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IMMUNOHISTOCHEMICAL CHARACTERISTIC OF MYOMA TISSUE IN PATIENTS WITH UTERINE LEIOMYOMA AFTER TREATMENT WITH ULIPRISTAL ACETATE

The study was performed as a part of scientific research work "Improvement of minimally invasive surgical methods for treatment of certain diseases of vessels, internal and reproductive organs, abdominal wall, thyroid and parathyroid glands, joints, particularly with the use of implants with individually modified surface based on nanobiosensory technologies" (state registration number 0114U002120).

ABSTRACT. Background. Uterine leiomyoma is one of the most common benign tumors of the female genital organs. The main conservative treatment of leiomyoma is progesterone receptor blockers that suppress myoma growth and may lead to its regression. **Objective.** To study the immunohistochemical features of myoma tissue in patients with uterine leiomyoma after treatment with selective progesterone modulator - ulipristal acetate. **Methods.** Leiomyoma tissue obtained from 9 patients after ulipristal acetate treatment were investigated. Group for comparison - leiomyoma from patients without hormonal therapy. Immunohistochemical study of progesterone and estrogen receptors, proliferative activity marker Ki-67 and inhibitor of apoptosis Bcl-2 was performed. **Results.** In the group of patients without preoperative hormonal treatment progesterone receptors were expressed in 76,4±6,8% of the nuclei, estrogen receptors - in 32,8±2,6%. In the group of patients after treatment with ulipristal acetate there was a significant decrease of progesterone receptor expression – 36,8±1,28% ($p < 0,05$) and a nonsignificant decrease of estrogen expression – 30,7±3,4% ($p > 0,05$). Bcl-2 in the control group was found in 65,4±7,2% cells, in leiomyoma after treatment there was a significant decrease of bcl-2 – 42,6±3,2% ($p < 0,05$). In leiomyomas without hormonal treatment Ki-67 was determined in 11,8% of the nuclei of smooth muscle cells, and in leiomyomas after ulipristal acetate – in 7,2% leiomyoma cells. **Conclusions.** In patients after three months of ulipristal acetate treatment there was a significant decrease of expression of progesterone receptor, bcl-2, and Ki-67. Taken together these data evidence reduced action of progesterone on leiomyoma cells, induction of apoptosis and decreased proliferation processes that may cause involution of fibroids.

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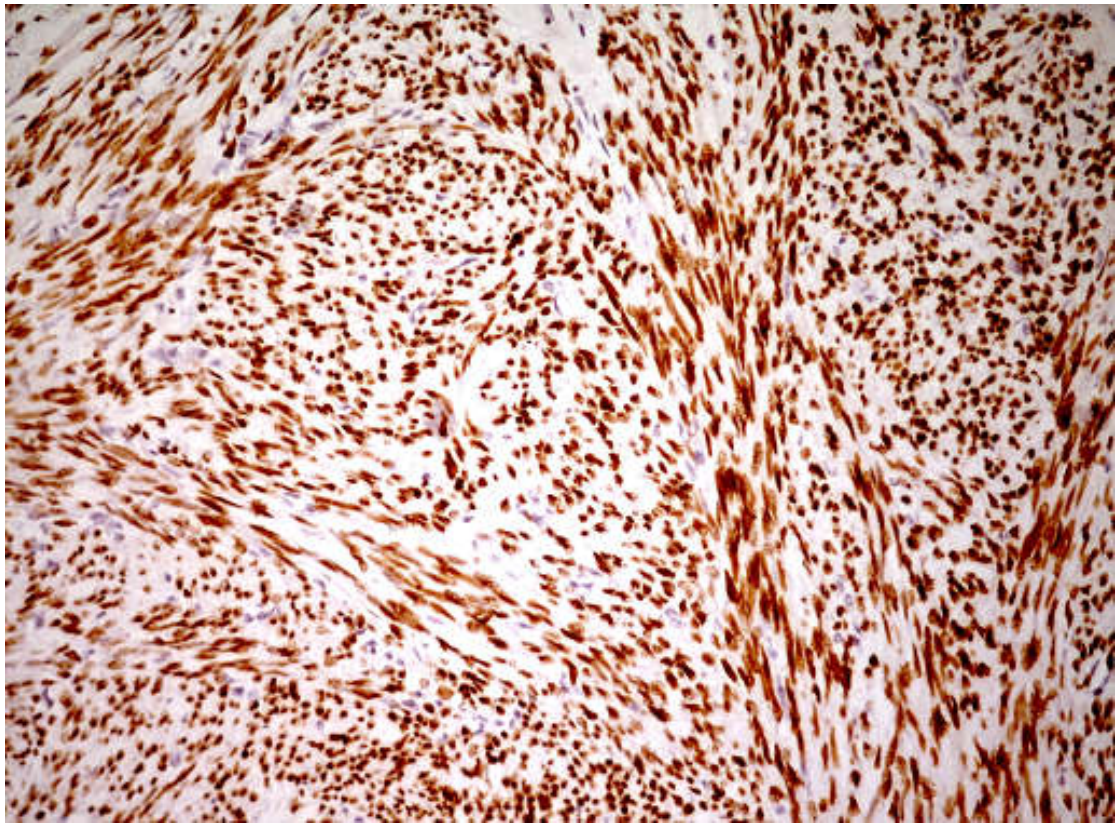


Fig. 1. Expression of receptors for progesterone in the nuclei of leiomyoma smooth muscle cells. Control group. Immunohistochemical investigation. $\times 200$.

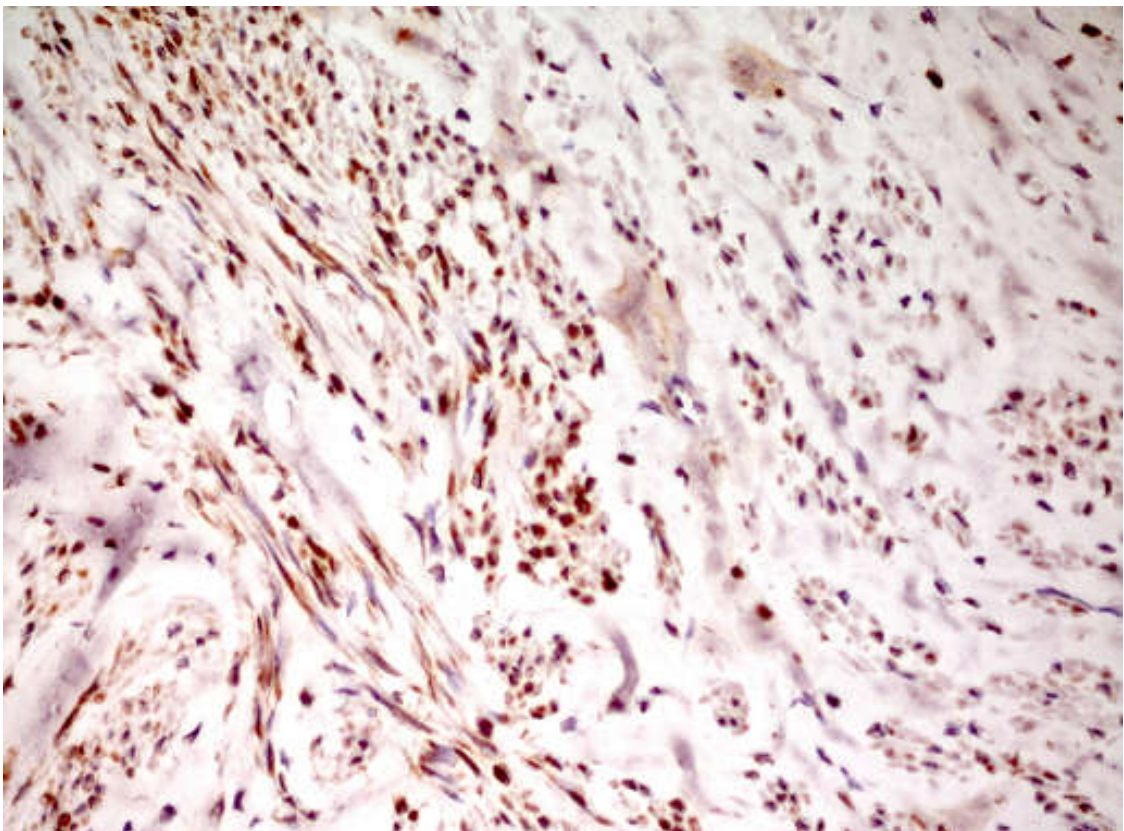


Fig. 2. Expression of receptors for progesterone in the nuclei of leiomyoma smooth muscle cells. Group of patients who received ulipristal acetate. Immunohistochemical investigation. $\times 200$.

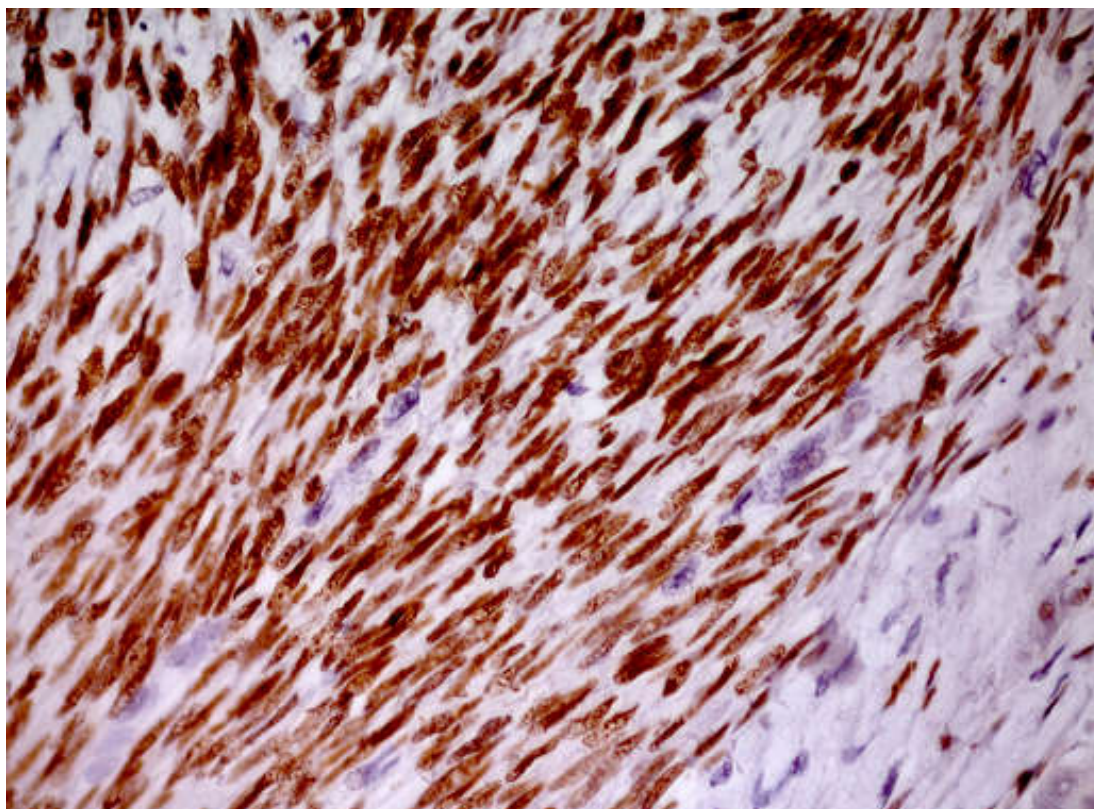


Fig. 3. Expression of apoptosis inhibitor bcl-2 in the nuclei of leiomyoma smooth muscle cells. Control group. Immunohistochemical investigation. $\times 400$.

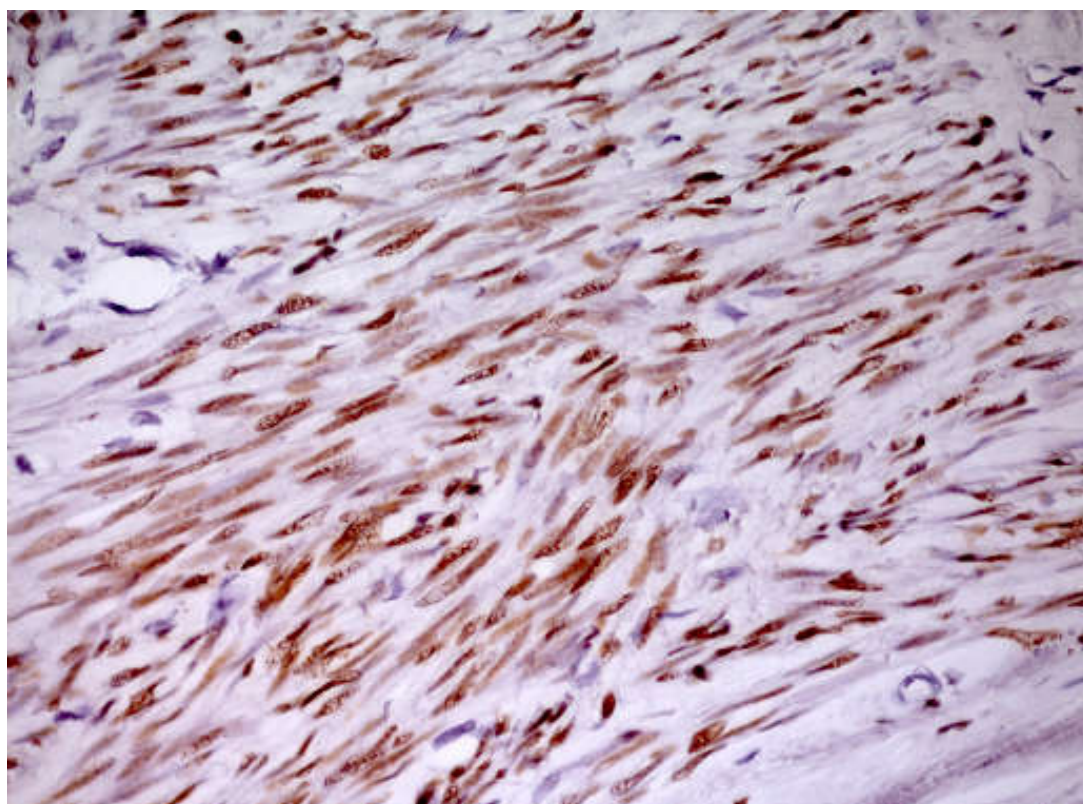


Fig. 4. Expression of apoptosis inhibitor bcl-2 in the nuclei of leiomyoma smooth muscle cells. Group of patients who received ulipristal acetate. Immunohistochemical investigation. $\times 400$.

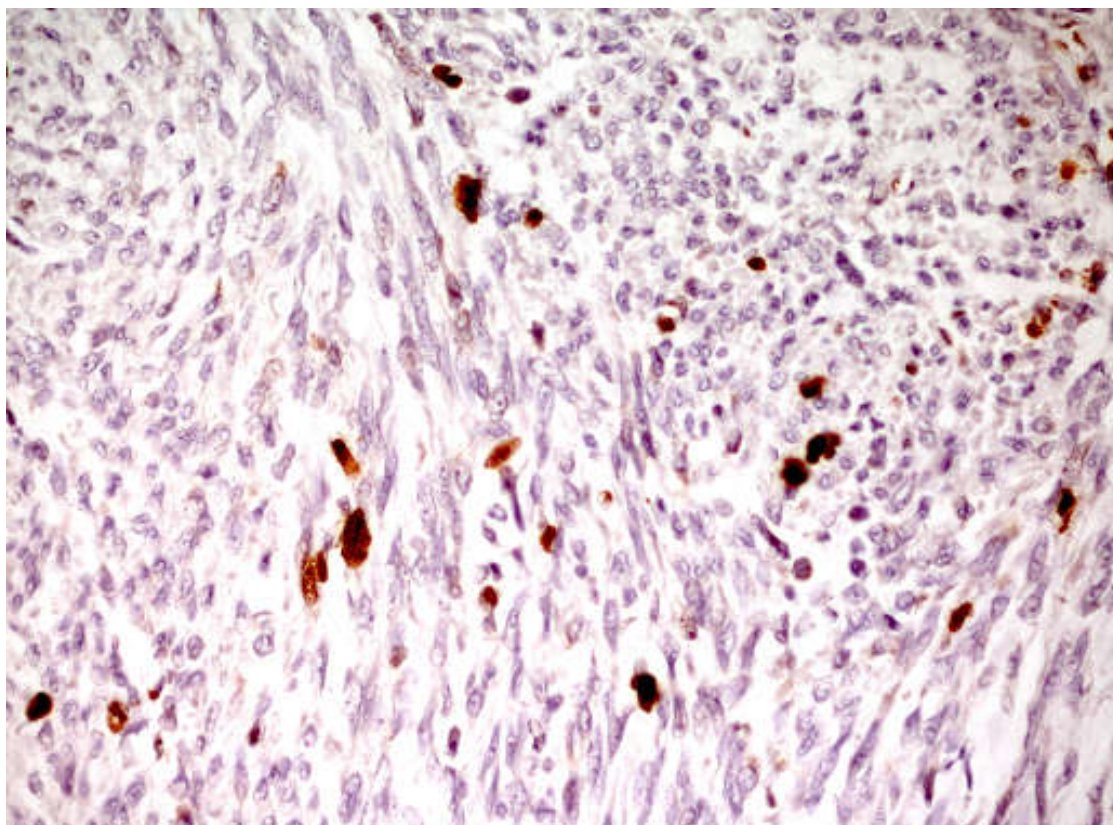


Fig. 5. Expression of Ki-67 protein in the nuclei of leiomyoma smooth muscle cells. Control group. Immunohistochemical investigation. $\times 400$.

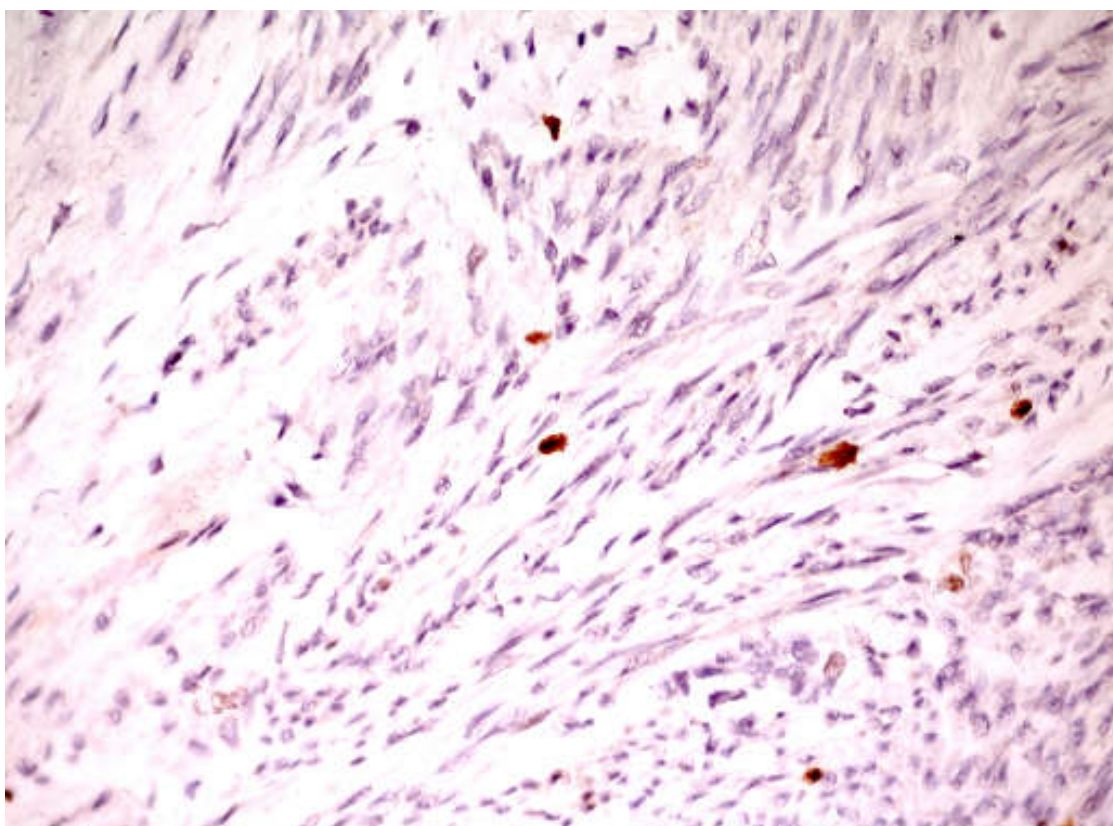


Fig. 6. Expression of Ki-67 protein in the nuclei of leiomyoma smooth muscle cells. Group of patients who received ulipristal acetate. Immunohistochemical investigation. $\times 400$.

References

1. Radzinskiy VE, Totchiyev GF. [Uterine myoma: course for organ preservation. Newslettes]. M: Publishing office of StatusPraesens journal; 2014. P. 24. Russian.
2. Yoshida S, Ohara N, Xu Q, Chen W, Wang J, Nakabayashi K, Sasaki H, Morikawa A, Maruo T. Cell-type specific actions of progesterone receptor modulators in the regulation of uterine leiomyoma growth. *Semin Reprod Med.* 2010 May;28(3):260-73. doi: 10.1055/s-0030-1251483. PMID: 20414849
3. Talaulikar VS, Manyonda I. Progesterone and progesterone receptor modulators in the management of symptomatic uterine fibroids. *Eur J Obstet Gynecol Reprod Biol.* 2012 Dec;165(2):135-40. doi: 10.1016/j.ejogrb.2012.07.023. PMID: 22901974.
4. Talaulikar VS, Manyonda IT. Ulipristal acetate: a novel option for the medical management of symptomatic uterine fibroids. *Adv Ther* 2012;29(8):655–63. doi: 10.1007/s12325-012-0042-8. PMID:22903240
5. Biglia N, Carinelli S, Maiorana A, D'Alonzo M, Lo Monte G, Marci R. Ulipristal acetate: a novel pharmacological approach for the treatment of uterine fibroids. *Drug Des Devel Ther.* 2014 Feb 20;8:285-92. doi: 10.2147/DDDT.S54565. PMID: 24591818.
6. Donnez J, Vázquez F, Tomaszewski J, Nouri K, Bouchard P, Fauser BC, Barlow DH, Palacios S, Donnez O, Bestel E, Osterloh I, Loumaye E; PEARL III and PEARL III Extension Study Group. Long-term treatment of uterine fibroids with ulipristal acetate. *Fertil Steril.* 2014 Jun;101(6):1565-73.e1-18. doi: 10.1016/j.fertnstert.2014.02.008. PMID: 24630081.
7. Berger C, Boggavarapu NR, Menezes J, Lalitkumar PG, Gemzell-Danielsson K. Effects of ulipristal acetate on human embryo attachment and endometrial cell gene expression in an in vitro coculture system. *Hum Reprod.* 2015 Apr;30(4):800-11. doi: 10.1093/humrep/dev030. PMID: 25740886.
8. Tikhomirov AL, Zayratyants OV. [A clinico-morphological characteristic of uterine myoma after using the selective progesterone receptor modulator ulipristal]. *Voprosy ginekologii, akusherstva i perinatologii.*2014, 13(1):67-72. Russian.
9. Tikhomirov AL, Kazenashev VV, Zayratyants OV, Manukhin IB. [First clinical morphological tendencies of the treatment of patients with myoma of womb with ulipristal acetate]. *Gynecology (Moscow).* 2014;16(2):29-33. Russian.
10. Nisolle M, Gillerot S, Casanas-Roux F, Squifflet J, Berliere M, Donnez J. Immunohistochemical study of the proliferation index, oestrogen receptors and progesterone receptors A and B in leiomyomata and normal myometrium during the menstrual cycle and under gonadotrophin-releasing hormone agonist therapy. *Hum Reprod.* 1999 Nov;14(11):2844-50. PMID: 10548634.

11. Potapov VA, Donskaya YuV, Medvedev MV. [Histological and immunohistochemical evaluation of leiomyoma and endometrial tissue in patients with uterine leiomyoma and endometrial hyperplasia]. Morphologia. 2014;8(1):80-4. Ukrainian.

12. Engman M, Granberg S, Williams AR, Meng CX, Lalitkumar PG, Gemzell-Danielsson K. Mifepristone for treatment of uterine leiomyoma. A prospective randomized placebo controlled trial. Hum Reprod. 2009 Aug;24(8):1870-9. doi: 10.1093/humrep/dep100. PMID: 19389793.

13. Murdoch M, Roberts M. Selective progesterone receptor modulators and their use within gynaecology. The Obstetrician & Gynaecologist. 2014;16(1):46-50. DOI: 10.1111/tog.12072.