

Gestational trophoblastic disease in the Gynaecologic and Obstetric Institute of Sassari in the period 1976-89

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Summary: 61 cases of gestational trophoblastic disease (GTD) were examined retrospectively in the period 1976-89 (60 cases of simple vesicular mole and one case of chorionepithelioma), analysing them from the epidemiologic point of view. The incidence of GTD were 3.6/1000 live births, higher than the Italian and European average, with a very low incidence, on the contrary, of chorionepithelioma (0.06/1000 live births). No significant epidemiological data emerged, with the exception of age (11 cases of over 40 years) and of ABO typing (a notable incidence of ORh+ group). The gestational capacity of the patients returning for checking was 78.9%, similar to that of the general population.

INTRODUCTION

Gestational trophoblastic disease (GTD) in its various forms (simple vesicular mole, invasive mole, chorionepithelioma) represents a pathology with marked variations of incidence and with epidemiologic characteristics differing according to the geographic area (2).

In one of our preceding studies conducted on all the cases in the Province of Sassari, we noticed a high incidence of this disease in its most benign form (simple vesicular mole), with, on the contrary, a very low incidence of malignant forms (chorionepithelioma) (1).

For this reason we reexamined the cases of GTD observed in our Clinic during the last 14 years.

MATERIAL AND METHODS

In a retrospective study we examined all the cases of GTD observed during the last 14 years (January 1976 - December 1989) in our Clinic.

In particular we found 60 cases of vesicular mole, no cases of invasive mole, and one case of chorionepithelioma, in a patient who had presented a vesicular mole 4 years before.

Altogether, therefore, 61 cases of GTD were encountered in 60 patients.

In these patients, up to November 1982 a double revision of the uterine cavity was carried out, alternating with a cycle of prophylactic chemotherapy with Metotrexate (10 mg/die \times 5 days), which was repeated after the second revision. Since November 1982 a single revision of the uterine cavity has been carried out, preceded, in case of diagnosis of certainty of vesicular mole, by an "aggressive" treatment with MTX (25 mg e.v. in a single dose) and induction with PgE of the molar emptying. In all cases the patients were treated after uterine revision with three cycles of prophylactic treatment with MTX (10 mg/die \times 5 days with an interval of 30 days).

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The patients follow-up was carried out with monitoring of their urinary HCG until they showed negative; from August 1979 the RIA dosage of Beta-subunit of HCG was used in 44 of the 60 patients, with serial withdrawals (once a month for year) and a chest X-ray repeated every 6 months.

In patients with persistence of positive levels of Beta-HCG beyond the 15th week of uterine revision, a further cycle of MTX followed, until the findings of the hormonal samples were completely negative. Patients were submitted to hormonal contraception with advice to avoid a pregnancy for at least a year after treatment.

We considered:

- the distribution over the years of the cases, with rates/1000 live births;
- the age, parity and blood group of the patients;
- the gestational period at the moment of diagnosis;
- the relationship between uterine size and gestational age;
- the histological grading (degree of activation of cytotrophoblast);
- the urinary HCG and Beta-HCG levels in the follow-up of the patients;
- the gestational capacity in the patients reexamined (46/60).

RESULTS AND DISCUSSION

The distribution of the cases per year with rates/1000 live births is reported in Table 1. There is no evidence of a particular trend with the minimum number of cases observed between 1978 and 1985 (only one case), and the maximum number of cases in 1979 (8 cases equal to a rate of 6.6/1000 live births).

The only case of chorionepithelioma came under observation in 1980. No case of relapse of vesicular mole was observed the only patient with chorionepithelioma had had a simple vesicular mole 4 years before. The incidence of vesicular mole proved in total to be 3.6/1000 live births, that of chorionepithelioma of 0.06/1000 live births. The relation between chorionepithelioma and vesicular mole was 1:60, almost double in respect to the large American case-series which reported an average the value of 1:35.

Table 1. - Analysis of the case-series and rates/1000 live births.

Year	Hydatidiform mole		Invasive mole	Chorion-epithelioma	
	No. cases	Rates/1000 live births		No. cases	Rates/1000 live births
1976	6	4.0	-	-	
1977	5	3.3	-	-	
1978	1	0.7	-	-	
1979	8	6.6	-	-	
1980	2	1.6	-	1	0.7
1981	6	5.0	-	-	
1982	4	3.3	-	-	
1983	7	6.0	-	-	
1984	4	3.7	-	-	
1985	1	0.9	-	-	
1986	6	5.8	-	-	
1987	5	4.7	-	-	
1988	3	2.8	-	-	
1989	2	1.8	-	-	
Total	60	3.6	-	1	0.06

Age of the patients: under 20 years there were 6 cases (10%), between 21 and 30, 29 cases (48.3%), between 31-40 (23.3%), between 41-50 8 cases (13.3%) and over 50 years 3 cases (5%). The highest number of cases resulted concentrated between 21 and 30 years, in the group of a woman at highest fertility; 6 cases below 20 years and 3 cases over 50 years, must be especially noted because at the age considered most at risk for this disease.

Parity: 21 patients (35%) were in their first pregnancy, 5 (8.3%) had only had abortions before, and 34 (56.6%) were pluriparous.

Blood group: of the 60 patients, 28 (46.6%) presented ORh+ group, 15 (25%) a Rh+ group, while the remaining 17 (28.3%) presented other different groups.

Gestational age: before the 10 week, 17 cases (28.3%) were diagnosed, between 11th-15th week 32 cases (53.3%), between 16th-20th week 9 cases (15%) and beyond 21st week 2 cases (3.3%).

There were 11 cases diagnosed in relatively advanced gestational age (beyond the 16th week). These cases, however, refer to the first years of the case-series before the introduction of routine echographic examination, which has permitted diagnosis at much earlier gestational age.

Relationship between uterine size and gestational age: in 22 cases (36.6%) the uterine size was greater than the amenorrhea, in 27 cases (45%) it was equal, and in 11 cases (18.3%) it was less.

Degree of proliferation of the cytotrophoblast: in 32 cases (53.3%) there was

Picture 1 shows the monitoring of Beta-HCG levels in the 44% of patients in whom it was possible to carry out the examination, in 7 patients (11.6%) the Beta-subunit remained, even if modestly positive after 5 months from the uterine revision. Therefore in 4 of these patients a further treatment with MTX became necessary. In the remaining 3 patients Beta-HCG values were negative after the 20th week without further treatment.

Gestational capacity: the patients who returned to control (one patient had died in 1980 from chorionepithelioma) were

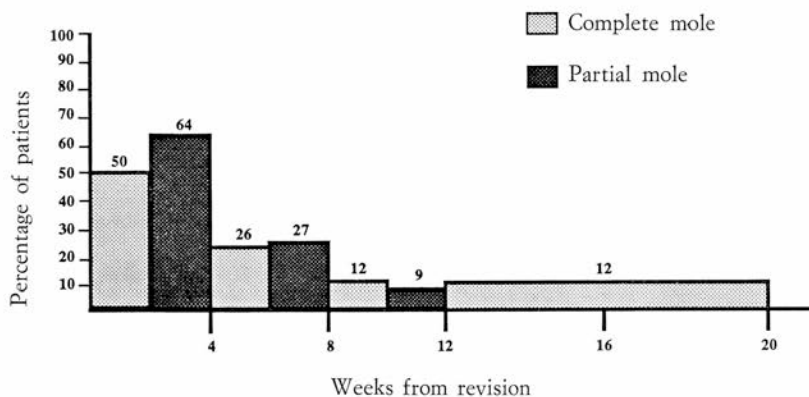


Fig. 1. — β -hCG levels in gestational trophoblastic disease.

a low trophoblastic activation (G1), in 21 cases (35%) there was a moderate proliferation (G2), and only in 7 cases (11.7%) was there high activation (G3).

Hormonal monitoring: the urinary HCG assay, showed 3 cases (5%) which were already negative at the moment of observation (mole so-called "extinguished" from the hormonal point of view), and a very high level (1.827.000 IU/l) observed in the only patient who after 4 years had had a chorionepithelioma. Of the 60 cases, 59 (98.3%) had been negated from urinary point of view within 15 days of the uterine revision; the remaining case was negated 30 days later.

46 (77%): of these 12 (29%) had had 20 pregnancies following hydatiform mole. Of these 20 pregnancies, 15 were carried to term with spontaneous delivery, 3 ended in abortive pregnancy and one in a endouterine fetal death. In the sum total, one of the patients reexamined who is not included, is now pregnant and carrying her pregnancy to term.

The gestational capacity was 78.9%, similar on that of the general population.

CONCLUSION

From the analysis of the case-series, first of all emerges the high incidence of

GTD which we met (3.6/1000 live births) higher than the Italian average (0.8/1000 live births) ⁽²⁾, and than that we reported in a previous study on all the cases observed in the Province of Sassari (1.46/1000 live births) referring to the period 1974-83 ⁽¹⁾. However, it must be considered that the majority of the cases observed in our territory are concentrated in our Institute, so that it is possible for such incidence to be overestimated.

On the contrary, our study confirms the very low incidence of chorionepithelioma (0.06/1000 live births) which is placed at the lowest levels of all literature worldwide ⁽²⁾, with similar values to that we met in the study conducted on the whole Province (0.04/1000 live births) ⁽¹⁾.

This, together with the datum of a very low percentage (11.6%) of moles with a high proliferative trophoblastic activity, leads us to consider that the high incidence of benign trophoblastic disease encountered in our Region, is not accompanied by an evolution of this pathology, even if we remember that all the cases we have observed have been treated with prophylactic chemotherapy.

With regard to epidemiologic characteristics, no important data have emerged with the exception of age (11 cases over 40 year and 6 cases under 20 years) and of the ABO typing (notable incidence of ORh+ group), factors which agree with the hypothesized chromosomal genesis of the disease.

The follow-up of our patients revealed the inadequacy of monitoring only urinary HCG, considering that the negativization

in these cases occurred within 15-30 days from the uterine revision, while the serial monitoring of the Beta-HCG levels allowed the early individuation of cases with persistent trophoblastic disease, to undergo further treatment.

Finally the gestational capacity of patients who returned to control proved to be high, with an abortion rate similar of the general population. Therefore with absence of negative consequences by previous chemotherapeutic treatment.

It is, however, extremely important, for this reason, to avoid patients entering a further pregnancy before a year from the end of treatment, after an accurate clinical, echographic and, above all, hormonal control, with a demonstration of complete absence of the serum finding.

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