INADEQUATE LUTEAL PHASE AND BENIGN BREAST DISEASE

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SUMMARY

The Authors compare E2 and Progesterone plasma levels in the luteal phase of twelve normally menstruating women whose basal body temperature curves were biphasic and in which breast micronodularity and mastodynia were present, with those of ten breast disease-free controls.

The significant difference ($p < 0.001$) found in Progesterone levels gives strength to the opinion that Progesterone supply therapy can effectivley improve both mastodynia and the clinical picture objectively documented.

Mastosis can be defined as a degenerative breast disease the origin of which is neither phlogistic nor neoplastic; it is very frequent in women's reproductive age and mostly affects women who are nulliparous, or never breast-fed, or more frequently present anovulatory cycles as do neurolabile and obese subjects.

Scientifical experiences already demonstrated that E2 induces cell-proliferation in galactophorous ducts while Progesterone, rhythmically secreted in the menstrual cycle, interrupts the proliferative process and promotes acinar differentiation.

Mastosis, which developes on a dysendocrine ground, often remains clinically silent and appears as a frequent ([1]), though incidental, autoptic finding; sometimes, on the contrary, mastodynia is present, which mainly affects the premenstrual phase.

The purpose of our study is to investigate the endocrine back-ground of symptomatic patients whose menstrual cycles are quite regular, to make the rationale clear of an eventual hormonal supply therapy.

MATERIAL AND METHODS

Twenty-two out-patients were investigated: ten were normal controls; twelve were affected with mastodynia which mainly affected the premenstrual phase, and presented a picture of micronodularity widely interesting one or both breasts, which was diagnostically confirmed through plate-thermography, transillumination, echography and, when necessary, mammography.

The affected patients' mean age was 27 ± 7 years; their menstrual cycles lasted 29 ± 4 days; their basal body temperature curves were biphasic and galactorrhea was absent.

Blood was drawn from every patient's cubital vein between 8 A.M. and 10 A.M. in the 3rd, 6th and 9th day from the thermal rise: Progesterone and Estradiol R.I.A. was then performed on each sample (Serono-Biodata Kit; assay sensitivity of 15 ng/ml and 10 pg/tube, respectively).

The significativity of the differences between the averages of the two hormones in both groups was calculated by the Student's t test.

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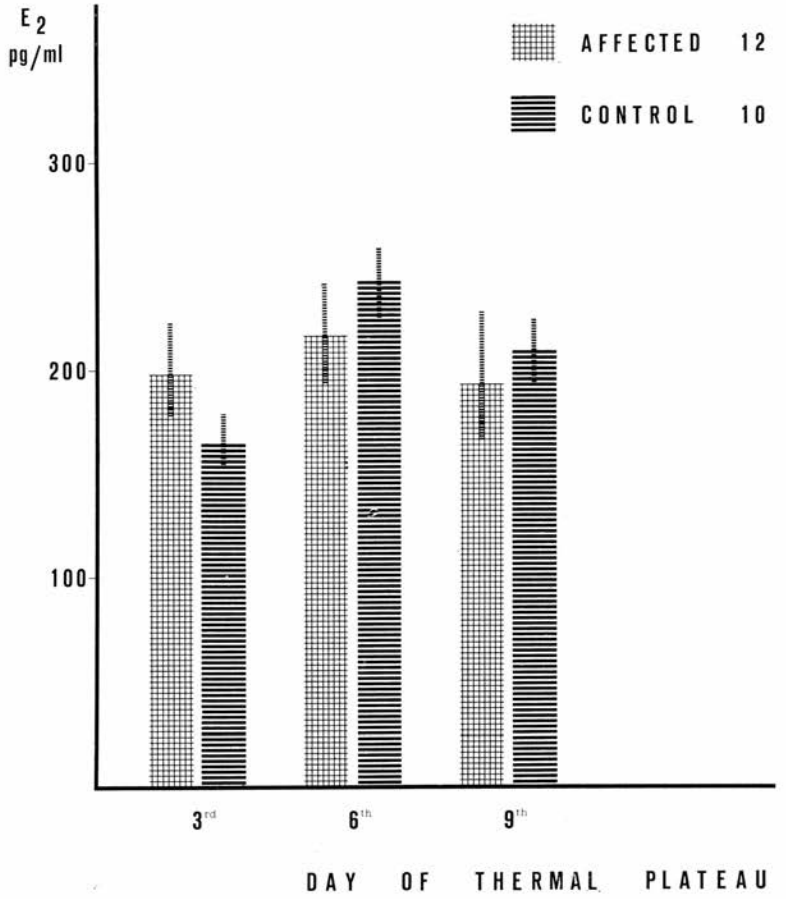

Fig. 1. — E2 plasma levels in the 3rd, 6th and 9th day of the thermal plateau in the control and affected patients.

The luteal phase ratio P/E2 was then calculated in both groups according to the formula [2]

$$PEL = \frac{P\ (pg/ml)}{E2\ (pg/ml)} \times 0.001$$

RESULTS

E2 plasma levels were 203.9 ± 11.4 (SE) pg/ml in the control group and 134.3 ± 16.8 (SE) pg/ml in the affected group: no statistically significant difference was found between these values ($t = 1.8$; $p = NS$).

Progesterone plasma levels were 23.4 ± 1.5 (SE) ng/ml in the control group and 10.9 ± 0.7 (SE) ng/ml in the affected group: the value-difference was statistically significant ($t = 8.6$; $p < 0.001$).

Estradiol and Progesterone average plasma levels in the 3rd, 6th and 9th day of the thermal plateau are shown for both groups in figs. 1 and 2.

The PEL value was 0.52 in the affected patients and 1.13 in the controls.

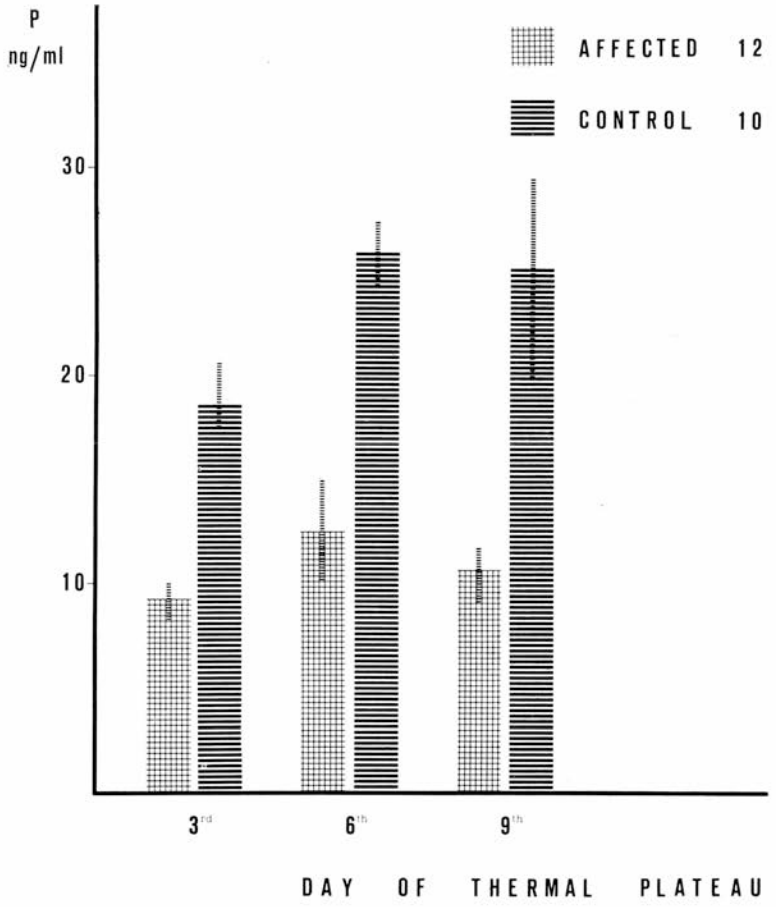

Fig. 2. — P. plasma levels in the 3rd, 6th and 9th day of the thermal plateau in the control and affected patients.

DISCUSSION AND CONCLUSIONS

Almost ([3]) every ([2, 3, 4, 5, 6, 7, 8]) Author reports that patients affected with benign breast disease associated or not with mastodynia, also present a luteal deficit of the type of the short or inadequate luteal phase.

Our data (figs. 1 and 2) seem in agreement with that and support the opinion according to which breast normal development can only be achieved when an ideal ratio is present between Estradiol and Progesterone activities.

While Estradiol plasma levels are quite similar in both groups, Progesterone levels are significantly lower in the women presenting micronodular breast disease associated with mastodynia.

We think that the mainly involved factor in the etiopathogenesis of this disease is the luteal-phase relative hyperestrinism.

The luteal deficit, both in the short and inadequate luteal phase, makes the estrogen action free from the physiological modulation exerted by Progesterone in target-tissues, where it lowers E2-receptor

levels and increases the intracellular concentration of 17-beta-OH-dehydrogenase, the enzyme which converts E2 to E1.

When Estradiol and Progesterone actions are not synchronized, breast-tissue is thought to undergo alterations [9] which lead to cancer through hyperplasia and dysplasia, even if many Authors [10, 11] don't believe that this is true.

The examination of our series points out the presence of normal menstrual cycles and biphasic basal body-temperature curves in all the patients affected with micronodularity, and demonstrates that a clinical investigation simply based on the two above mentioned parameters is quite ineffective to detect a luteal pathology with the characteristics of the short and the inadequate luteal phase.

Particularly, the finding of a biphasic basal body-temperature curve only indicates that ovulation intervened, but only Progesterone Radio-Immuno-Assay can assure about a correct luteal function.

Only when Progesterone levels are lower than 3 ng/ml [6, 13], in fact, a lack of the rise in basal body temperature is found; a smaller decrease in Progesterone levels, however, is considered sufficient to rise breast symptoms, and in our opinion, whenever Progesterone levels are lower than 10 ng/ml, a Progesterone supply should be considered, to improve mastodynia and breast premenstrual tension together with the breast micronodular picture [12]. Progestin therapy in these patients' luteal phase, besides its effects against subjective symptoms, should be considered, at last, a very important step in the prophylaxis of much more serious breast diseases.

BIBLIOGRAPHY

1) Kramer W. M., Rush B. F.: *Cancer, 31*, 130, 1973.
2) Mauvais-Jarvais P., Kutten F., Mowszowicz I., Sitruk-Ware R.: *Nouv. Presse Med., 6*, 4115, 1977.
3) Geller S., Grenier J., Nahoul K., Scholler R.: *Ann. Endocrinol., 40*, 45, 1979.
4) Mauvais-Jarvais P., Ware R., Sterkers N., Tamborini A.: *Ann. Endocrinol., 37*, 309, 1976.
5) Mauvais-Jarvais P., Ware R., Sterkers N., Ohlgiesser C., Tamborini A.: *Ann. Endocrinol., 37*, 347, 1976.
6) Sitruk-Ware R., Sterkers N., Mowszowicz I., Mauvais-Jarvais P.: *J. Clin. Endocrinol. Metab., 44*, 771, 1976.
7) Sitruk-Ware R., Sterkers N., Mauvais-Jarvais P.: *Obst. Gyn., 53*, 457, 1979.
8) Gairard B.: *Rev. Med., 9*, 477, 1979.
9) Donelly P. K., Baker K. N., Carney J. A., O'Fallon W.: *Mayo Clin. Proc., 50*, 640, 1975.
10) Silverberg S. G.: *Cancer, 29*, 574, 1972.
11) Devitt J. E.: *Lancet, 1*, 793, 1976.
12) Mauvais-Jarvais P., Sterkers N., Kutten F., Beauvais J.: *J. Gyn. Obst. Biol. Repr., 7*, 477, 1978.
13) Abrahm G. E., Maroulis G. B., Marshall J. R.: *Obst. Gyn., 44*, 522, 1974.