

Morphofunctional Characteristics of the Ovaries in Proliferative Uterine Myoma

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Morphofunctional changes in the ovaries in women of reproductive age with proliferative uterine myoma were studied. Disorders in folliculogenesis with primordial follicles degeneration of different degree, cystic degeneration of follicles at different stages of their development, paralleled by hyperplasia of the theca-granulosa complex and hyperestrogenemia, were detected. Morphological equivalent of hyperestrogenemia is increased content of lipid inclusions in granulosa cells, ultrastructural hyperplasia, increased volume and quantity of secretion-containing Cull-Exner bodies.

Key Words: *proliferative myoma; ovarian theca-granulosa complex; histochemistry; ultrastructure*

Proliferative uterine myomas are little studied, particularly their patho- and morphogenesis, characteristics of cell proliferation, angiogenesis, and parenchyma-stroma relationships [2,4]. Hyperestrogenemia and progesterone, as well as growth factors, play an important role in the development of uterine myomas [2]. A node can grow as a result of intensive proliferation and be due to limitation of cell death [5].

Myoma is a hormone-dependent local hyperplasia of smooth-muscle cells, and hence, the ovaries play a special role in the development of this condition and regulation of proliferative processes. Folliculogenesis and steroid synthesis are realized in the ovaries [3], with the theca interna and granulosa cells involved in these processes [6]. Estrogen excess and disorders in the adaptation mechanisms of the entire steroid homeostasis system are essential for the development of uterine myoma [4]. We failed to find reports on complex studies of the ovaries in patients with proliferative uterine myoma. These studies are particularly important for women

of reproductive age (under conditions of active functional activity of the ovaries).

Our complex study of the ovaries, including histological, histochemical, electron-microscopic, and morphometric analysis, was carried out in women of reproductive age with proliferative uterine myoma.

MATERIALS AND METHODS

The follicular system of the ovaries was studied in 7 women (aged 30-35 years) with proliferative uterine myoma. Operation for uterine myoma was carried out during the second phase on day 20 of the cycle. Specimens of the ovaries from women of the same age without diseases of the reproductive system, dead from accidents served as the control.

Specimens of the ovaries and myoma nodes of the corpus uteri collected during surgery were fixed in 12% formalin and embedded in celloidine. Sections (5-6 μ) were stained with hematoxylin and eosin. For detection of sudanophilic lipids, cryostat sections were made and stained with Sudan III. For electron microscopy, the material from cystic atretic follicles was fixed in 2.5% glutaraldehyde (pH 7.4), postfixed in 1% osmium tetroxide, and em-

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bedded in epon. After double contrasting with uranyl acetate and lead citrate ultrathin sections were examined in a Tesla BS 500 electron microscope at accelerating voltage of 70-90 kV.

Morphometric study was carried out using an ocular micrometer on preparations stained by hematoxylin and eosin ($\times 630$). The thickness of the theca interna was measured for each cystic follicle (a total of 100 follicles per case were evaluated). The volume of granulosa cells and Cull-Exner bodies was estimated by the formula: $V=0.523 LB^2$ (L the greater and B minor diameters) [1]; 100 cells were measured for each case [1].

Ten classes were distinguished from the resultant variation series using the formula:

$$K = \frac{\text{Maximum volume} - \text{Minimum volume}}{\text{Number of classes}}$$

The results were processed by methods of variation statistic using Student's *t* test.

RESULTS

Of 7 cases with proliferative uterine myomas, single-node myomas were detected in 4 patients (submucosa nodes 9 and 5 cm in diameter in 2 cases and intramural nodes 13 and 6 cm in diameter in 2 other cases). Multinodular myomas of different size (up to 9 cm) with submucosal nodes located in all layers of the myometrium were detected in 3 cases. Necrobiosis and hyalinosis in large nodes were detected in 3 and 3 cases, respectively.

Smooth muscle cell proliferation was observed mainly at the node periphery. Cell proliferates were located around blood vessels, presenting as muffs; no blood vessels were detected in some areas of the proliferative growth zone. Smooth muscle cells were slightly enlarged and characterized by low mitotic activity; no signs of cell atypia were detected. Structural components of the stroma were poorly pronounced in the tumors. Edema with myxomatous degeneration was seen in some nodes along with proliferative processes, more often in the central zone; hyalinosis was detected in some cases.

One ovary was removed in 5 cases, both ovaries in 2 cases. Small cystic degeneration of the ovaries was observed in almost all cases, with cysts 0.2-1.5 cm in diameter; large cysts (3-4 cm) were detected in only 2 cases.

The number of primordial follicles in the ovaries was decreased in patients with proliferative uterine myoma, with some of them at the stage of necrobiosis (Fig. 1, a). Cystic atretic follicles at

TABLE 1. Volume of Follicular Granulosa Cells in Proliferative Uterine Myoma

Class	Volume by classes, μ^3	Distribution by groups of observation, %	
		control	patients
I	40.4-79.3	58.9	8.6
II	79.4-118.3	23.9	21.1
III	118.4-157.4	17.2	43.0
IV	157.5-196.4	0	7.1
V	196.5-235.5	0	5.1
VI	235.6-274.6	0	4.3
VII	274.7-313.6	0	3.7
VIII	313.7-352.7	0	3.3
IX	352.8-391.6	0	1.9
X	391.7-430.6	0	1.9

TABLE 2. Volume of Follicular Cull-Exner Bodies in Proliferative Uterine Myoma

Class	Volume by classes, μ^3	Distribution by groups of observation, %	
		control	patients
I	108.0-426.2	64.4	55.7
II	426.3-744.4	30.8	15.7
III	744.5-1062.6	4.8	8.6
IV	1062.7-1380.8	0	2.8
V	1380.9-1699.0	0	2.8
VI	1699.1-2017.2	0	2.8
VII	2017.3-2335.4	0	2.9
VIII	2335.5-2653.6	0	2.9
IX	2653.7-2971.8	0	2.9
X	2971.9-3290.0	0	2.9

TABLE 3. Thickness of *Theca Interna* in Cystic Follicles in Proliferative Uterine Myoma

Class	Volume by classes, μ^3	Distribution by groups of observation, %	
		control	patients
I	4.7-14.7	9.5	13.8
II	14.8-19.4	28.4	17.2
III	19.5-24.1	53.7	27.6
IV	24.2-28.8	6.3	7.5
V	28.9-33.5	2.1	6.9
VI	33.6-38.2	0	6.9
VII	38.3-42.8	0	6.9
VIII	42.9-47.6	0	6.3
IX	47.7-52.3	0	3.5
X	52.4-57.0	0	3.4

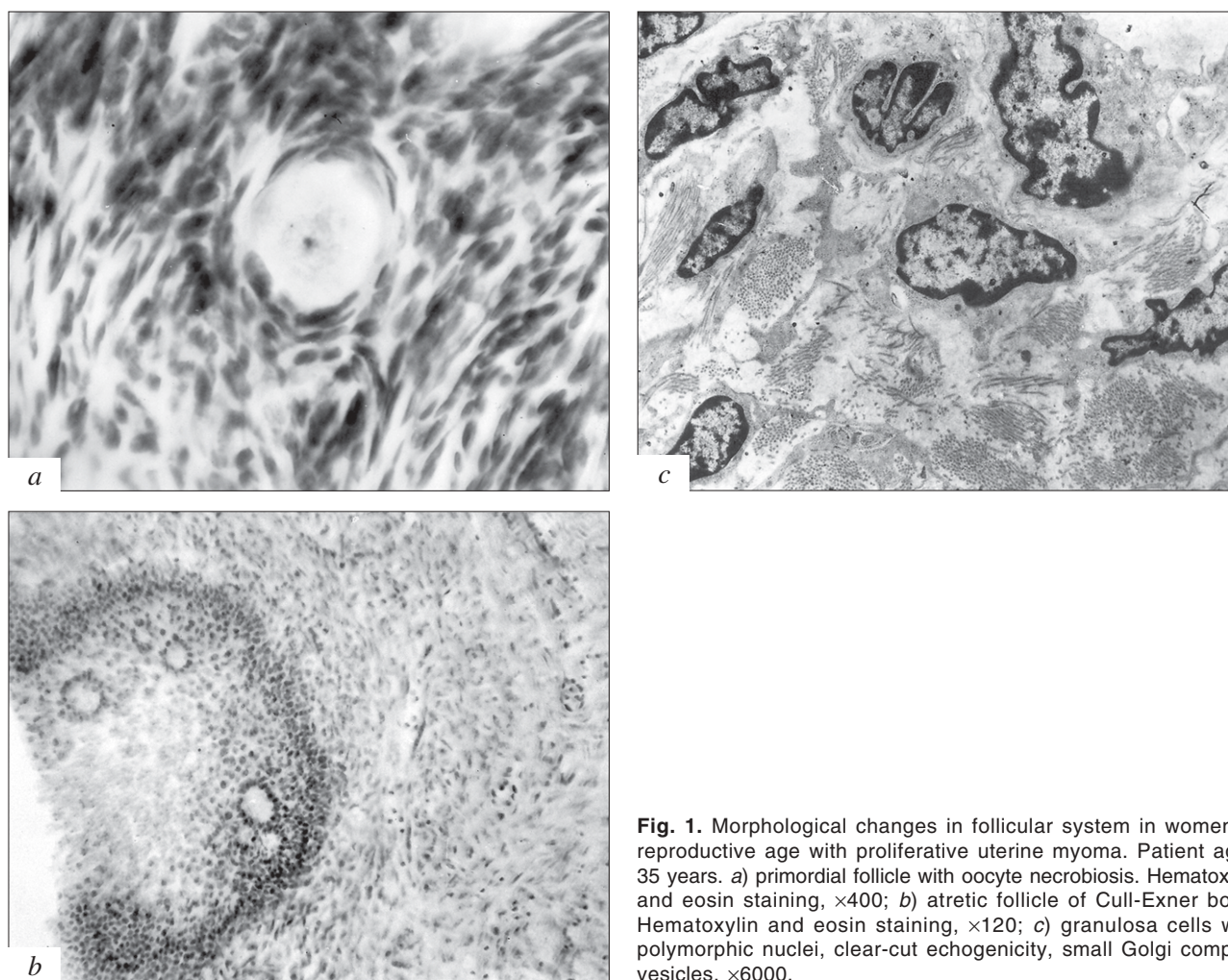


Fig. 1. Morphological changes in follicular system in women of reproductive age with proliferative uterine myoma. Patient aged 35 years. a) primordial follicle with oocyte necrobiosis. Hematoxylin and eosin staining, $\times 400$; b) atretic follicle of Cull-Exner body. Hematoxylin and eosin staining, $\times 120$; c) granulosa cells with polymorphic nuclei, clear-cut echogenicity, small Golgi complex vesicles, $\times 6000$.

different stages of development were seen. Granulosa cells were polygonal, sometimes oval, with round hyperchromatic nuclei and pale cytoplasm; their volume increased in comparison with the control (Table 1). The content of lipid incorporation (medium-sized droplets, usually diffusely filling the entire cytoplasm) also increased. Mitotic activity of granulosa cells was retained. The content and volume of cavities in Cull-Exner bodies located between granulosa cells increased (Table 2). They were oval or round and contained eosinophilic substance (Fig. 1, b).

Light microscopy showed thickened follicular theca interna (Table 3), thecomatosis was detected in 2 cases. The cells in cystic follicles were oval or polygonal, with light, sometimes vacuolated cytoplasm; their nuclei were cyst-like and round. Theca interna was well delineated from the granular layer by the basal membrane. These cells were characterized by high mitotic activity and contained lipid

inclusions. Pronounced vascularization of this layer was observed.

Electron microscopy showed that numerous granulosa cells contained large polymorphic nuclei with discernible nucleoli (Fig. 1, c). Small vesicles of the Golgi complex were seen in the cytoplasm, indicating biosynthetic activity of granulosa cells.

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