rs16928751 *ADIPOR2* genes in women of the Russian population.

KEYWORDS: obesity, metabolic syndrome, genotypes of the polymorphisms.

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FERTILITY RESTORATION IN A PATIENT WITH RESISTANT PROLACTINOMA AFTER COMPLEX THERAPY OF DOPAMINE AGONIST AND SELECTIVE ESTROGEN RECEPTOR MODULATOR

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Introduction. Prolactinomas are the most common pituitary adenomas and dopamine agonists (DA) still remain the first choice of treatment. Nevertheless it does not always exert an adequate effect and endocrinologists face the challenge of resistant prolactinomas more frequently. This problem is very important for women of reproductive ages who desire to recover fertility. We present a clinical case of a woman with DA resistant prolactinoma and primary amenorrhea who had recovered regular menstrual cycle and ovulation after one year of combination treatment with cabergoline and tamoxifen. **Clinical case.** In 2002 a 12-year old woman was referred to our tertiary care center with hyperprolactinemia (prolactin (PRL) level 5000 IU/l (90—540), no macroprolactinemia) and macroprolactinoma 10×18×10 mm by MRI. Administration of cabergoline with maximum dose 3.5 mg a week did not result in significant clinical or laboratory improvement. In 2004 transnasal transsphenoidal adenomectomy was performed. Postoperative prolactin levels remained high. For short period the patient received injections of octreotide without effect. In 2006 the repeat operation was conducted because of additional tumor tissue of 8×7×10 mm on MRI. After surgery PRL decreased to 3000 IU/l, cabergoline therapy was restarted in dose 1 mg per week with gradually increasing up to 4.5 mg that allowed to stabilize tumor growth, but without recovery of menstrual cycle. During examination in 2015 PRL level was 6000 IU/l, endoparasellar adenoma visualized on MRI and hypoplasia of the uterus with the lineal endometrium were detected. As an antitumor agent, the patient was assigned a treatment with selective estrogen receptors modulator (SERM) tamoxifen — in a dose 20 mg per day in combination with cabergoline in a dose 4.5 mg per week. After one year of such therapy the prolactin was 15000 IU/l, adenoma's MR-characteristics didn't reveal any negative trend. At the same time the patient noted that menstrual function restored in 3 months after starting tamoxifen. Ultrasound examination confirmed normal uterus size and adequate endometrial thickness; also, the left ovary contained corpus luteum. The therapy was prolonged with recommendations of careful ultrasound control of endometrium state and barrier contraception. **Conclusion.** This case demonstrates reversion of symptoms of hyperprolactinemic hypogonadism in a patient with DA resistant prolactinoma due to SERM treatment without prolactin level normalization. The pathophysiological mechanisms underlying the phenomenon are not clear but may be due to the changers in interactions of kisspeptin neurons involved in GnRH secretion due to modulation of negative and positive estrogen feedback.

KEYWORDS: hyperprolactinemia, plolactinoma, tamoxifen, cabergoline.

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EPIGENETIC ASPECTS OF BONE METABOLISM REGULATION IN PATIENTS WITH ENDOGENOUS HYPERCORTISOLISM

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Objective. To investigate mRNA and microRNA related to bone of remodeling in bone tissue samples from patients with Cushing's disease (CD). **Material and methods.** Patients with clinically evident and biochemically proven active CD and patients with hormonally inactive pituitary adenoma matched by age, sex and BMI were invited to participate. Bone samples were taken during transsphenoidal adenomectomy from the base of the sella-turcica, immediately placed in lysis buffer (QIAzol) and subjected to homogenization. 24h urine free cortisol (24hUFC) was measured by an immunochemiluminescence assay on a VitrosECi (60-413 nmol/24 h). Total RNA isolation from bone tissue with on-column digestion of the genomic DNA was carried out with miRNeasy Mini Kit on the automatic station «QIAcube». Reverse transcription was carried out using a High-Capacity RNA-to-cDNA Kit. Gene expression analysis was performed by Real-Time PCR on StepOnePlus instrument with Custom TaqMan Array 48 Plus plates. MicroRNA expression analysis was carried out by TaqMan Advanced miRNA Assays. **Results.** We enrolled 24 subjects (15 patients with CD and 9 with hormonally inactive pituitary adenomas); 18 females and 6 males, the mean age was 41 years (confident interval (CI) 95% 36—46) mean BMI — 29 (CI 95% 26—32) kg/m^2. There were no significant difference between the groups. Mean 24h UFC in subjects with CS — 1168 (CI 95% 702—1634) nmol/24h. Expression of osteoblast activity and bone formation genes was decreased in patients with CD: ALPL 0.34 (CI 95% 0.24—0.43; p<0.001), BGLAP 0.41 (CI 95% 0.28—0.54; p<0.001), COL1A1 0.26 (CI 95% 0.14—0.37; p<0.001), COL1A2 0.51 (CI 95% 0.33—0.69; p<0.001), MMP2 0.52 (CI 95% 0.41—0.62; p<0.001). The expression of SOST 5.3 (CI 95% 1.8—8.8; p<0.001), WNT10B 10.24 (CI 95% 5.26—15.22; p<0.001), WNT3A 1.44 (CI 95%