HYPOTHESIS: THE NATURE OF PULMONARY METASTASES IN CHORIOCARCINOMA

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SYNOPSIS

Between July 1966 and December 1970 ninety-seven patients with hydatidiform molar pregnancies were treated in the University Unit of Kandang Kerbau Hospital, Singapore. Ten developed pulmonary metastatic trophoblastic disease. Methotrexate was given to all except to one that had prolonged hepatitis. Two patients had total hysterectomy for perforating mole. Of the 10 patients 8 are alive and 2 have died. It is emphasised that the diagnosis of early malignant trophoblastic disease following molar pregnancy and treatment with chemotherapy will improve the prognosis.

INTRODUCTION

The incidence of hydatidiform molar pregnancy in Singapore is about 1 in 800 births[4] and 10 to 15 per cent of molar pregnancies[3] are followed by malignant trophoblastic disease. Manahan[1] described the spectrum of trophoblastic neoplasia as benign hydatidiform mole through chorioadenoma destruens to choriocarcinoma. Prawirohardjo[2] and then Tow[5] modified this to benign hydatidiform mole, villous choriocarcinoma and avillous choriocarcinoma. The aim of this paper is to try to elucidate the nature of malignant trophoblastic disease following molar pregnancy and the modification of the natural history by treatment.

TABLE I

CLASSIFICATION OF TROPHOBLASTIC NEOPLASIA

Manahan 1954	Tow 1965
Hydatidiform mole	Hydatidiform mole
Chorioadenoma destruens	Villous choriocarcinoma
Choriocarcinoma	Avillous choriocarcinoma

MATERIAL

From July 1st 1966 to December 31st 1970, the University Unit at the Kandang Kerbau Hospital, Singapore treated and followed up 97 patients with hydatidiform molar pregnancy. Ten of these had pulmonary metastatic trophoblastic disease thus giving a malignancy rate of 10 per cent. Among the 10 patients there were 9 Chinese and 1 Malay. Their average age was 26·6 years and 5 were nulliparous, the molar pregnancy being their first pregnancy. All the 10 patients had radiological evidence of pulmonary metastases and a positive H.C.G. test in urine varying from 3,750 i.u./litre to 640,000 i.u./litre as assayed by the haemagglutination-inhibition technique. Four patients had lung metastases concomitant with the molar pregnancy and subsequently 2 of them had perforating moles 5 and 7 weeks later. Six patients had lung metastases after the mole had been evacuated, the period ranging from 3 weeks to 3 months. Tissue for histology from the uterine lesions was obtained from 5 of the 10 patients and all showed villous trophoblastic tissue except for one where the histological diagnosis was not possible due to faulty preservation. Clinically this patient had a perforating mole. In only one instance was tissue obtained from the pulmonary lesion. This was from a patient whose lesion was resistant to treatment even after a year. Lobectomy is not carried out initially for diagnostic or therapeutic reasons.

RESULTS

The mainstay of treatment is chemotherapy with methotrexate but one patient earlier on in the series had in addition 6-mercaptopurine. Repeated courses of Methotrexate are given until the H.C.G. becomes negative and the pulmonary shadows have disappeared. Evacuation of the uterine cavity or hysterectomy for perforating mole is performed if indicated. Nine patients were treated as outlined above; eight went into remission usually after 3 or 4 courses of chemo-

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therapy, the H.C.G. becoming negative after an average of 5 (range 2 to 12) weeks and the pulmonary shadows disappearing after an average of 3½ (range 1 to 12) months. One of the 9 patients treated (T.S.I. M669) did not respond to methotrexate therapy inspite of 10 courses spread over 8 months; she later underwent bilateral thoracotomy and lobectomy and viable avillous choriocarcinomatous tissue was obtained. She eventually died from cerebral metastases. The tenth patient (Y.W.C. M663) was not given methotrexate because of prolonged hepatitis. She developed a small pulmonary shadow and a positive H.I. test 14 weeks after evacuation of her molar pregnancy. The pulmonary shadow regressed and the H.I. test became negative spontaneously a week later. At the time of analysis 8 of the 10 patients are alive and show no sign of the disease from 4 to 48 months after treatment was started. Two patients died, one from cerebral metastases from a methotrexate resistant tumour and the other from pulmonary embolism arising from intravenous administration of methotrexate via a polythene catheter in the right external jugular vein although she was in remission from the disease.

TABLE II

RESULTS IN 10 PATIENTS

9 treated	-	-	-	7 alive 2 dead
1 untreated	-	-	-	Alive

DISCUSSION

Malignant trophoblastic disease is a sequel to benign hydatidiform molar pregnancy in about 10 per cent of cases. Diagnosis is made from careful evaluation and follow-up of patients with molar pregnancy. The nature of the pulmonary metastases in cases concomitant or following soon after a molar pregnancy is likely to be that of villous trophoblastic tissue. This would conform to the diagnosis of "villous choriocarcinoma". At this stage of the disease, it is amenable to treatment with methotrexate with a good prognosis. If the disease is not detected early or controlled with treatment, the "villous" stage may progress to "avillous choriocarcinoma" with a poor prognosis. A very small number of patients with metastatic trophoblastic disease may undergo spontaneous regression. Thus, the early diagnosis of malignant trophoblastic disease by close follow-up of patients who have had molar pregnancy at a Mole Follow-up Clinic is a sine qua non for ensuring good prognosis in the treatment of patients suffering from choriocarcinoma.

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