A STUDY OF TROPHOBLASTIC NEOPLASM

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Introduction

Trophoblastic neoplasms include three related pathological entites hydatidiform mole, invasive mole and choriocarcinoma. In recent years a lot of work has been done on various aspects of these lesions—geographical distribution, morphology, aetiology, pathogenesis, histopathology, biological behaviour, hormonal function, transplantation, tissue culture experiments and therapy. Information as to the incidence of trophoblastic tumours in India is limited. Kerala registers a very high incidence of the neoplasms and hence a statistical and histological reappraisal of 212 cases of trophoblastic neoplasms was undertaken in this study.

Material and Methods

Two hundred and twelve biopsies on trophoblastic tumours consisting of 126 hydatidiform moles, 56 invasive moles and 30 choriocarcinomas were studied from a total number of 38699 biopsies examined in the Department of Pathology, Medical College, Trivandrum during the period January 1965 to May 1969. Endometrial curettings, hysterectomy specimens and biopsies from secondary sites were available for this study.

A histological study was done on all the trophoblastic neoplasms received during the period. The following histological criteria were used for the classification of lesions.

1. Presence or absence of chorionic villi.
2. Changes in the chorionic villi—extent of hydropic degeneration—presence or absence of blood vessels—proliferation of cytotrophoblast—proliferation of syncytiotrophoblast.
3. Changes in myometrium—evidence of myometrial invasion—proliferation of cytotrophoblast—proliferation of syncytiotrophoblast—presence of tumour emboli—evidence of haemorrhage and necrosis—nature of stromal reaction.
4. Cytological observation—presence of pleomorphism—presence of mitotic figures—presence of giant cells.

Results

Table 1 shows the incidence of trophoblastic tumours in a total of 38099 biopsies studied during the period 1965 January to 1969 May in the Department of Pathology, Medical College, Trivandrum. The number of biopsies on trophoblastic tumours was 212 and the percentage in relation to the total number of biopsies is shown in Table I.

Out of the 212 biopsies on trophoblastic tumours, 126 were of hydatidiform mole, 56 invasive or malignant mole and 30 choriocarcinoma. Out of the 119 hyda-

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TABLE I

No. of Trophoblastic Tumours in Relation to Total Biopsies

	1965	1966	1967	1968	Upto May 69	Total	%
No. of biopsies	8191	8561	8840	9060	3447	38099	100
No. of trophoblastic tumours	38	50	58	52	14	212	0.56

tidiform moles, 44 malignant moles and 28 choriocarcinomas were from S.A.T. Hospital. Obstetric history of the patients admitted other than S.A.T. Hospital was not known.

Relationship to Total No. of Pregnancies

During the period of this study 26,677 cases of pregnancies were admitted to S.A.T. Hospital. The number of pregnancies and the number of trophoblastic lesions in each year is shown in Table II.

Relationship to Abortion

During the period of this study there were 4043 abortions in S.A.T. Hospital (Table III).

Age distribution

The age distribution of 205 cases of trophoblastic neoplasms were studied as shown in Table IV. 46% of the trophoblastic growths occurred in age groups below 30 years. The peak incidence for hydatidiform mole and invasive mole was third decade. Choriocarcinoma did not show any predilection for any particular age group.

Relationship of Incidence of Parity

Out of 212 biopsies, obstetrical history was known in 151 cases (Table V).

TABLE II

No. of Pregnancies and No. of Trophoblastic Lesions Seen During the Same Period

No. of	1965	1966	1967	1968	Upto May 69	Total	Incidence
Pregnancies	5602	5023	6052	6915	2480	26677	
H. moles	12	25	36	36	10	119	1/228
Invasive moles	8	11	16	7	2	44	1/606
Choriocarcinomas	9	7	3	7	2	28	1/953

TABLE III

Relative Incidence of Abortions, Hydatidiform Moles and Invasive Moles During the Same Period

	1965	1966	1967	1968	Upto May 69	Total	Incidence
Abortions	853	726	939	1113	412	4043	
Hyd. moles	12	25	36	36	10	119	1/37
Inv. moles	8	11	16	7	2	44	1/91

TABLE IV

Age distribution of Trophoblastic Tumours

		Below 20	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55 & above	Total
Vesicular mole	No. of cases	16	30	22	19	13	10	9	-	-	119
	%	13.5	25.2	18.5	16.0	10.9	8.4	7.5	-	-	100
Invasive mole	No. of cases	3	9	11	7	11	9	4	2	-	56
	%	5.1	16.2	19.7	12.5	19.7	16.2	7.1	3.6	-	100
Choriocarcinoma	No. of cases	4	4	4	5	4	3	6	-	-	30
	%	13.3	13.3	13.3	16.5	13.6	10.0	20.0	-	-	100

TABLE V

Parity in Relation to Trophoblastic Tumours

		Primi-para	1	2	3	4	5	6	7	8	9	10	Total
Vesicular mole	No. of cases	23	11	18	13	4	7	2	7	3	1	2	91
	%	25.2	12.9	19.7	14.3	4.3	7.7	2.2	7.7	3.3	1.1	2.2	100
Invasive mole	No. of cases	2	4	4	5	2	3	3	3	3	1	2	32
	%	6.3	12.5	12.6	15.6	6.3	9.3	0.3	9.3	9.3	3.2	6.3	100
Choriocarcinoma	No. of cases	6	5	1	2	3	1	1	4	2	2	1	28
	%	21.4	17.8	3.6	7.2	10.5	3.6	3.6	14.3	7.2	7.2	3.6	100

Blood Group

Out of 212 cases of trophoblastic neoplasms, blood group of 100 patients could only be studied (Table VI).

Type of Pregnancy Preceding Choriocarcinoma

52% of choriocarcinoma followed molar pregnancy, 27% full-term deliveries and 21% abortions. (Table VII).

Sites of Metastasis from Choriocarcinoma

Out of 30 cases, metastasis were seen only in 22 cases. In 8 cases the tumour was localised to the uterus and did not produce any metastasis. The various sites of metastasis are shown in Table VIII.

Discussion

Classification of Trophoblastic Neoplasia.

The classification followed in this study is the one proposed in the conference on trophoblastic diseases held in Baguis City, Philippines in 1965 for submission at the IX International Cancer Congress for consideration and which was accepted as the International classification.

Trophoblastic neoplasia

A. Gestational
B. Non-gestational.

Morphological diagnosis

1. Hydatidiform mole—(a) Non-invasive, (b) Invasive.
2. Choriocarcinoma.

TABLE VI

Distribution of Blood Groups in 100 Cases of Trophoblastic Tumour

	A	B	AB	0
Vesicular mole	18	17	—	17
Invasive mole	9	7	3	6
Choriocarcinoma	9	4	3	7
Blood bank series and control	25.4	23.8	4.9	45.9
Total percentage	36	28	6	30

TABLE VII

Type of Pregnancy Preceding Choriocarcinoma—30 cases

	Vesicular mole	Abortion	Full-term deliveries
No. of cases	12	6	8
Percentage	52	21	27

TABLE VIII

Sites of Metastasis from Choriocarcinoma

Lungs	Suburethral	Intracranial	Ovaries	Bladder
11	6	3	1	1

3. Uncertain—"Syncytial endometritis"—not considered as neoplasia.

Incidence of Trophoblastic Tumours

As to the incidence different authors give extremely varying reports (Table IX). The difference has been attributed to social conditions, low intake of protein and vitamins, early marriage and high fertility rate may all play a part in the causation of this disease.

TABLE IX

Incidence of Vesicular Mole and Choriocarcinoma Reported by Various Authors

Country	Year	Author	Vesicular mole	Chorio-carcinoma
U.K.	1959	Ian Donald	1:2,000	
U.S.A.	1947	Hertig & Sheldon	1:2,062	
U.S.A.	1950	Hertig		1:40,000
U.S.A.	1947	Novak	1:25,000	
Rhode Island	1968	Stella Yen & Brian Macmohan	1:1,502	
China	1956	King	1:530	1:3,700
Japan	1959	Hasegawa	1:232	
Philippines	1959	Acosta Sison	1:200	
Mexico	1963	Marquez-Monter et al	1:218	
Taiwan	1963	Wei-Ping-Yen et al	1:125	1:483
Australia	1958	Coppleson	1:820	
Singapore	1964	Tow		1:382
Calcutta	1956	P. C. Das	1:447	
Madras	1961	K. Bhaskar Rao	1:361	1:2,058
Bombay	1968	Shantha A. Shetty & Thakur	1:467	
Guntur	1961	Reddy D. J. et al	1:295	1:748
Ahmedabad	1964	Mathur & Shah	1:200	
Vellore	1968	Paranjothy		1:5,000
Visakapatanam	1969	Srinivasa Rao & Ray	1:191	1:950
Trivandrum (Kerala)	1970		1:206	1:953

Age

The incidence of hydatidiform mole and choriocarcinoma is more common in the higher age groups, especially after 35 or 40 years (Essen Moller, 1925). The joint project for study of trophoblastic tumours reported the relationship of these to malnutrition, parity and old age (Sison, 1959; King, 1956; Hasegawa, 1959). In the present series 43.7% of hydatidiform moles occurred in the third decade. In invasive mole, third and fourth decades showed almost an equal distribution. Regarding chorionepithelioma the average age found by most authors was 30-33 years. In our series fourth and fifth decades showed the maximum incidence. A comparison of the age distribution of trophoblastic disease in Taiwan, U.S. and in India—Trivandrum, Kerala is shown in Table X. Our series mainly correspond to that of Taiwan where the incidence of trophblastic lesions is very high.

Parity

Multiparity is considered as one of the possible predisposing factors (Sison 1960). In the present study the relationship between parity and trophoblastic

TABLE X

Age Distribution of Trophoblastic Tumours in Taiwan, U.S. and Kerala

Age	Hydatidiform mole			Invasive mole			Choriocarcinoma		
	Taiwan	U.S.	Trivandrum	Taiwan	U.S.	Trivandrum	Taiwan	U.S.	Trivandrum
15-20	4	12	16	-	5	3	1	6	4
20-24	34	32	30	-	4	9	2	10	4
25-29	39	17	22	5	3	11	3	7	4
30-34	38	12	19	4	3	7	5	7	5
35-39	2	4	13	4	2	11	3	4	4
40-44	14	1	10	2	-	9	3	1	3
45-49	7	-	9	6	-	4	2	-	6
50 and above	-	-	-	-	-	2	3	-	-
Unknown	-	4	7		-				
Average	30	25	28.8	32	25	32.4	36	28	32

tumours is considered in Table V. Parity associated with a low level of nutrition, especially due to diminished protein intake may cause changes in placental tissues giving rise to abnormal villi and malignant transformation. There is circumstantial evidence to postulate parity as a predisposing aetiological factor. However the related factors of undernutrition and a study of further aspects of diet in Kerala may contribute further to the understanding of aetiology of trophoblastic tumours.

Blood group factors

Distribution of blood groups of patients with trophoblastic tumours is given in Table VI. Scott in a survey of the Albert-Mathew Chorionepthelioma Registry records found that the blood groups of 46 cases of chorionepithelioma showed a shift from O to A, B and AB. This may be related to a possible lack of maternal antibody response as a factor in the development of malignant trophoblastic tumours. In the present series A group shows a comparatively higher incidence.

Type of pregnancy preceding choriocarcinoma

In approximately 50% of cases the neoplasm follows a hydatidiform mole (Hertig, 1950; Novak & Seah, 1954; King, 1956). Thus hydatidiform mole is the commonest type of complication of pregnancy preceding a malignant trophoblastic neoplasm.

Metastasis from Choriocarcinoma

The commonest site for metastasis is the lung and the next, the vulva and vagina. The rarer sites are liver, brain, thyroid, bones, skin, kidney and bladder.

Conclusion

A critical analysis of 212 trophoblastic

tumours out of a total of 38,099 biopsies (0.56%) studied in the Department of Pathology, Medical College, Trivandrum is presented here.

It was found that of the total pregnancies 1/228 was a hydatidiform mole, 1/606 an invasive mole and 1/953 a choriocarcinoma. The incidence of trophoblastic tumours was found to be high in lower age group compared with other reported series. A higher incidence of blood group 'A' was noted in these cases. Majority of the cases of choriocarcinoma was preceded by hydatidiform mole. The present study showed there is a very high incidence of trophoblastic tumours in Kerala as compared with the figures reported from other countries.

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