of the treatment and thereafter it became negative. In January 1966, she attended the antenatal clinic with 4 months' amenorrhoea. Pregnancy and labour were uneventful. She delivered a healthy female child weighing 2700 Gms on 2/7/66. Mother and child were discharged in good condition.

Case 2.: P. M., aged 17 years, primigravida, was admitted in Maternity Hospital, Pondicherry, on 15/4/65 with 4 months' amenorrhoea, bleeding and abdominal pain for 10 days. She was anaemic. Uterus was

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A HOPEFUL OUTLOOK FOR TROPHOBLASTIC GROWTHS

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24 weeks' size and slightly tender. Foetal heart sounds were absent. A provisional diagnosis of vesicular mole was made. The bleeding continued and urine showed albumin. Male toad test was positive in one in 200 dilution, X-ray abdomen showed no foetal parts. A molar pregnancy was evacuated under general anaesthesia and she had 2 pints of blood. Histological examination revealed a necrotic degenerating mole with trophoblastic activity. Bleeding continued and so a dilatation and curettage was done on 19/5/65 and the report was choriocarcinoma. The frog test was positive on the 6th, 19th and 24th day of molar evacuation. Patient had 3 courses of Methotrexate orally. The patient was discharged on 2/7/65. She did not attend the follow-up clinic. On 20/4/67 she attended the antenatal clinic at the Medical College, Pondicherry, with 7 months amenorrhoea. Her general examination, B.P. and urine were normal. Uterus was 28 week size and foetal heart sounds were present. On 27/7/67 she delivered a healthy, male boy weighing 2560 gms. The placenta which was adherent was removed manually and histologically was found to be normal. Mother and child were discharged in good condition.

The accumulating evidence on the effectiveness of Methotrexate in choriocarcinoma suggests that the role of hysterectomy in the treatment deserves reconsideration. It may be remembered that successful pregnancy is no proof of cure or safeguard against subsequent malignancy.

The number of patients potentially capable of future pregnancies following chemotherapy in trophoblastic tumours are increasing.

Paranjothy reviewed 58 cases of choriocarcinoma and 17 cases of malignant mole, all treated at Christian Medical College and Hospital, Vellore, South India. A comparative study between the two has revealed some interesting facts. The average age for choriocarcinoma was 28 years and for malignant mole 27 years. In both, 75% of the cases occurred below 30 years of age. 75.8% in both the groups were gravida 3 and over.

Symptomatology

Bleeding was the main symptom in both and was present in over 90% of cases. Anaemia emaciation, debility, cough and breathlessness were the next group of important symptoms and were common to both. There were however few differences, Haemoptysis was present in 23% of malignant moles as against 7% in choriocarcinoma. Severe toxaemia with raised blood urea was present in 18% of malignant moles as against nil in choriocarcinoma. Massive haemothorax needing repeated aspirations occurred in 11.7%, in malignant moles as against nil in choriocarcinoma.

Treatment

We do hysterectomy in all cases with few exceptions. This is followed by chemotherapy a week after surgery. Hysterectomy includes removal of ovaries however young the patient may be. This attitude is taken, as one of our patients in whom one ovary was left behind at the time of hysterectomy came to us 12½ years later with secondaries in the pelvis and succumbed to the disease (before the advent of chemotherapy).

We withhold or postpone surgery in presence of extensive lung metastasis and in very young patients. We treat them with Methotrexate only.

The drug of choice in our series is Methotrexate. We give Methotrexate orally in divided doses. Total dose per course varies from 60-120 mg. Total number of courses varies from 1-11. Toxic symptoms are very severe in our patients. When the patients become resistant to Methotrexate, we have tried 6 mercaptopurine and chlorambucil along with

Methotrexate. Our results in Methotrexate resistant cases are very poor. We have not tried combination of drugs from the start to reduce drug resistance.

Results of therapy in choriocarcinoma

With surgery alone survival was 0.0%. With surgery and Methotrexate, we had complete remission in 48.2%, partial remission in 44.4% and no response in 7.4%. The longest survival in our series is 7 years.

Results of therapy in malignant mole

With surgery alone, survival was 100.0%. With surgery and Methotrexate, we had complete remission in 100.0% of cases.

Although there is similarity in age, parity and symptomatology with few exceptions between choriocarcinoma and malignant mole, we see significant difference between the two in mortality and in response to Methotrexate. The exact relationship between the two is yet to be defined. We do not know if all or only some of the malignant moles progress to choriocarcinoma and if so at what interval.

Prophylactic use of Methotrexate in molar pregnancy

We have started to give Methotrexate prophylactically in the following groups: (a) Age over 40. (b) Gravidity over 3. (c) When mole is associated with large lutein cysts. We aim at giving 3 courses of Methotrexate, but in some cases due to severe toxic symptoms, further courses had to be abandoned.