TROPHOBLASTIC TUMOURS—A REVIEW*

by

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At the 15th biennial All India Obstetric and Gynaecological Congress, 12 papers on trophoblastic tumours were presented from 8 centres in India. The historical aspect of this subject has been dealt with by Saxena and Manjrekar.

Incidence

The material presented in these papers gives us a total of 1094 trophoblastic tumours—931 hydatidiform moles, 42 cases of chorioadenoma destruens and 121 cases of choriocarcinoma (Table 1). Thus, in the order of frequency we have hydatidiform mole, choriocarcinoma and chorioadenoma destruens. These tumours are common in South-east Asian, Far Eastern, and Latin American countries. Though the exact cause is not known, contributory factors were high fertility associated with malnutrition, folic acid deficiency and chronic infections. In India, it appears to be fairly common as shown in Table 2.

The incidence of hydatidiform mole varies from about 1 in 200 (in Trivandrum, Madurai and Visakhapatnam) to 1 in 650 (Hyderabad) and that of choriocarcinoma from 1 in 500 in Trivandrum to 1 in 10,000 in Hyderabad. This wide disparity may be due to certain centres receiving more cases because of special facilities for management of these tumours. A true incidence considering all pregnancies in a city would give a more correct idea of its prevalence. It may be thus seen that the incidence of hydatidiform mole for the teaching hospital and Madurai city was 1 in 194 and 1 in 592 pregnancies respectively. The correspond-

TABLE 1

Distribution of Trophoblastic Tumours in different teaching centres in India

City	Duration of Study (Years)	Hydatidiform mole	Choriocarcinoma	Chorioadenoma destruens
Ahmedabad	5 yrs.	78	2	1
Calcutta	6 yrs.	50	7	8
Delhi	10 yrs.	146	28	3
Hyderabad	8.5 yrs.	170	11	3
Jabalpur	10 yrs.	61	5	4
Madurai	9 yrs.	281	41	15
Visakhapatnam	10.5 yrs.	145	27	8
Total		931	121	42

**Review of papers on Trophoblastic tumours at the 15th All India Obstetric & Gynaecological Congress, Goa, 28-30th December, 1969.*

TABLE 2
Incidence of Trophoblastic tumours in different teaching centres

City	Hydatidiform mole	Chorio-carcinoma	Chorio-adenoma destruens
Ahmedabad	1 in 431 pregnancies	..	..
Calcutta	1 in 589 „	1 in 4207	..
Delhi	1 in 409 „	1 in 1808	..
Hyderabad	1 in 654 „	1 in 1000	..
Madurai: Hospital	1 in 194 „	1 in 1338	1 in 3685
City	1 in 592 „	1 in 4061	1 in 11000
Visakapatnam	1 in 191 „	1 in 950	1 in 2891

ing figures for choriocarcinoma were 1 in 1338 and 1 in 4061 pregnancies respectively (Rao and Ammini).

Hydatidiform mole

There seems to be no correlation between age and parity in relation to trophoblastic tumours in most papers. Rao and Reddy from Visakhapatnam consider that the risk of molar pregnancy increases with age and that molar abortions occur thrice as often in women over 30 years as compared to ordinary abortions. Rao and Ammini are of the opinion that the risk increases with age and not with parity.

Clinical diagnosis of hydatidiform mole appeared easy in most cases. The uterus was disproportionately enlarged in 60-75% of cases (Table 3). It was seen as early as the 6th week of pregnancy in some. The maximum duration of pregnancy was 36 weeks in one case where it was mistaken for accidental haemorrhage (Vohra and Madan). Pre-eclamptic toxaemia was noticed in 20-27% of moles but no case of eclampsia was reported. Lutein cysts were seen in 7.8% (Mehta) to 30% of cases (Rao and Reddy). The diagnosis was confirmed in most cases by radiological and biological tests except when they were admitted as emergencies.

In 9 cases (0.96) a foetus was associated with the mole suggesting binovular twins.

Recurrence of mole was seen in 1.06% to 1.8% of patients and was considered an indication for hysterectomy in view of the high degree

TABLE 3
Clinical findings in molar pregnancy; uterine size & Toxaemia

	Rao and Reddy (Visakhapatnam)	Mehta (Ahmedabad)	Vohra and Madan (Delhi)
(1) Size of uterus			
More than period of amenorrhoea	74%	60%	51.3%
Corresponds to period of amenorrhoea	11%	8%	30.3%
Less than period of amenorrhoea	15%	24%	12.3%
Not known	..	8%	6.1%
(2) Pre-ecl. toxaemia	27.7%	7.5%	19.4%

of malignancy in them. Kanaka Durgamba and Rajaram reported 5 consecutive molar pregnancies in one patient and 3 in another.

A case of cancer cervix with mole was mentioned in the series reported from Delhi.

Most of these cases were evacuated vaginally when necessary, after a high dose of pitocin or following injection of intrauterine hypertonic saline. Laminaria tents were used in the earlier series at certain centres only.

Hysterotomy was done in 2.5% to 10% of moles. Though in some hospitals (Jabalpur and Ahmedabad) the size of the uterus influenced the performance hysterotomy, most workers did not consider it so. Except in those emergencies when the cervix was tightly closed and the uterus tense and tender with internal haemorrhage, a hysterotomy was not indicated.

Hysterectomy was done in 0.6 to 16.6% of moles for cases in the higher age (35 years and above) and higher parity groups. Here again the size of the uterus was not considered an indication for hysterectomy. Even after spontaneous molar abortion, in the high risk group a hysterectomy is advisable after correcting the anaemia. Rao and Ammini reported a mortality of 4.9% in a series of 281 cases of moles. Most of these deaths were due to haemorrhage.

In most centres the uterus is curetted with a blunt curette either soon after evacuation or a few days later to make sure that the evacuation is complete. The histological grading of the molar tissue and the curettings were not found helpful in assessing the changes of chorionic malignancy, but Rao, Reddy and Ray felt that it might indicate lesions progressing to chorioadenoma destruens.

All papers stressed the importance of follow-up after molar pregnancy. However, a low follow-up rate was reported by several workers, especially, from Hyderabad and Ahmedabad, justifying chemoprophylaxis in these patients. In 25 patients treated with prophylactic methotrexate from Ahmedabad no choriocarcinoma was seen. In these patients 10 pregnancies occurred subsequently without any congenital foetal abnormalities. Similar observations have been made by Rao and Ammini in another series of 25 cases. Commenting on drug toxicity they, however, feel that choriocarcinoma cases tolerate the drug better than post-molar patients and reported 2 deaths due to the drug alone following molar pregnancies before citravorum factor was available. Vohra and Madan advised oral contraceptives for these patients as chorionic gonadotrophin levels are unaffected by these substances during follow-up. The chances of malignancy following a mole varied from 3.9% (Rao and Ammini) to 6.0% (Rao, Reddy and Ray).

Chorioadenoma destruens

There were 42 cases of chorioadenoma destruens reported in 8 papers. Except in one case which followed an abortion, all had molar pregnancies earlier. These patients often complain of irregular vaginal bleeding persisting even after repeated curettage. Histological examinations of the curettings may reveal trophoblastic villi (active and degenerating) or may not show any chorionic tissue if the curette has not reached the

tumour buried deep in the myometrium. The biological tests are mostly positive except when the tissue is necrotic and degenerated. Ten out of these 42 cases (23.8%) had secondaries mostly in the lungs and vagina. The risk of perforation with fatal intraperitoneal haemorrhage should always be borne in mind in the management of these cases. One death due to this cause was reported in a series of 15 cases by Rao and Ammini. These authors agree with the observations of Bhattacharjee and Sengupta that chorioadenoma destruens is not likely to lead to choriocarcinoma. From the therapy point of view, therefore, hysterectomy is advised for parous women to avoid risk of perforation or anaemia due to recurrent bouts of vaginal bleeding. In nulliparous women on the other hand, chemotherapy, and if it fails and the growth is localised, surgical resection of the tumour bearing area of the uterus and repair has been advocated by several authors (Vohra and Madan; Bhattacharjee and Sengupta; Rao and Ammini).

Choriocarcinoma

Choriocarcinoma formed 11% of trophoblastic tumours presented at the Congress. The youngest patient was 15 and the oldest 50 years. The preceding pregnancy was mostly a molar one (Table 4). The interval between pregnancy and the onset of choriocarcinoma varied from 6 weeks to 9 years (Vohra and Madan). In another series, over 50% had irregular vaginal bleeding following the last pregnancy till the chorionic malignancy was discovered (Kanaka Durgamba and Rajaram).

In one case choriocarcinoma was seen along with intrauterine gestation of 32 weeks. This patient was admitted for antepartum haemorrhage caused by ulcerating vaginal nodules. Her death was due to extensive pulmonery secondaries after a premature delivery (Chatterjee).

In a typical case the patient was anaemic. On pelvic examination, suburethral nodules were seen in 25% of cases. The cervix was normal and the uterus enlarged to 12-16 weeks size with bilateral cystic ovaries. In some the cervix was open and the growth was palpable as a necrotic, friable, easily bleeding mass in-utero simulating incomplete abortion or a submucus myoma. In 3 cases, it was mistaken for carcinoma cervix as it had involved the cervix (Rao and Ammini). The biological tests were not done in all cases. In a few histologically confirmed fatal cases these tests were repeatedly negative (Chatterjee, Rao and Ammini).

TABLE 4

Preceding pregnancy in choriocarcinoma

Authors	Hydatidiform	Abortion	Term delivery	Not known
Rao & Reddy	50 %	26 %	18.5%	4.5%
Kanaka Durgamba & Rajaram	46 %	16 %	30 %	8 %
Vohra and Madan	46.6%	30 %	23.4%	..
Chatterjee, P.	62.5%	12.5%	25.0%	..

The histopathology of choriocarcinoma was discussed at length in a paper by Rao and Reddy. They stressed the importance of curettage in the diagnosis and did not come across any perforation or fatal haemorrhage due to this procedure. However, in some cases the curettings might show only encrotic tissue with few trophoblastic cells. All workers considered absence of villous pattern in favour of choriocarcinoma. The trophoblastic cells may either be of the Langhan's or syncytial type or mixed; but in none of the anaplastic lesions the Langhan's cells dominated. Giant cells in variable numbers and vacuolation of cytoplasm of syncytial cells were seen in some cases. The myometrial invasion by sheets of trpohoblastic cells with coagulation necrosis and haemorrhage was a feature in most specimens (Saxena and Manjrekar) Early haemotogenous spread, delay in admission and diagnosis are responsible for the high incidence of metastases in these tumours.

In 66% of cases of choriocarcinoma secondaries were noticed. The commonest site were the lungs (56%) of cases. Vagina, cervix liver, ovary, brain, lymph node, skin etc. were also involved (Table 5).

TABLE 5

Site of metastases in choriocarcinoma

Total number of patients with choriocarcinoma	..	121
Those with secondaries	..	80(66.1%)
Lungs	.. 70	
Vagina	.. 38	
Cervix	.. 8	
Ovary	.. 4	
Liver	.. 6	
Brain	.. 6	
Vulva	.. 3	
Lymph node	.. 1	
Other sites	.. 5	

Four papers on choriocarcinoma discussed the current trend in its management (Vohra and Madan; Chatterjee; Kanaka Durgamba and Rajaram; Rao and Ammini). All these authors are of the opinion that chemotherapy has improved the prognosis. When the lesion is limited to the uterus, after improving the general condition, total hysterectomy with bilateral salpingo-oophorectomy should be done and followed up with at least 2 courses of methotrexate. Whenever secondaries are present, the accessible metastatic lesions should be resected besides the panhysterectomy and chemotherapy should be commenced promptly in the postoperative period and continued till at least 2 courses are given after complete regression is noted clinically as well as by radiological and biological tests. Though the toxicity is higher, to reduce the drug resistance, Rao and Ammini advocate combined therapy with methotrexate and 6-Mercaptopurine. All these patients have to be continuously watched for toxic reactions during and after chemotherapy.

Vohra and Madan reported a mortality of 61.2% in 28 cases. In another series of 41 patients of choriocarcinoma Rao and Ammini found 23 deaths (56.1%). With surgery and chemotherapy they reported a survival (6 years to 1 year with an average of 3 years) rate of 62.5 per cent. The overall mortality was 52.5% amongst 97 cases of choriocarcinoma reported from 5 centres (Table 6). With a longer and better follow-up, the death rate would perhaps be even more, considering the fact that nearly two-thirds of these patients were admitted with secondaries.

TABLE 6
Mortality in choriocarcinoma from 5 teaching centres

Teaching Centre	No. of cases	Deaths
Calcutta	7	3
Delhi	31	18
Hyderabad	13	5
Jabalpur	5	2
Madurai	41	23
	97	51

(Mortality: 52.5%)

There is a definite place for conservative therapy in choriocarcinoma especially if the tumour is limited to the uterus and the patient is anxious to have a child. After the diagnosis was confirmed by histological and biological tests, chemotherapy alone was successfully tried in 2 cases who conceived 2 years later and delivered a term live healthy child (Rao and Ammini; Chatterjee).

The contraindications of chemotherapy, its toxic reactions and their management have been mentioned by Rao and Ammini who feel that with these powerful drugs caution should be exercised to see that the patient does not succumb to these agents in our attempt to eliminate the disease from her.

Summary

Twelve papers on trophoblastic tumours presented at the 15th All India Obstetric and Gynaecological Congress held at Goa in 1969 have been reviewed.

The material consisted of 1094 trophoblastic tumours 931 moles, 42 chorioadenoma destruens and 121 choriocarcinoma. These tumours seem to be as common in India as in South east Asian and Far eastern countries. Recurrence of molar pregnancy was noted in 1.06 to 1.08% of cases. In 0.96% a foetus was found associated with the mole. The treatment of hydatidiform mole, including the place for chemoprophylaxis, has been discussed.

Out of 42 cases of choriocarcinoma destruens 10 showed secondaries.

Choriocarcinoma constituted 11% of trophoblastic tumours presented at the Congress. Sixty-six per cent of them showed secondaries. The overall mortality amongst 97 cases reported from 5 centres was 52.5%. With surgery and chemotherapy the survival was 62.5% in one large series. The trends in the management of choriocarcinoma have been discussed.