

SOME SPECIAL ASPECTS OF MALIGNANT TROPHOBLASTIC DISEASE

(Review of 4 Cases)

by

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Introduction

Malignant trophoblastic diseases often vary in their modes of clinical manifestations. While the diagnostic criteria are sometimes confusing, course of the disease and as such results of treatment are almost always unpredictable. Four cases of trophoblastic diseases presented here were considered worth reporting because in 2 of them the presenting features were not classical and in the other 2 the course of the disease had different outcome. These cases were admitted in the department of Obstetrics and Gynaecology, N. R. S. Medical College and Hospital, Calcutta, during the period from 1971 to 1973.

Case 1

Mrs. S. G., 35 years, P1+0 had her first delivery by lower segment caesarean section on 3rd August, 1972 in an outside hospital. She had a sudden bout of postpartum haemorrhage on the 25th postoperative day and this was followed by two further bouts at weekly interval. Each time she had to be resuscitated by blood transfusion. Endometrial biopsy performed on 20.9.72 showed atypical proliferation of

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chorionic epithelium suggestive of malignancy (Fig. 1). However, biological male toad test of urine was negative. The patient was given Methotrexate (5 mgm. T.D.S. for 5 days) for two courses at four weeks' interval. This controlled the vaginal bleeding and she was discharged from hospital on 19.11.72 after a chest X-Ray which showed no abnormality.

The patient was re-admitted on 8.1.73 with severe vaginal bleeding. Emergency hysterectomy with bilateral salpingo-oophorectomy was performed on the same day. The size of the uterus was normal. The cavity of the uterus, on opening up, showed a small haemorrhagic nodule (appearing like granulation tissue) on the right end of lower segment scar. Both ovaries looked normal. Histopathological examination of the uterus at the site of the nodule revealed evidence of chorioadenoma destruens (Fig. 2). She made an uneventful recovery and was discharged from hospital on 19.1.73. She is well and free from the disease since then.

Case 2

Mrs. C. M., 18 years, PO+1, had vaginal evacuation of a hydatidiform mole on 18.11.71. Her first urine examination done two weeks after evacuation of mole was positive but after one month it became negative. Uterine curettage performed on 30.11.71 showed no evidence of chorionic tissue. In February, 1972 she had irregular intermenstrual spotting for which she was admitted to the hospital. Immunochemical test for urinary gonadotrophins in the urine was strongly positive. The uterus on bimanual examination, appeared normal in size without any other detectable pelvic pathology. Her chest X-Ray was normal and second uterine

curettage performed on 19.2.72 showed no evidence of chorionic tissue. She received two courses of Methotrexate (15 mgm. daily in divided doses for 5 days, each course) following which, she was symptom free and urine was negative. She was alright since then but on routine check up in December, 1972 biological test of urine was found to be strongly positive. She was menstruating regularly though the flow was scanty. Bimanual pelvic examination revealed a normal sized uterus without any pelvic mass. Possibility of normal uterine pregnancy was excluded by another pelvic examination, a month later. Third uterine curettage was done on 20.1.73. It failed to reveal any trophoblastic tissue. She was put on Methotrexate for 3 courses in the same dose as before. While on Methotrexate, immunochemical tests of urine were either negative or weakly positive. But, since then she complained of amenorrhoea and as soon as methotrexate treatment was discontinued her urine showed presence of persistently high titre of chorionic gonadotrophins. She was admitted again on 19th November, 1972. Exploratory laparotomy was done on 9.6.73 with a view to obtain biopsy from uterine myometrium. On laparotomy, the uterus was found smaller than normal in size. The ovaries apparently looked healthy. There were two bluish cysts on the fallopian tubes, one on each side. The cysts were on the serous coat and could easily be enucleated. These measured about half inch in diameter. Uterine cavity was opened and cut surface of the myometrium looked apparently healthy. There was no growth in the cavity. A small piece of the myometrium was excised which was sent for histopathological examination. Abdomen was closed in layers. Histopathological examination showed decidua like changes in the wall of the cysts without any evidence of chorionic tissue. Biopsy from the uterus revealed no abnormality. She made an uneventful recovery and was discharged from the hospital on 21-6-73. At the time of discharge her urine was negative. She was being followed up since then with periodic check-up of urine and radiological examination of chest. Her urine showed positive pregnancy test twice and it became negative with cytotoxic drugs. Radiological examination of chest never revealed any abnormality. On 27.12.72 at about 11 P.M. she

had sudden severe bout of haemoptysis and she expired next morning at 8 A.M.

Case 3

Mrs. N. M., 30 years P5+O had a molar pregnancy which was evacuated vaginally in October, 1972. Uterine curettage done at that time showed hydatidiform mole of dark syncytial mass suggesting secondary change in the mole. She was discharged from hospital with the advice of Tab. Methotrexate (5 mgm thrice daily for 5 days for 2 courses). During the next four months she suffered from irregular vaginal bleeding and was re-admitted in January, 1973. On examination, she was found to be anaemic, the uterus was enlarged to the size of 10-12 weeks pregnancy. Pelvis was otherwise free. Biological male toad test of urine was positive. Five days after her admission, she was operated upon and total hysterectomy with bilateral salpingo-oophorectomy was done. Hysterectomy specimen showed uterus enlarged to about 10-12 weeks' size. Both ovaries were cystic measuring about 2" in diameter. The cavity of the uterus contained a homogenous haemorrhagic mass. Histopathologically, the uterine specimen showed chorioadenoma destruens with prominent atypism of cells. In both ovaries multiple lutein cysts were noticed. Her postoperative period was uneventful and was discharged from hospital. She was re-examined after six months and was found well and clinically free from the disease.

Case 4

Mrs. K. L., 30 years, P5+O had a molar pregnancy for which abdominal hysterotomy with bilateral partial salpingectomy was done on 12.4.72. Histopathological report of uterine scraping collected at the time of operation showed hydatidiform mole without any evidence of malignancy. Her chest X-Ray was normal. The patient had uneventful postoperative recovery and was discharged from the hospital. She received two courses of Methotrexate with periodic blood examination. She was symptom free and urine was negative upto 20.7.72—the date on which she was last seen. She was readmitted in the hospital on 2.12.72 with complaints of haemoptysis and irregular vaginal bleeding. She was anaemic. She had an abdominal lump palpable just above and to the left inguinal ligament. Bimanual pelvic examination revealed that the uterus was enlarged to the

size of 12 weeks pregnancy. The left ovary was enlarged tender and cystic. Biological male toad test of urine was positive and chest X-Ray showed multiple secondary deposits. She was given a course of Methotrexate (5 mgm. TDS for 5 days) from 24.12.72. This was followed by abdominal hysterectomy with bilateral salpingo-oophorectomy after two weeks. The enlarged uterus had its cavity filled with haemorrhagic mass. Both the ovaries appeared normal (left one was found enlarged at the time of admission). Histological report showed the picture of chorionadenoma destruens. Methotrexate treatment was continued with periodic blood examination and repeated transfusion. After a month's stay in hospital, she improved, secondaries in the lung disappeared and biological test of urine became negative. She was discharged from hospital but was readmitted after 4 months with extreme degree of cachexia and features of intestinal obstruction. She died before anything more could be done to her.

Discussion

Chorioadenoma destruens as a cause of secondary postpartum haemorrhage after caesarean section is extremely rare. Macvicar and Graham (1973) observed that infection rather than malignancy was the cause of secondary postpartum haemorrhage following caesarean section in the two cases reported by them. Evidence of malignant chorionic tissue was detected in the endometrial curettings and on sections from uterine myometrium, though immunochemical test of the urine was negative. Brewer (1964) has pointed out that in some cases of trophoblastic disease, this test may be negative because the capability of chorionic tissue to produce gonadotrophin is variable. Jeffcoate (1967) has further stated that in choriocarcinoma biological pregnancy test may be negative where the malignant chorionic tissue is covered by fibrin deposit.

In the second case, in spite of persistent presence of chorionic gonadotrophic hormone in the urine, the exact location of

primary or secondary deposit of chorionic tissue could not be detected. Magrath *et al*, (1971) have suggested that sometimes malignant chorionic tissue is lodged as a vascular embolus leaving completely its primary site and remains clinically undetectable for some period before it produces detectable secondary deposit. During the quiescent embolic phase, the only feature of the disease is high urinary gonadotrophic level. Jeffcoate (1967) believes that many such cases cure themselves and all evidence of disease disappears. On the other hand, after months or years, frank and virulent choriocarcinoma supervenes. This happened in the present case where secondary deposit was evident only by fatal haemoptysis. Another unusual feature in this case was a long period of amenorrhoea which is usually not present in malignant trophoblastic disease. Magrath *et al*, (1971) have presented two such cases of choriocarcinoma where classical gynaecological features of the disease were absent and both had periods of amenorrhoea.

The third and fourth cases exhibit varied behaviour of malignant mole with regard to progression and response to therapy. Prophylactic cytotoxic drug was used in both the cases. Both progressed to chorioadenoma destruens and hysterectomy was performed. Case 4 ultimately died of frank malignancy with pulmonary deposits. The exact relationship among hydatidiform mole, chorioadenoma destruens and choriocarcinoma is yet to be defined. Brewer (1964) has tried to explain the varied behaviour of trophoblastic tumour on maternal factors, which destroy chorionic tissue at all implantation sites. If these maternal factors are absent or weak, then the disease has a fair chance to progress to malignancy and the available treatments are ineffective. Paran-

jothy (1970) has observed that average age incidence of malignant mole and chorionepithelioma is around 30 and average gravidity is 3 and over. Based on this observation and corroborated by the findings of two cases reported here, it seems rational to perform prophylactic hysterectomy in hydatidiform mole at the age of 30 and over, where the woman does not desire to have any further conceptions.

Pulmonary deposits are the commonest forms of secondary metastasis in choriocarcinoma (Bhaskar Rao, 1970; Novak and Seah, 1954; Park and Lees, 1950). These generally mean an early death for the patients (Lewis 1964).

Summary

Four cases of different types of trophoblastic tumours have been presented and discussed in relation to diagnosis, treatment and prognosis. In one chorionic tissue with suspicion of malignancy was the cause of severe postpartum haemorrhage after caesarean section. In another the urinary gonadotrophin level was found high even two years after evacuation of the mole which was her first pregnancy. No primary growth nor any secondary deposit was detectable. She ultimately died of haemoptysis, obviously due to secondary pulmonary metastases. The other two cases of chorioadenoma des-

truens had varied behaviour as regards malignant change. One case is alive and well after hysterectomy. The other died from progression of the disease with pulmonary deposits.

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See Figs. on Art Paper VIII