'EUTHYROIDAL' GOITER AND MENSTRUAL DISORDERS

M. GANGEMI, M. BENATO,
G. MENEGHETTI, D. LICORI,
D. MARCHESONI

Department of Obstetrics and Gynecology,
University of Padua (Italy)

SUMMARY

We selected 5 patients, between 18 and 31 years of age, presenting menstrual irregularities and thyroidal goiter with no apparent functional change (normal T_4 and T_3 tests). These patients underwent further examinations: TSH (basal and after TRH stimulation), HPRL (basal-circadian rhythm and after TRH stimulation), FSH and LH (basal and after Gn-RH stimulation), thyroidal scintiscan, search for antithyroidal antibodies.

Basal and post-stimulation TSH was fundamental in 2 cases of subclinic hypothyroidism. The positive antibody search confirmed the autoimmunitary origin.

In the same patients, the HPRL circadian rhythm and TRH test highlighted a secondary hyperprolactinemia which would not have been revealed by a single basal sample.

The hypothalamus - hypophysis - ovary and hypothalamus - hypophysis - thyroid axes increasingly appear to be closely correlated.

A decreased ([1, 2]) or increased ([3, 4]) incretion of thyroidal hormones (the main metabolic regulating agents in human organisms) originates a wide range of menstrual disorders, showed by menorrhagias and menometrorrhagias in hypothyroid women and by hypomenorrhea and amenorrhea in hyperthyroid women.

There is a close relation between the regulation of hormones and prolactin secretions. In particular, in primitive hypothyroidism, TRH overproduction often causes prolactin hypersecretion resulting in amenorrhea and galactorrhea ([5]). The endocrine relations between menstrual disorders and a palpable thyroidal goiter, with no apparent thyroid misfunctioning, are difficult to understand.

We studied a group of apparently euthyroidal patients, whose thyroidal functionality had been screened on the basis of the usual parameters, with normal results. Our study aimed at finding possible endocrine connections between objective evidence of thyroidal goiter and concomitant menstrual disorders.

MATERIAL AND METHODS

Among the patients who came to our Endocrinology Centre we chose five women presenting association of thyroidal goiter, though with normal T_4 and T_3 tests, and altered menstrual rhythm.

The following parameters were evaluated in all the patients, to establish their hormonal profile:

— T_4 and T_3 basal tests;

— TSH, basal and after TRH stimulation (200 mcg e.v.) at 20′ and 60′;

— prolactin circadian rhythm (HPRL) through blood sampling every 2 hours for 24 hours, in basal conditions;

— plasma HPRL after TRH stimulation (200 mcg e.v.) at 10′, 20′, 30′, 40′, 50′, 60′, 90′;

— FSH and LH, basal and after double Gn-RH (Relisorm, Serono, 100 mcg e.v.) stimulation.

Sampling was performed at 0′ (9 a.m.) and after 15′, 30′, 45′, 60′ from stimulation; the

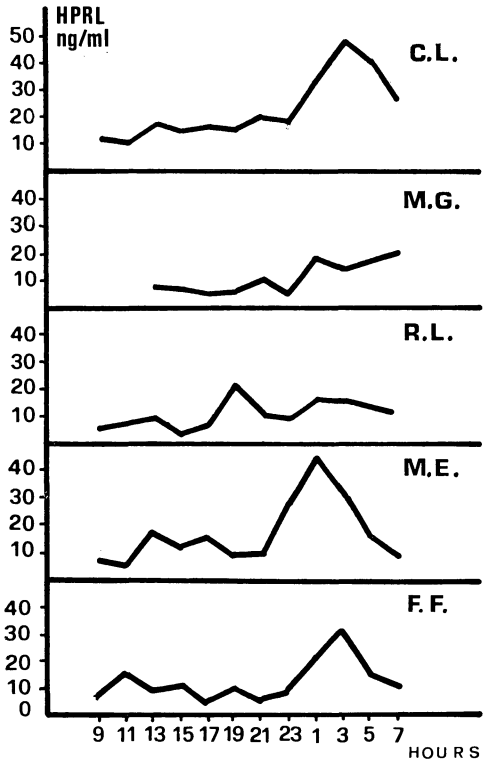

Fig. 1. — HPRL basal circadian rhythm.

second stimulation, 120′ (11 a.m.) after the first, was followed by sampling after 15′, 30′, 45′, 60′ and, finally, at 1 p.m., 3 p.m. and 5 p.m.

The dosage of all hormones was performed in plasma by the radioimmunologic method, using Biodata kits for HPRL-FSH-LH, Abbot kits for TSH and Medical System kits for T_4 and T_3 tests.

Finally, all patients underwent thyroidal scintiscan with Te^{99} and I^{131}, to confirm the clinical report of goiter and look for antithyroid antibodies, so as to disclose possible autoimmunitary processes.

RESULTS

Fig. 1 reports HPRL plasma concentrations, evaluated in basal conditions for 24 hours. During the first few hours, in C.L., M.E. and F.F., HPRL exceeded normal levels, reaching clearly pathologic values.

Fig. 2 reports HPRL response to TRH stimulation. In all 5 patients, notably in C.L., M.E. and F.F., the prolactinemic response reached abnormally high values, particularly in the early phase of stimulation. Furthermore, in C.L. and M.E., basal values were resumed after longer periods.

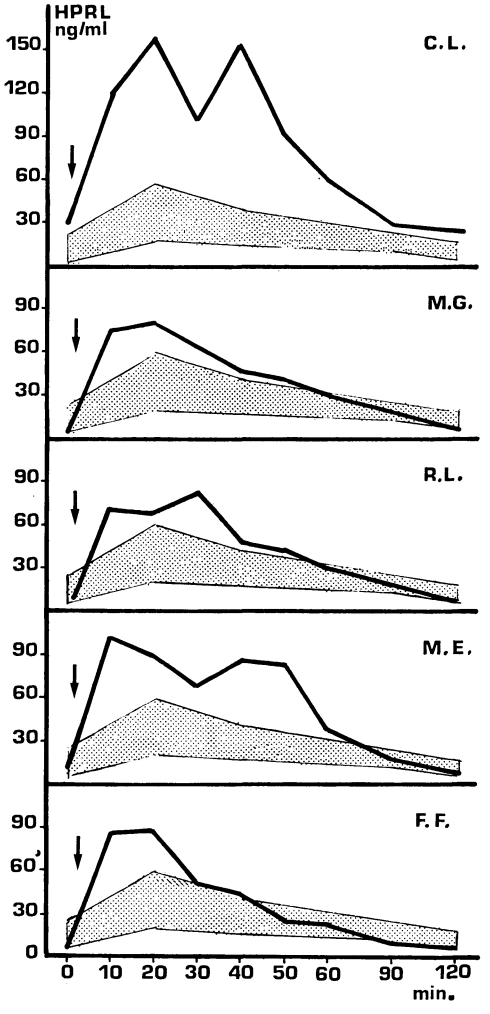

Fig. 2. — HPRL response to TRH test.
↓ = TRH 200 mcg e.v. Normal values are in the dotted area.

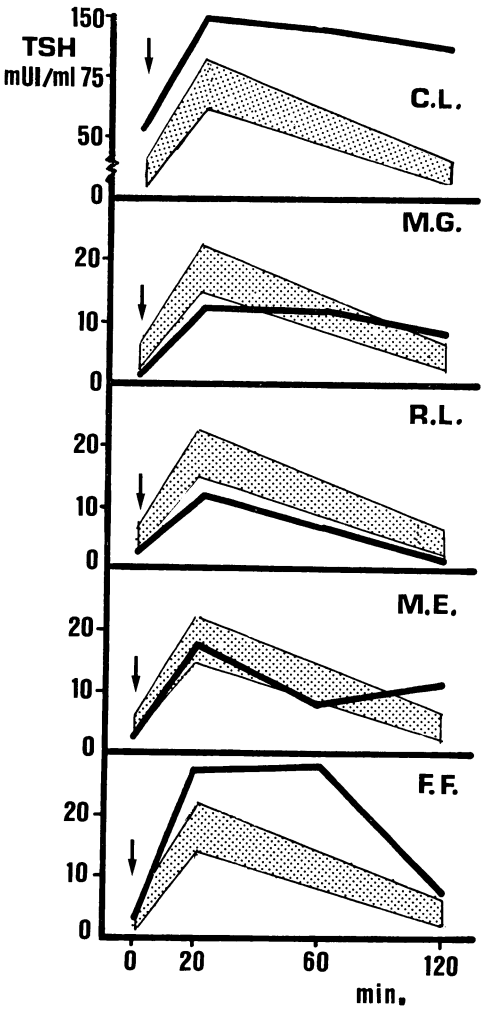

Fig. 3. — TSH response to TRH test.
↓ = TRH 200 mcg e.v. Normal values are in the dotted area.

Fig. 3 reports TSH results, both basal and after TRH stimulation. C.L. and F.F. showed clearly increased TSH responses. In C.L. values were already high in basal conditions (0') whereas the remaining patients presented normal values.

Fig. 4 reports FSH and LH values (basal and after Gn-RH stimulation). They differ widely according to the patient. R.L. presented high basal gonadotrophins, but poor responsiveness to stimulation. The other patients presented more complex responses. C.L., M.E. and F.F. showed LH hyperresponses; C.L. showed no FSH response and M.G. had a normal response.

Table 1 reports a synthesis of the anamnestic, clinical, instrumental (thyroidal scintiscan) and laboratory (search for antibodies) data which, together with the hormonal profiles, enabled us to understand the thyroidal picture within the gynecologic pathology that had led the examined patients to our Centre of Gynecologic Endocrinology.

DISCUSSION

At the beginning of this work we said that our patients were selected on the basis of the association of thyroidal goiter with normal T_4 and T_3 test values (being these the most commonly used parameters of thyroidal functionality). We also pointed out that the thyroid is almost as important as the gonads in the screening of amenorrhea or, rather, menstrual disorders. The reported data show that the first diagnostic approach was unable to highlight any change in the thyroidal functionality of these patients, presenting normal HPRL basal values and normal parameters of thyroidal screening (T_4 and T_3 tests). Only the clinical report of goiter could suggest the presence of thyroidal misfunctioning. However, the subsequent more thorough diagnosis highlighted extremely useful data, revealing a pathology that the usual parameters had failed to show.

In our opinion, TSH evaluation must always match the screening for thyroidal functionality.

C.L. and F.F. were affected by subclinic hypothyroidism of autoimmunitary

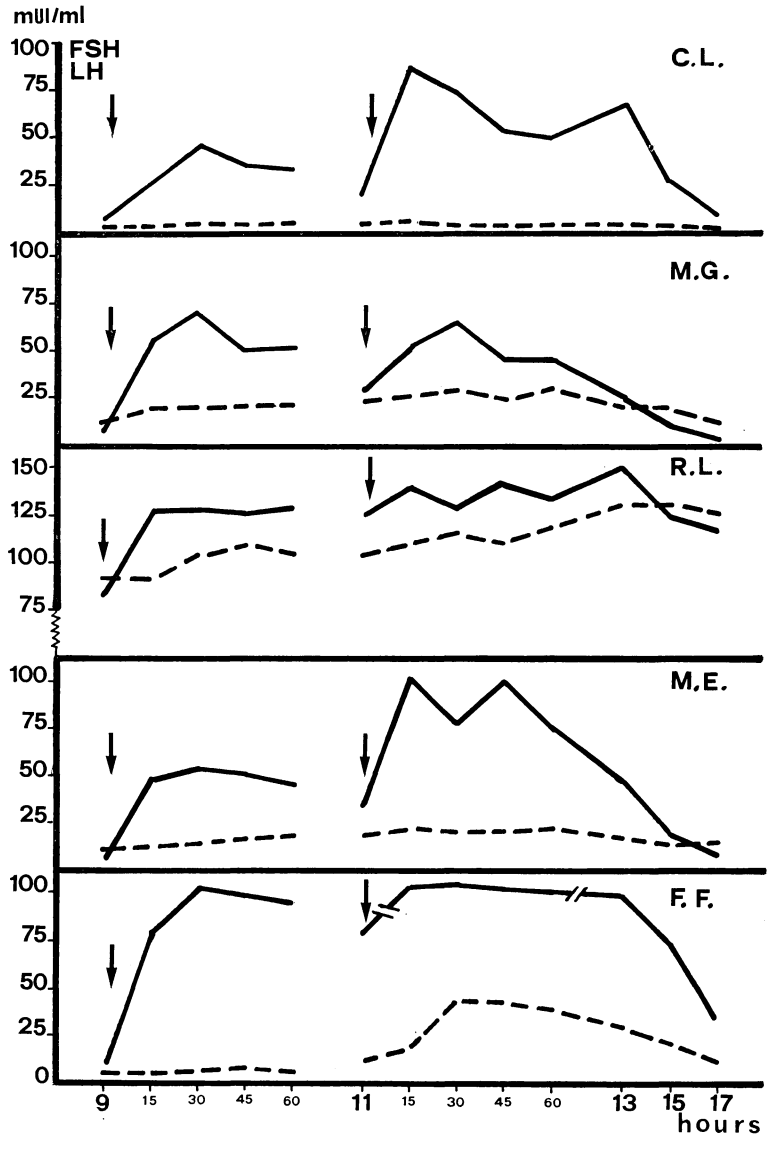

Fig. 4. — FSH and LH response to GnRH test (GnRH double stimulation).
↓ = Relisorm 100 mcg e.v.; —— LH; - - - FSH.

Table 1. — *Anamnestic, clinical and laboratory data of patients affected by asymptomatic goiter and menstrual disorders.*

Name	Age	Anamnesis	Thyroid P.E.	Gynecologic P.E.	Thyroid scintiscan	Thyroid antibodies	Diagnosis
C. L.	26	Oligomenorrhea	Enlarged hard	Normal finding	Normal right lobe; small adenomatous nodule in the left lobe	Anticytoplasmic Ab 1:160 Low positivity of gastric parietal cells Ab	Autoimmune thyroiditis Atrophic gastritis
M. G.	18	Amenorrhea	Enlarged	Hypoplastic uterus; normal finding	Enlarged thyroid with normal morphology	Negative	Thyroidal goiter
R. L.	31	Amenorrhea	Enlarged	Hypoplastic uterus; normal finding	»	»	Thyroidal goiter Precocious menopause
M. E.	30	Amenorrhea	Enlarged hard	Normal finding	»	»	Thyroidal goiter
F. F.	18	Oligomenorrhea	Enlarged hard - parenchymatous	Hypoplastic uterus; normal finding	Enlarged with irregular iodine accumulation	Anticytoplasmic Ab 1:80	Autoimmune thyroiditis

origin, as the finding of antithyroidal antibodies confirms (see tab. 1).

The case of R.L. presents particular features. She came to our Centre of Gynecologic Endocrinology because suffering from secondary amenorrhea since a few months. She was chosen and included in the study group according to the already mentioned criteria (association of goiter, normal T_4 and T_3 tests and menstrual disorders). It was only after all the examinations envisaged by our protocol that her precocious menopause was clearly established. A few months earlier, the FSH and LH tests had given normal results!

Prolactin data can enable us to draw useful conclusions. Single evaluations of this hormone are often rather useless, given circadian variations and the very fast pulsation rhythm. But, through various samples taken every two hours for 24 hours, three patients showed differing pathologic hikes in the early hours of the morning.

In C.L. and F.F. this is readily explained by their subclinic hypothyroidism. Hence the presumably high TRH values and the relative HPRL hyperproduction in hours when this hormone is normally mainly produced. The data obtained after TRH stimulation confirm the anomalous prolactin secretion, which is likely to play an important role in the pathogenesis of C.L.'s and F.F.'s menstrual disorders.

The other data are harder to understand. The evaluation of FSH and LH (basal and after Gn-RH stimulation) is of little help.

In conclusion, while thyroidal functionality must always be assessed when studying menstrual disorders, TSH evaluation is always advisable in the screening for thyroidal hypofunctionality. In case of further doubts, a TRH test to assess TSH changes under stimulation should follow. Several HPRL dosages or, rather, a circadian rhythm are advisable before ruling out hyperprolactinemia in these secondary cases.

Besides providing useful data on TSH secretion, the TRH test gives important information on HPRL hypophyseal release.

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