THYROID FUNCTION TEST IN TROPHOBLASTIC TUMOUR CASES

by

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Introduction

Odell (1968) described 14 patients with neoplasia containing trophoblastic cells, and an unusual form of hyperthyroidism. These patients had no convincing clinical evidence of hyperthyroidism but investigations revealed definite abnormalities. In all the patients both the P.B.I. and the 24 hour thyroid iodine uptake were raised. Goldstein (1967) reported the incidence of hyperthyroidism as 10% of 189 molar pregnancy cases. A thyroid 'storm' with cardiac failure may ensure as noted in the recent review by Hershman and Higgins (1971). Novak (1974) has reported that such a crisis—immediately post-hysterectomy occurred in their clinic.

Material and Methods

In the present study in order to find out the incidence of hyperthyroidism in trophoblastic tumours in 30 cases, thyroid function test has been done. The material of the present study were collected from Eden Hospital, Medical College and Hospitals, Calcutta from January 1976 to June 1980. During this four and half years period total 138 trophoblastic tumours have been treated in this institution. The trophoblastic tumours have been classified and described under five different heads as, (1) hydatidiform mole, (2) metastatic mole, (3) invasive or perforating mole, (4) choriocarcinoma and (5) undetermined group. Of the 30 cases where thyroid function test has been performed, 2 were choriocarcinoma, 2 invasive moles, 2 metastatic moles and the rest were benign hydatidiform holes.

There are several methods of assessing the functional state of thyroid gland. Radioactive isotopes of iodine are now readily available everywhere and afford a simple means of making direct observations on the state of thyroidal iodine turn over. The principle upon which these tests depend is that radioactive isotopes of iodine behave in the body in exactly the same manner as the stable naturally occurring isotopes, but their radioactivity enables to follow their movement without difficulty and to measure the concentrations in the thyroid and various body fluids. Although a number of radioactive isotopes of iodine have been produced, for measuring the thyroid function, usually I^{131} with a half life of 8 days are used, since a longer period of study with I^{131} is possible. In practice, where patients suspected of thyroid disease are investigated, the assumption is made that they have a normal renal clearance for iodine. In the present series, the thyroid function

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Accepted for publication on 30-3-82.

was studied by using radioactive Iodine (I^{131}). Odell (1968) in addition to this test, also estimated P.B.I. of the patients. But P.B.I. (the serum protein bound iodine) though it is one of the most useful tests of thyroid function since during pregnancy the level of thyroxine binding proteins are raised by oestrogens, it has got very little value during pregnancy. Hence in the present study P.B.I. has not been estimated.

On an average 48 to 72 hours after evacuation of molar pregnancy the test was performed, since there were technical difficulties to do the test before evacuation of moles. But in choriocarcinoma cases the test was performed before treatment either surgery or chemotherapy. The patients who showed hyperthyroidism by investigation the thyroid function test was repeated after 4 weeks in these cases. A tracer dose of 100 μC of Carrier free I^{131} was given to each patient on an empty stomach. The average state of accumulation of radio iodine by thyroid during the first three hours and the maximum concentration reached were then measured by Geiger-Muller Counter. In order to avoid uncertainties in the absorption of iodine in the stomach immediately after its administration, the average rate of accumulation during the first three hours was always measured. This was obtained by dividing by three the percentage accumulated at the third hour after administration. The line of demarcation between euthyroid and hyperthyroid groups was taken as a maximum concentration of 40% of the administered dose or a maximum average rate of accumulation of 6%/hour during the first 3 hours.

Analysis of Cases and Discussion

Out of 30 cases where thyroid function test has been performed, in 9 (30%) hyperthyroidism was detected. The incidence is high as compared to other authors. When the test was repeated after 4 weeks in 7 cases the results became normal, whereas in 2 cases there was still hyperthyroidism for which the patients were referred to endocrinological department for further treatment. Table I shows the details of the cases where thyroid function test was performed and Table II shows the relationship of thyroid function with B.P. lutein cysts of ovary, gonadotrophin excretion rate and extension of the disease in hyperthyroid cases only Tables I and II. From this Table it has been noted that out of 9 cases where thyroid function test showed hyperthyroidism clinically there was toxaemea of pregnancy with hypertension in 6 cases. In cases 5 and 7, in addition, the patients developed acute cardiac failure mimiking thyrotoxicosis with cardiac failure. Dewherst (1976) mentioned that an interesting event which may be observed with hydatidiform mole and also choriocarcinoma is the development of thyrotoxicosis and this is apparently due to a substance produced by chorionic tumours which is a thyroid stimulant, but which differs in characteristics from other known thyroid stimulators. The exact nature of this thyroid stimulant is not definitely known even at the present moment. Hennen (1965), Hershman and Starnes (1969) mentioned that normal human chorionic tissue contains a thyroid stimulating agent. According to Hall *et al* (1974) the normal placenta produces 2 thyroid stimulating agents termed H.C.T. (Human chorionic thyrotrophin) and H.M.T. (Human molar thyrotrophin-, the latter so designated because it is produced in large amounts in some patients with hydatidiform mole and choriocarcinoma. It is possible that H.M.T. may act as a precursor of H.C.T. but firm evidence for

this is lacking. The role of H.M.T. and H.C.T. in normal pregnancy is virtually unknown. However, current evidence suggests that trophoblastic tumours can produce a T.S.H. like material which may be responsible for abnormal thyroid function tests and occasionally for overt hyperthyroidism. Hall *et al* (1974) are of opinion that in view of the similarities in structure between T.S.H., F.S.H., L.H. and H.C.G. it might be expected that trophoblastic tumours could secrete materials with T.S.H. like activity. Kenimer *et al* (1975) in an interesting study showed a close correlation between H.C.G. and T.S.H. level in serum and tissue preparations. It appeared that serum H.C.G. levels in excess of 100 units per ml. are associated with increased thyroid function probably accounting for the signs and symptoms of hyperthyroidism, noted in some patients with H. Mole and Choriocarcinoma. They also mentioned that probably H.C.G. ß. sub-unit contains no thyrotropic activity and all H.C.G. immunoreactive fractions with a p.H. between 3.5 and 5 contained thyrotropic activity in proportion to their H.C.G. content. Odell (1968) has also reported that in all patients of his series, Urinary gonadotrophin exeretion was very high but this material did not have an intrinsic T.S.H. like activity. In the present series only in two hyperthyroid cases (4, 5) the gonadotropin titre in urine was higher than 150 units/ml. In four cases (13, 18, 21 and 27) where thyroid uptake showed hyperthyroidism, the gonadotropin exeretion was less than 100 units/ml. and in five cases (6, 12, 17, 25 and 29) where gonadotropin exeretion was 200 units/ml. or more, the thyroid function was normal. So the findings of the present study does not correlate with that of Kenimer *et al* (1975). Out of 9 hyperthyroid cases, in 5 there were bilateral polycystic ovaries. Thus hyperthyroidism in trophoblastic tumour cases was related to toxaemea of pregnancy (in 6 cases) and presence of luteine cysts of ovaries (in 5 cases) but there was no definite relation with amount of gonadotropin excretion and also extension of the disease. Thus in 2 invasive mole cases (2 and 6) and 2 metastatic moles (1 and 12) though there were invasion of myometrium and blood vessels with vaginal metastasis, the thyroid function showed normal value. In 1 recurrent molar pregnancy case (17) the thyroid function showed normal value.

Thus out of 30 cases where thyroid function test with radio active iodine uptake has been performed, in 9 cases (30.1%) hyperthyroid activity was detected. Hyperthyroidism has been noted specially in toxaemia cases and there is a possibility of some relation of hyperthyroid activity with toxaemia in these cases. Whether anti-thyroid drugs could be used routinely in these trophoblastic tumour cases with toxaemia and hyperthyroidism will be tried in future. Several workers (Hennen 1965; Hershman 1971) have used antithyroid drugs in choriocarcinoma cases along with thyrotoxicosis but in the present study no such drug was used.

Acknowledgement

We are grateful to Prof. A. Basu, Department of Radiotherapy, Medical College and Hospitals for his valuable discussions and kind help for carrying out the thyroid function test using radio active iodine in his department. Our thanks are also to Superintendent, Medical College and Hospitals for allowing us to use the hispital records.

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TABLE I

Details of 30 Cases Where Thyroid Function Was Done

Case No.	Nature of tropho-tumour	Age	Parity	B.P.	Chief complaints	Ht. of uterus
1.	2.	3.	4.	5.	6.	7.
1.	Metastatic H. Mole	23 yrs.	P1÷0	110/70 mm.Hg.	Amenorrhoea for 3 months Bleeding P.V. 7 days	16 wks
2.	Invasive mole	30 yrs.	P5÷0	128/80 mm.Hg.	Amenorrhoea 5 months. Bleeding P.V. 4 months Passage of grape-like materials	14 wks
3.	Chorio-carcino-ma	30 yrs.	P5÷1	128/80 mm.Hg.	Bleeding P.V. 5 months. Lump-abd. 3 months.	16 wks
4.	Benign H. Mole	30 yrs.	P3÷0	110/70 mm.Hg.	Bleeding P.V. swelling of lower abd.	20 wks
5.	H. Mole with Thy-rotoxico-sis	20 yrs.	P0÷0	160/80 mm.Hg.	Amenorrhoea 4 months. Bleeding P.V. 4 days-Dyspnoea	24 wks
6.	Invasive mole	48 yrs.	P5÷0	140/70 mm.Hg.	Amenorrhoea. Bleed-ing P.V. 6 weeks	20 wks
7.	H. Mole with Thy-rotoxi-cosis	19 yrs.	P1÷0	182/90 mm.Hg.	Amenorrhoea 3 months. Bleeding P. V. 1½ months	28 wks
8.	Benign H. Mole	12 yrs.	Unmarried	116/70 mm.Hg.	Amenorrhoea 4 months. Bleeding P.V. 1 month	24 wks
9.	Benign H. Mole	20 yrs.	P2÷0	160/80 mm.Hg.	Amenorrhoea 3 months. Bleeding P.V. 15 days	24 wks
10.	Benign H. Mole	25 yrs.	P1÷0	105/65 mm.Hg.	Amenorrhoea 6 months. Bleeding P.V. 2 days	22 wks
11.	Chorio-carcinoma	30 yrs.	P1÷0	130/80 mm.Hg.	Irregular bleeding P.V. 6 months	16 wks
12.	Metasta-tic mole	36 yrs.	P5÷0	110/60 mm.Hg.	Amenorrhoea 1 month. Bleeding P.V. 10 days	16 wks.
13.	Benign H. Mole	19 yrs.	P1÷0	150/100 mm.Hg.	Amenorrhoea 5 months. Bleeding P.V. 4 days	—
14.	Benign H. Mole	28 yrs.	P4÷0	110/70 mm.Hg.	Amenorrhoea 6 months. Bleeding P.V. 2 days	24 wks
15.	Benign H. Mole	28 yrs.	P1÷0	110/70 mm.Hg.	Pain abdomen Amenor-rhoea 4 months. Bleed-ing P.V. 6 days	14 wks
16.	Benign H. Mole	17 yrs.	P0÷0	110/70 mm.Hg.	Amenorrhoea 5 months. Bleeding P.V. 2 days	20 wks

TABLE I—(Cont.)

Extension of disease	Lutein cysts of ovaries	Urinary H.C.G.	Thyroid I^{131} Uptake	Treatment
8.	9	10.	11.	12.
2 vaginal nodules	Not palpable	1 in 100 dil. +ve	1 hour 4.4% 24 hours 18.6%	S.E. & Excision of Vag. Nodules
No metastasis	Bilateral cysts	90,000 IU/L.	1 hour 6.6% 24 hours 30.5%	S.E. Hysterectomy & Methotrexate
Vaginal wall Lungs	Bilateral cysts	1 in 200 dil. +ve	1 hour 6.4% 24 hours 38.6%	Hysterectomy Methotrexate
No metastasis	Bilateral cysts	1,200,000 units/L.	1 hour 8.8% 24 hours 57%	S.E. Hysterectomy
No metastasis	Bilateral cysts	640,000 units/ Litre	1 hour 6.7% 24 hours 42%	S.E. Treatment of Cardiac failure Methotrexate
No metastasis	No cysts	1 in 200 dil. +ve	1 hour 8.7% 24 hours 30.4%	S.E. Hysterectomy Methotrexate
No metastasis	Bilateral cysts	Negative in all dil. (one wk. after evacuation)	1 hour 10% 24 hours 51.7%	S.E.
No metastasis	Not palpable	1 in 100 dil. +ve	1 hour 6.6% 24 hours 16.3%	S.E.
No metastasis	Bilateral cysts	Negative in all dils.	1 hour 4.4% 24 hours 41.6%	S.E.
No metastasis	Not palpable	1 in 10 dil. +ve	1 hour 8.8% 24 hours 28.4%	S.E.
Vaginal wall Lungs	Not palpable	1 in 100 dil. +ve	1 hour 5% 24 hours 21.9%	Methotrexate
Vaginal nodules vesicles	No cysts	640,000 units/L.	1 hour 2.6% 24 hours 21.9%	S.E. Hysterectomy Methotrexate
No metastasis	Not palpable	50,000/L. units	1 hour 13.9% 24 hours 57%	S.E.
No metastasis	Bilateral cysts	50,000/L. units	1 hour 7.9% 24 hours 40.8%	S.E.
No extension	Not palpable	6,000/L. units	1 hour 5.5% 24 hours 50.4%	S.E.
No extension	Both ovaries palpable	10,000/L. units	1 hour 8.3% 24 hours 25%	S.E.

TABLE I—(Contd.)

Details of 30 Cases Where Thyroid Function Was Done

Case No.	Nature of tropho-tumour	Age	Parity	B.P.	Chief complaints	Ht. of uterus
1.	2.	3.	4.	5.	6.	7.
17.	Rècur-rent H. Mole	22 yrs.	P0÷2	120/80 mm.Hg.	Amenorrhoea 4 months. Bleeding P.V. 3 days	18 wks
18.	Benign H. Hole with foe-tus	32 yrs.	P2÷0	220/110 mm.Hg.	Amenorrhoea 6 months. Swelling lower units Bleeding P.V.	32 wks
19.	Benign H. Mole	18 yrs.	P0÷0	110/70 mm.Hg.	Amenorrhoea 5 months. Bleeding P.V. 5 days	28 wks
20.	Benign H. Mole	25 yrs.	P2÷0	130/70 mm.Hg.	Amenorrhoea 2 months. Bleeding P.V. Pain ab-domen	26 wks
21.	Benign H. Mole	27 yrs.	P1÷1	60/?	No A/O amenorrhoea. Bleeding profuse	28 wks
22.	Benign H. Mole	26 yrs.	P1÷0	105/65 mm.Hg.	Amenorrhoea 4½ months. Bleeding P.V. 2 days	18 wks
23.	Benign H. Mole	24 yrs.	P2÷0	100/60 mm.Hg.	No complaints. Admit-ted for M.T.P.	20 wks
24.	Benign H. Mole	25 yrs.	P3÷0	110/70 mm.Hg.	Amenorrhoea 4 months. Serosanguinous dis-charge	16 wks
25.	Benign H. Mole	17 yrs.	P0÷0	104/60 mm.Hg.	Pain abdomen Amenor-rhoea 4 months. Bleed-ing P.V.	20 wks
26.	Benign H. Mole	22 yrs.	P0÷0	150/110 mm.Hg.	Amenorrhoea 4 months. Bleeding P.V. Pain—abdomen	34 wks
27.	Chorio-carcinoma	45 yrs.	P6÷0	120/80 mm.Hg.	Irregular Bleeding 14 weeks P.V. Pain around vulva	14 wks
28.	Benign H. Mole	30 yrs.	P3÷3	110/60 mm.Hg.	Amenorrhoea 4 months. Bleeding P.V. 7 days	18 wks
29.	Benign H. Mole	24 yrs.	P2÷0	110/70 mm.Hg.	Bleeding P.V. continu-ously. No amenor-rhoeoa	24 wks
30.	Benign H. Mole	24 yrs.	P3÷0	140/50 mm.Hg.	Amenorrhoea 6 months. Bleeding P.V. 7 days	24 wks

TABLE I—(Cont.)

Extension of disease	Lutein cysts of ovaries	Urinary H.C.G.	Thyroid I^{131} Uptake	Treatment
8.	9	10.	11.	12.
No extension	Not palpable	640,000/L. units	1 hour 5.9% 24 hours 31.7%	D.E.
No extension	Not palpable	6,000/L. units	1 hour 10.3% 24 hours 57%	Spontaneous Expulsion Curettage
No extension	Not palpable	Negative	1 hour 3.6% 24 hours 14.9%	D.E.
No extension	Not palpable	10,000/L. units	1 hour 5.5% 24 hours 11.9%	S.E.
No extension	Rt. ovary cystic	5,000/L. units	1 hour 6.8% 24 hours 4.3%	Hysterectomy
No metastasis	Bilateral cysts	4,000/L. units	1 hour 5.9% 24 hours 23.6%	Spontaneous expulsion digital exploration
No metastasis	No cysts	5,000/L. units	1 hour 9.6% 24 hours 39%	Hysterotomy
No metastasis	Not palpable	2,000/L. units	1 hour 5% 24 hours 31.4%	S.E.
No metastasis	Not palpable	320,000/L. units	1 hour 4.7% 24 hours 22.6%	D.E.
No metastasis	Bilateral cysts	8,000/L. units	1 hour 6.8% 24 hours 56%	Hysterotomy
Vaginal vulva Lungs Brain	No cysts	50,000/L. units	1 hour 13.5% 24 hours 51.4%	Hysterotomy
No metastasis	No cysts	6,000/L. units	1 hour 4.5% 24 hours 30%	Hysterotomy
No metastasis	No cysts	320,000/L. units	1 hour 4.8% 24 hours 16.5%	D. & E.
No metastasis	Not palpable	Not done	1 hour 2.6% 24 hours 15.3%	Spontaneous Expulsion Exploration

TABLE II

Hyperthyroid Activity in Trophoblastic Tumour Cases

Case No.	B.P. mm/Hg.	Urinary Gonadotropin	Lutein cysts ovaries	Thyroid uptake I^{131}
4	110/70	1,200,000 Units/L	Bilateral cysts	1 hr. 8.8% 24 hrs. 57%
5	160/80	640,000 Units/L	Bilateral cysts	1 hr. 6.7% 24 hrs. 42%
7	182/90	Negative	Bilateral cysts	1 hr. 10% 24 hrs. 51.7%
9	160/80	200,000 Units/L	Bilateral cysts	1 hr. 6.4% 24 hrs. 48.2%
13	150/100	50,000 Units/L	Not palpable	1 hr. 13.9% 24 hrs. 57%
18	220/110	6,000 Units/L	Not present	1 hr. 10.3% 24 hrs. 57%
21	60/?	5,000 Units/L	Not present	1 hr. 6.8% 24 hrs. 43%
22	120/80	50,000 Units/L	Not present	1 hr. 13.5% 24 hrs. 51.4%
26	150/110	6,000 Units/L	Bilateral cysts	1 hr. 6.8% 24 hrs. 58%

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