Gestational Trophoblastic Disease

B.A.K. Peiris[1], I.M.R. Goonewardene[2]

[1]Registrar, [2]Senior Lecturer

Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Ruhuna, Teaching Hospital, Galle.

Abstract

A comparative study of the incidence, clinical presentations, and diagnosis of gestational trophoblastic disease was carried out 5 years apart viz 1983 and 1988.

There was no significant change in incidence (1 in 180 pregnancies in 1983, 1 in 246 pregnancies in 1988). In both studies the majority of patients were in the 21-30 year age group, and in second and third pregnancies, probably reflecting the proportions in the general population. Bleeding per vaginam following a period of amenorrhoea was the commonest presentation and the majority presented during the second trimester. There was a significant number of cases with uterine enlargement smaller than dates, 9 cases out of 22 in 1983 and 11 cases out of 22 in 1988. In 1983 due to an almost total dependence on clinical criteria for diagnosis, in 50% of cases the diagnosis was completely missed initially. After introduction of ultrasonography there was a dramatic improvement in diagnosis and none were missed.

Keywords: Gestational trophoblastic disease.

Introduction

In 1889, Sanger suggested the occurrence of a tumour arising from the decidu . of pregnancy. Marchand reported a series of choriocarcinoma in 1895, but it was Gottchalk in 1894 who first suggested that the disease was of trophoblastic origin. Gestational trophoblastic disease is not a single entity. It is a spectrum of diseases with varying clinical presentations. It ranges from the benign hydatidiform mole to the highly malignant avillous choriocarcinoma.

Patients and Methods

Admissions to the University Obstetric and Gynaecology Unit of the General Hospital, Galle during the period August 1st 1986 to December 1st 1987 were studied. In the absence of radio-immuno assays for the measurement of Human chorionic gonadotrophin (β H.C.G) in the serum, the Gravindex 90 slide test was used for urine analysis, during the first ten months of the study. This is a latex particle agglutination inhibition test with a sensitivity of 3.5 international units per mililitre. During the last six months, a

more sensitive reagent Neoplanotest Duoclon was used with a sensitivity of 0.5 international units per mililitre. During the period under study ultrasonography was carried out almost in all the patients presenting with first trimester bleeding.

The data obtained were compared with a similar study carried out in the unit in 1983.[8]

Results

Incidence: There were 22 cases of gestational trophoblastic disease out of a total of 5407 pregnancies inclusive of abortions, giving an incidence of 1 in 246 pregnancies.

In1983 there had been 22 cases out of a total of 3953 pregnancies giving, an incidence of 1 in 180 pregnancies.

In 1988 there was one case with a coexisting fetus. In 1983 there had been two such cases, one of which had delivered an active viable fetus and this patient had an interesting manifestation of a hyperthyroid state.

Discussion

Incidence

This paper examines data obtained on the incidence of gestational trophoblastic disease in two studies; one in 1983 and the other in 1988. Calculating the incidence of a condition from hospital based studies is unreliable. In 1964 an incidence of 1 in 200-300 pregnancies was reported in Hong Kong[6]. Various workers especially Acosta Sison from the Phillipines, have found a similar incidence in Asia, in contrast to the much lower incidence of approximately 1:2000 pregnancies reported in North America and Europe[9,1]. The highest incidence of 1:82 pregnancies has been reported in Taiwan[24]. Several theories have been postulated as to the cause of this significant geographical variation. Low socio-economic status, malnutrition, that the common food eaten in these areas rice, beans and corn are cooked by prolonged boiling resulting in depletion of folic acid, have all been incriminated[15]. One interesting postulate is that it may be related to the higher levels of circulating human chorionic gonadotrophin found in normal Asian pregnancies compared to the lower values in normal Caucasian pregnancies[17].

Partial molar change could occur in the placenta rarely, without death of the fetus[5,3,12]. All cases with coexistant fetuses detected in the unit had their own, separate and normal placentae. Twin conceptuses could be the answer[11].

The delivery of a coexisting fetus, alive and viable, is extremely rare[19,4,21].

Thyroid stimulating hormone (TSH) and human chorionic gonadotrophin (HCG) have almost identical subunits. A relative lack of specificity of the thyroid stimulating hormone receptors in the thyroid follicular cells could result in binding of the increased human chorionic gonadotrophin and explain the hyperthyroid state seen in one case[15].

Age and Parity

The distribution of age and parity in the two studies were similar.

The majority were in 21-30 year age group and in the 2nd and 3rd pregnancies, probably reflecting their proportions in the general population.

At the extremes of the reproductive age group, viz under 20 years and over 40 years of age, the incidence of gestational trophoblastic disease is greater[2,20,7,1,10]. The role of parity

Table I

Influence of age and parity

Present Study 1988

Parity / Age	1	2	3	4	5	6	7	8	9	10
15-20 yrs	1	1	-	-	-	-	-	-	-	-
21-30 yrs	3	7	3	-	1	-	-	-	-	-
31-39 yrs	1	2	-	2	-	-	-	-	-	-

Goonewardene 1983

Parity / Age	1	2	3	4	5	6
15-20 yrs	1	-	-	-	-	-
21-30 yrs	2	8	4	1	-	-
31-39 yrs	-	-	1	1	3	-
>39 yrs	-	-	-	-	-	1

however is not clear. It has been postulated that the elderly primigravida carried the highest risk for choriocarcinoma. However, Bagshaw considered 3rd and 4th pregnancies were high risk while para 1,2 or more than 4 were considered to have a lower risk[2]. Cytogenetic studies have revealed that gestational trophoblastic disease arise as a result of androgenesis [13,22]. This may account for the higher incidence of the condition at the extremes of the reproductive age groups, as chromosome aberrations are probably commoner during these periods.

Amenorrhoea

As seen in both studies the majority of gestational trophoblastic disease present after fourteen weeks of amenorrhoea[17].

Table II

The Distribution of cases according to the amenorrhoea and the occurence of the first bleed.

Present Study 1988

Amenorrhoea in weeks / 1st bleed in weeks	<13	13-26	27-40	>40	NK	%
<13	2	6	-	-	-	36
13-26	-	6	2	-	-	36
27-40	-	-	1	-	-	05
NK	-	-	2	-	3	23
%	9	55	23	-	13	100

Goonewardene 1983

Amenorrhoea in weeks / 1st bleed in weeks	<13	13-26	27-40	>40	%
<13	3	2	1	-	28
13-26	-	11	3	-	67
27-40	-	-	-	1	05
%	14	62	19	05	100

Table III

Uterine enlargement in relation to the amenorrhoea and other associated features of trophoblastic disease.

Present Study 1988

Associated features / Uterine enlargement	Proteinuric hypertension	Ovarian cysts	Hyperemesis gravidarum	Total
Larger than dates	2	2	3	6
Corresponding to dates	-	-	1	2
Smaller than dates	-	-	1	2
Indefinite	-	-	-	3

Goonewardene 1983

Associated features / Uterine enlargement	Proteinuric hypertension	Ovarian cysts	Hyperemesis gravidarum	Total
Larger than dates	3	3	3	9
Corresponding to dates	-	-	-	3
Smaller than dates	2	2	-	9*

Uterine Size

It is interesting to note that only 27% (1988) and 41% (1983)[8] had uterine enlargement larger than dates. Fifty percent in 1988 and 41% in 1983[8] had uteri smaller than dates. Uterine enlargement excessive for the period of gestation has long been considered as the characteristic feature of gestational trophoblastic disease. It is also associated with a higher incidence of malignant sequelae[16,14]. However, it is important to be aware that an uterus which corresponds in size to, or is smaller than that expected for the period of amenorrhoea does not exclude a molar pregnancy.

Cystic Ovaries

Two cases in 1988 and five cases in 1983[8] had cystic ovaries and one in each, required chemotherapy. The presence of cystic ovaries, arising as a result of the lutenizing effect of the high concentration of human chorionic gonadotrophin found in these patients, has been corelated with malignant sequelae[18]. Although these cysts may increase in size even after the evacuation of the H.mole and require chemotherapy, the majority regress spontaneously after the tumour is evacuated.

Table IV

Methods of Diagnosis

	Present Study 1988	Goonewardene 1983
Clinical criteria alone	3	9
Amniogram	-	1
Metastases + Persisting urinary HCG	-	1
During evacuation of incomplete abortion	5	11
Ultrasonography	13	-
Persisting urinary HCG	1	-

Associated Syndromes

Fifty percent of cases with hyperemesis gravidarum had uteri larger than dates in 1988 while all 3 cases that presented with hyperemesis gravidarum in 1983[8] had uteri larger than dates.

Both cases of proteinuric hypertension in 1988 had uteri larger than dates while 3 out of 5 cases in 1983[8] had uteri larger than dates.

Gestational trophoblastic disease is the commonest cause of pregnancy induced proteinuric hypertension[8,17]. Rates of 10% to 50% have been reported in gestational trophoblastic disease[8,6,17]. In 1988 it was detected in 9% of cases.

Although the aetiology of pregnancy induced hypertension is not known, it is reasonable to postulate that it is a failure of maternal adaptation to trophoblastic tissues, and evidently the presence of a fetus is not essential. Further research into this aspect may help in solving this vexing problem.

Metastases

There were no cases with metastases in 1988 while there was one case with bilateral pulmonary metastases in 1983[8].

Malignant sequelae and the role of the antecedant pregnancy

Both patients requiring chemotherapy in 1988 were following hydatidiform moles (H.Mole). One was a perforating mole and the other had persistant urinary human chorionic gonadotrophin levels. In 1983[8] out of the 3 cases requiring chemotherapy, 2 followed H. moles. One had persisting urinary human chorionic gonadotrophin and pulmonary deposits, the other one had massive enlargement of cystic ovaries inspite of evacuation of the mole. The third was a case of invasive mole.

Generally, about 10-15% of H. moles will have malignant sequelae[23,2]. It is believed that about 50% of cases of choriocarcinomata are preceded by H.moles, 25% by normal pregnancy and the remaining 25% by abortions and ectopic pregnancies. However in 1982 in Singapore, 82.5% of choriocarcinomata were preceded by molar pregnancies[17].

Choriocarcinoma following a normal delivery carries the worst prognosis. The prognosis is better if the antecedant pregnancy had been an abortion. The best prognosis is after a previous mole. The shorter the interval between the antecedant pregnancy and the diagnosis of malignant sequelae, the better the prognosis is. If it is less than 4 months it is favourable, but a period of one year or more is a high risk factor[2].

Conclusion

In order to establish the true incidence of gestational trophoblastic disease in the region, and its epidemiological characteristics, a population based study has to be carried out. It is important to note that about half the number of gestational trophoblastic disease present with uterine size corresponding to or smaller than that expected for the gestational age. Although a high index of clinical suspicion may be helpful in the early diagnosis of gestational trophoblastic disease, routine ultrasonography of all cases of early bleeding in pregnancy is invaluable in the diagnosis of this condition. The key to the aetiology of pregnancy induced proteinuric hypertension may well lie in the study of gestational trophoblastic disease.

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