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THE ROLE OF MUTATIONS IN THE PI3K / AKT / mTOR SIGNAL PATHWAY IN DECREASING OVARIAN RESERVE IN REPRODUCTIVE PATIENTS WITH DEEP INFILTRATIVE ENDOMETRIOSIS

Name: Oxana A. Melkozerova, Ekaterina O. Okulova, Anna A. Mikhelson, Tatyana B. Tretyakova
Affiliation: Ural Scientific Research Institute of Maternity and Child Care
Ministry of the Public Health of the Russian Federation
Country: Russia
Email ID: abolmed1@mail.ru

ABSTRACT

The aim: To evaluate the spectrum of mutations in the PIK3CA gene among patients with infiltrative form of external genital endometriosis.

Patients and methods. The main group of the study included 50 patients of reproductive age with deep infiltrative endometriosis (DIE), in 18 of whom deep infiltrative endometriosis was combined with ovarian endometriomas. The comparison group included 25 patients of reproductive age who underwent laparoscopic metroplastics of an inconsistent uterine scar from a cesarean section. All patients underwent determination of the level of anti-Müllerian hormone, follicle-stimulating hormone and estradiol in the blood by enzyme immunoassay, as well as counting the number of antral follicles in the ovaries during transvaginal ultrasound examination. The search for activating mutations of the PIK3CA gene was carried out by sequencing a new generation of DNA in tissue samples of ovarian endometriomas in patients with a combination of infiltrative endometriosis and endometrioid ovarian cysts (n=18), as well as in biopsies of healthy ovarian tissue in all patients of the main group (n=50) and comparison groups (n=25).

Results. When assessing the state of the ovarian reserve in the patients of the two groups, it was found that the AMH level was lower in the patients with the infiltrative form of external genital endometriosis than in the patients of the comparison group by an average of 1.0 ng/ml (2.6±2.2 ng/ ml in the main group, 3.6±3.5 ng/ml in the comparison group), however, the difference did not reach statistical significance, $p>0.05$. The number of antral follicles according to transvaginal ultrasound was significantly lower in the main group (8.5±4.5) than in the comparison group (12.2±4.1), $p=0.001$. This difference was statistically significant both for patients with ovarian endometriomas (6.0±4.2, $p<0.001$) and for patients without ovarian endometriomas (9.8±4.2, $p=0.04$).

Our study did not reveal PIK3CA gene mutations in any of the ovarian endometrioma tissue samples from patients with a combination of infiltrative endometriosis and endometrioid ovarian cysts, as well as in none of the healthy ovarian tissue biopsies from patients of the main group and the comparison group using the new generation DNA sequencing method.

Conclusion. Thus, the presence of deep infiltrative endometriosis is associated with a decrease in ovarian reserve in patients of reproductive age, regardless of the presence of endometrioid ovarian lesions. Population studies are needed to identify mutations of this gene in endometriosis, as well as to study mutations of other genes encoding proteins regulating the antiapoptic signaling pathway PI3K/AKT/mTOR, to identify the mechanism of ovarian reserve depletion in infiltrative form of external genital endometriosis.

BIOGRAPHY

Dr Oksana Melkozerova received her doctorate from the Ural Initial Research Institute of Maternity and Infancy, Yekaterinburg, Russia, at the age of 45. She is the Deputy Director for Research at the Ural Initial Research Institute for the Protection of Mothers and Infants, Yekaterinburg, Russia. She has over 100 publications that have been cited over 150 times, and her Hirsch Publication Index is 8.

Presenter Name: Dr Oxana Melkozerova
Mode of Presentation: Oral
Contact number: +7 922 219 45 06
abolmed1@mail.ru