0.3—2.57; p=0.016), CD40 3.5 (CI 95% 3.13—3.91; p<0.001), BMP7 2.03 (CI 95% 1.22—2.83; p<0.001) was increased in subjects with hypercortisolism as compared to inactive pituitary adenoma. An increase in the expression of microRNA 133a-3p 1,74 (CI 95% 0.14—3.34; p=0,037), that stimulate osteoclastogenesis, and microRNA 204-5p 0,54 (CI 95% 0.06—1.02; p=0.031), that block the differentiation of osteoblasts was found. **Conclusion.** Suppression of osteoblastogenesis in patients with endogenous hypercortisolism is explained by an increase in the expression of the SOST, which codes the main inhibitor of the Wnt signaling pathway — sclerostin. Reduction of osteoblast differentiation is also realized through increased expression of 133a-3p microRNA and 204-5p microRNA.

KEYWORDS: microRNA, osteoblastogenesis, hypercortisolism.

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MCCUNE-ALBRIGHT SYNDROME (MAS): CLINICAL CASE

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Introduction. McCune-Albright syndrome (MAS) — a systemic disease associated with a mutation in the gene GNAS1, responsible for the activation of a G protein subunit (Gsa), is characterized by symptoms: fibrocystic dysplasia, skin pigmentation, precocious puberty. **Clinical case.** A 29 — y. o. male patient during past 12 years noted a gradual change in his appearance. Began to seek a medical attention only 3.5 years ago due to reduced vision. Hormonal tests revealed marked elevation of GH to 106 (<20 mIU/ln), and IGF-1 to 567 (121—336 ng/ml), decrease in testosterone levels to 1.91 (3-12 ng/ml), other gormons within the reference range. MRI of the brain showed a 4×7 mm adenoma of the anterior part of the pituitary. CT brain scan with contrast described poliostic dysplasia of the skull bones. Octreotide depot injections therapy was initiated 20 mg/28 d. Than levels of GH and IGF-1 were still high in spite of medical treatment — 119 (<20 mIU/ln) and 1033 (121—336 ng/ml), respectively. At the age of 27 years the patient was 205 cm tall (BMI 29.5 kg/m^2) at admission to Endocrinology Research Centre. His facial features were acromegaloid with sloped towered skull. "Café au lait" pigmentation of the skin was noted at the chest, back, and abdomen. Lab tests confirmed the presence of the active acromegaly (GH — 117 (< 20 mIU/ln), IGF-1 — 1412 (121—336 ng/ml)). Brain MRI with contrast showed a marked increase in the size of previously described adenoma 17×23×14 mm, and progression of the fibrous dysplasia (predominantly hypointense on T1) of the skull base, parietal, temporal bones, scales of the frontal and occipital bones, hypopneuma-tization of frontal sinus and ethmoidal labyrinth, narrowing of the internal and the external auditory canals on the left. All these symptoms allowed us to suspect the MAS. The progressive clinical course of the disease, insensitivity to octreoride treatment was the basis for the choice of further surgical treatment despite the pronounced fibrous dysplasia of the skull base. Then the patient underwent endoscopic endonasal removal of tumor using navigation BrainLab at Burdenko Neurosurgical Research Institute. Postoperatively levels of GH and IGF-1 decreased to - 27 (<20 mIU/ln) and 856 (121—336 ng/ml), visual function had improved markedly. He was then followed on depo octreotide injections 30 mg/28d and cabergoline 2 mg/w with later dose adjustments. The high-performance parallel sequencing was implemented with the gene panel (*MEN1, CDKN1B, PRKAR1A, GNAS, AIP, SDHA, SDHB, SDHC, SDHD, PRKCA, CDKN2C, CDKN2A, POU1F1, PTTG2*). **Conclusions.** The treatment of acromegaly in the setting of the MAS is characterized by multiple challenges that require the participation of a team of experienced endocrinologists and neurosurgeons. This patient with the MAS was identified heterozygous p.S163P replacement in *SDHB* gene.

KEYWORDS: McCune-Albright syndrome, acromegaly, parallel sequencing, pituitary adenomas.

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OBESITY PARADOX: CARDIOVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND OBESITY

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Introduction. Obesity and type 2 diabetes mellitus (T2DM) are commonly associated with cardiovascular complications. At the same time, obesity paradoxes are not new to the field of cardiovascular disease and have been observed in heart failure, acute coronary syndromes, and chronic kidney disease. **Clinical cases.** Two patients (both non-smoking men) comparable for age (48—50 years), BMI (32.1—34.4 kg/m^2) glycated hemoglobin (HbA_{1c}) (6.0—6.3%), hypoglycemic therapy (Sulfonylureas with Metformin) and diabetes duration (3—5 years) were treated in Endocrinology Research Centre during 2016 year. There was no significant differences in routine laboratory tests (total cholesterol, low-density cholesterol, high-density cholesterol, triglycerides, fasting glucose, microalbuminuria). First patient (50 years old, BMI 32.1 kg/m^2) had several cardiovascular complications at the time of hospitalization: including Myocardial infarction, coronary angiography revealed multi-vascular atherosclerotic lesion of coronary vessels (left anterior descending coronary artery, right coronary artery and circumflex artery were stenosed up to 90%) and athero-

sclerosis of lower limb arteries (up to 40%). There was no option for endovascular treatment for the patient, so he was recommended coronary artery bypass grafting. Leading cause of hospitalization was the presence of an ulcerative defect of the posterior surface of left tibia associated with neuropathic form of diabetic foot. Second patient (48 years old, BMI 34.1 kg/m^2) had no clinical and instrumental sings for the coronary artery disease (excluded after Tredmil-Test) or any other complications of T2DM. **Conclusion.** Patients with obesity need personalized strategy for management and treatment. Further studies are needed to evaluate novel markers for cardiovascular disease development in this group of patients. Promising can be the determination of the expression of cardiovascular associated microRNA and several growth factors.

KEYWORDS: microRNA, obesity, diabetes.

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MODY 3 AND PREGNANCY: COURSE AND TREATMENT

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Introduction. Diabetes caused by mutations in the HNF1-alpha gene (encoding hepatocyte nuclear factor-1 alpha) is one of the most common types of MODY. This gene contains is a blueprint for a transcription factor that is important in for the normal development of beta cells. MODY 3 is typically diagnosed before 30 years of age and is often misdiagnosed as Type 1 diabetes mellitus. MODY 3 usually manifests with symptoms associated with high blood sugars. These include increased frequency of urination (polyuria), increased thirst (polydipsia), and weight loss. Mutations can occur spontaneously but usually are passed on from a parent to a child. If a parent has MODY 3 there is a 50% chance that a child will inherit the mutation and be at risk of developing diabetes at a young age. Distinguishing MODY 3 from Type 1 diabetes can be difficult. In this case, we presents a woman with MODY 3 and pregnancy. **Clinical case**. A 44-year-old female patient diagnosed with MODY 3 Diabetes, during the first pregnancy, Ten years ago (GEN HNF_1A) mutation c.511 C> T (p.Arg171X.Treatment initial was insulin aspart 30 units day, after gestation received during 8 years glyclazide 30 mg daily. Second gestation was a year ago, treated with insulin lispro 14 units day. In both gestations there was hypertension treated with Trandate. In both gestations the delivery was cesarean due to fetal distress. Both deliveries were male, and the APGAR at 5 minutes was 10. No congenital anomaly was detected in any of the offspring. 8 months ago presented hypothyroidism due to Hashimoto's disease treated with 50 micrograms of levothyroxine. The patient's current state is stable. **Conclusion.** Monogenic diabetes is frequently mistakenly diagnosed as either type 1 or type 2 diabetes, yet accounts for approximately 1—2% of diabetes. Identifying monogenic forms of diabetes has practical implications for specific therapy, screening of family members and genetic counselling. The most common forms of monogenic diabetes are due to glucokinase (GCK), hepatocyte nuclear factor (HNF)-1A and HNF-4A, HNF-1B, m.3243A>G gene defects. In this case it was a MODY 3 diabetes that responded well to the use of Insulin. This knowledge is important for all physicians managing diabetes in pregnancy, given this is a time when previously unrecognised monogenic diabetes may be uncovered with careful attention to atypical features of diabetes misclassified as type 1, type 2, or gestational diabetes.

KEYWORDS: diabetes, HNF1-alpha gene, MODY 3.

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LIPODYSTROPHY SYNDROMES AND ASSOCIATED METABOLIC DISORDERS IN RUSSIAN POPULATION

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Background. Lipodystrophies are heterogeneous disorders characterized by selective loss of body fat, which can be generalized (GL) or partial (PL), inherited or acquired, and usually are associated with different metabolic disorders, like diabetes with marked insulin resistance, dyslipidemia, arterial hypertension, hepatic steatosis and hepatosplenomegaly, and so often remain not diagnosed, especially familial partial lipodystrophy (FPL). GL may be a sign of progeroid syndromes (PS). Genetic diagnostics may be challenging because of many candidate genes and similar phenotypes. There is a lack of information on clinical and molecular-genetic characteristics of lipodystrophy syndromes in Russian population and the condition is usually misdiagnosed. **Objective.** To assess the clinical and molecular-genetic characteristics of lipodystrophies in Russian population. **Material and methods.** 58 patients (45 adults and 13 children) from 51 families with different lipodystrophic fat loss patterns were included in the study: 40 (69%) patients with PL, 12 (20.7%) patients with GL, and 6 (10.3%) patients with PS. Detailed clinical examination and the assessment of metabolic abnormalities was performed. For genetic confirmation of the diagnosis 16 congenital lipodystrophies and progeroid syndromes with lipodystrophies candidate genes (*AGPAT2, BSCL2, CAV1, PTRF, LMNA, PPARG, PLIN1, AKT2, LIPE, LMNB2, POLD1, CIDEC, WRN (RECQL2), PPP1R3A, ZMPSTE24, BANF1*) were sequenced using a Custom Ion Ampliseq panel and PGM semiconductor sequencer (Ion Torrent). **Results.** There were considerable age differences between the groups with GL and PL: mean age