INCIDENCE OF INCREASED REACTIVE OXYGEN SPECIES ACTIVITY AND RAPID HYPOTHYROIDISM DEVELOPMENT IN PATIENTS WITH GRAVES' DISEASE DURING ANTITHYROID TREATMENT

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Introduction. Autoimmunity plays an important role in the development of thyrotrophin (TSH) receptor antibodies and the pathogenesis of Graves' disease (GD). The mechanism underlying the functioning status of thyroid stimulating antibodies (TSAb) and antibodies that block TSH action (TBAb) is still unclear. Clinical case. A-54-year-old woman was admitted to the hospital with manifest hyperthyroidism. She was diagnosed with GD. She had no ophthalmopathy similar to GD and had high titer of plasma TSH receptor antibodies (30,34 ED/L (0—1,0). The following characteristics of spontaneous chemiluminescent (CL) and zymosan-induced (ZiCL) activity of blood neutrophilic granulocytes (BNG) was studied: time to maximum (Tmax), maximum intensity value (Imax), reflecting the maximum reactive oxygen species (ROS) level synthesis, area under the curve (S), describing total ROS synthesis. In our patient we observed the increased Imax during luminol-dependent spontaneous- and Zi-CL. Index S changed depending on the kinetics of CL: from low index during luminol-dependent spontaneous to high S level in luminol- and lucigenin-dependent ZiCL. In her thyroid ultrasonography there were the alternation of hypoechoic and increased echogenicity areas, the volume of the gland were 31.03 ml. Color flow Doppler imaging showed typical findings of GD. Antithyroid drugs therapy were initiated in total daily dose of thiamazol 30 mg. Under additional beta-blockade the patient's condition significantly improved. After 3 weeks antithyroid treatment the clinical features and hormonal control of thyroid status demonstrated hypothyroidism, TSH – 37,96 mIU/ml (0.2—3.2), fT4 — 5.9 pmol/L (9.0—22.0). The block and replaced scheme was performed. We measured that the kinetics of BNG CL was varied with thyroid status and accompanied by increased of Imax in luminol-dependent spontaneous- and Zi—CL. Variability of S in luminol-dependent spontaneous CL markedly depressed, suggesting an immunosuppressive effect of the antithyroid drugs, and, than, increased only during lucigenin-dependent ZiCL. In contrast with manifest thyrotoxicosis, the hypothyroidism under antithyroid treatment of our patient entailed by high index T during luminol-dependent spontaneous and lucigenin Zi—CL. Sequentially after reversion euthyroid state and 2 weeks before radioiodine therapy (RIT) all medications were discontinued and given as treatment a fixed dose of 500 MBq radioiodine. Patient became hypothyroid at the 12 day post RIT and was maintained on 100 mcg of levothyroxine daily. **Conclusion.** This case demonstrates that both, the hyperthyroid state and antithyroid drugs mediated immunity upon BNG activity, release assay for ROS cytotoxicity. This phenomenon implies that pathogenesis of GD might be associated not only with self-limited changing TSAb or TBAb antibodies, but, also, the antithyroid drugs immunosuppressive exerted effects upon the BNG activity should be considered.

KEYWORDS: Graves' disease, antithyroid treatment, autoimmunity.

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EFFECT OF SUPPRESSION OF PUBERTY AND CROSS-SEX HORMONE THERAPY ON BONE TURNOVER MARKERS AND BMAD IN TRANSGENDER ADOLESCENTS

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Background. Puberty is highly important for the accumulation of bone mass. Bone turnover and bone mineral density can be affected in transgender adolescents when puberty is suppressed by gonadotropin-releasing hormone analogues (GnRHa), followed by treatment with cross-sex hormone therapy (CSHT). **Objective**. To investigate the effect of GnRHa and CSHT on bone turnover markers (BTMs) and bone mineral apparent density (BMAD) in transgender adolescents. **Material and methods.** Thirty four female-to-males (FtMs) and 22 male-to-females (MtFs) were divided into a young and old pubertal group, based on the bone age of 14 years in the FtMs and 15 years in the MtFs. All patients received GnRHa triptorelin. CSHT was prescribed in incremental doses from the age of 16 years. FtMs received testosterone ester mixture and MtFs were treated with 17-β estradiol. BTMs P1NP, osteocalcin and ICTP and the BMD of lumbar spine (LS) and femoral neck (FN) were measured at three time points. Furthermore, BMAD and Z-scores were calculated. **Results.** P1NP and 1CTP decreased during GnRHa treatment, indicating decreased bone turnover. Osteocalcin showed an aberrant pattern. A low BMAD Z-score of both FN and LS was observed in the MtFs at start of GnRHa treatment. The decrease in bone turnover upon GnRHa treatment was accompanied by an unchanged BMAD of both FN and LS, however BMAD Z-scores of predominantly the LS decreased. Twenty-four months after CSHT the BTMs P1NP and ICTP were even more decreased. During CSHT BMAD Z-scores increased and returned towards normal, especially of the LS. **Conclusion.** Suppressing puberty by GnRHa leads to a decrease of BTMs in transgender adolescents. The increase of BMAD and BMAD Z-scores predominantly in the LS as a result of treatment with CSHT

is accompanied by decreasing BTM concentrations after 24 months of CSHT. Therefore, the added value of evaluating BTMs seems to be limited and DEXA-scans remain important in follow-up of transgender adolescents.

KEYWORDS: transgender adolescents, gonadotropin-releasing hormone analogues, bone mineral density.

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DIFFERENT FORMS OF CONGENITAL ADRENAL HYPERPLASIA IN TWO SIBLINGS IN A FAMILY: A CASE REPORT

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Introduction. CAH — is a group of diseases with autosomal recessive type of inheritance. 21-hydroxylase deficiency is responsible for 95% of all cases of CAH. Depending on the severity of 21-hydroxylase deficiency the disease is divided into three forms: salt wasting, simple virile, and nonclassic. If both parents are known to be heterozygous carriers of pathogenic genes, each sib has only 25% chance of being affected. **Clinical case.** A 7-day-old female girl was referred to our hospital with ambiguous genitalia. According to the medical history, she was born at term to a 28-year old healthy mother from her second gestation with a spontaneous delivery without any complications. Birth weight was 3290 g. Genital examination revealed clitoromegaly, single urogenital onfice, posterior labial fusion. Karyotype analysis showed normal female karyotype 46XX. Biochemistry revealed hyponatriemia (Na 131 mmol/l), hyperpotassemia: (K 6,55 mmol/l). Blood hormone analysis showed increased levels of 17-hydroxyprogesterone (811 ng/mL) and dehydroepiandrosterone (989,8 mcmol/l), hypocortisolemia (69,6 nmol/l).These results suggested a salt wasting form of CAH. In the gene analysis of CYP21 heterozygous mutations IVS2-13A/C>G and 30-kb deletion were detected.Replacement treatment, including hydrocortisone at the dose of 41 mg/m^2/day and fludrocortisone at the dose of 0,15 mg/day was initiated. The dose of hydrocortisone was gradually decreased to 24 mg/m^2/day. On the therapy the child showed positive dynamics of electrolytes levels, the general status was compensated. Weight at the age of 37 days was 4060 g (meant weight 4090 g.).During collection of the family history the baby's mother marked special features of her older son. By the time of sister's birth the boy was 2 years 8 months old. The parents reported high velocity of growth since birth and acne after 2 years of age. Laboratory investigation showed high level of 17-hydroxyprogesterone (299,8 ng/l) and testosterone (12,6 nmol/l). The boy was admitted to the hospital. Physical examination revealed acne on the face and upper back, penile enlargement, pigmentation of the scrotum, though both testis were prepubertal in size. Height was 106 cm (> 97th percentile). Bone age was 6 years 10 months. His predicted height (159 cm) was significantly lower than genetic one (177 cm). Levels of blood electrolytes were normal. A diagnosis of virile form of CAH was considered. Hydrocortisone treatment at the dose of 13,3 mg/m^2/day was initiated. The boy showed a compound heterozygous mutation (IVS2-13 A/C>G and 30-kb deletion). **Conclusion.** Although the sibs had similar mutations, they exhibited different phenotypes. According to the literature, presence of IVS-2 mutation may determine both salt wasting and simple virile forms. It might result from the variable splicing of this mutation due to variation in RNA splicing factors.

KEYWORDS: congenital adrenal hyperplasia, 17-hydroxyprogesterone, hydrocortisone treatment.

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INDICATORS OF RESPIRATORY MITOCHONDRIAL FUNCTION IN DIABETES MELLITUS

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Changes in the level of mitochondrial dehydrogenases in the respiratory cells in patients with diabetes mellitus had been found in the earlier studies. However, the diagnostic criteria for verification of energy disturbances in the respiratory system in subjects with type 1 diabetes are not established. **The aim** of the study was to perform the cytochemical analysis of mitochondrial function in patients with diabetes. A total of 116 Caucasian subjects were recruited and studied: 57 person with type 1 diabetes, aged 54.2±1.3 years and 59 participants without diabetes, aged 47.8±3.5 years. Those with the history of respiratory disease and smoking history were specifically excluded. Cytochemical analysis was performed by analyzing the activity of succinate dehydrogenase (SDH) and lactate dehydrogenase (LDH) using computer morphometry. The substrate for the study was the bronchoalveolar secret. The viability of epithelial cells and alveolar macrophages of the bronchi was significantly decreased in patients with type 1 diabetes compared to control group — 49.6±1.5% and 73.2±2.8% vs 57.6±1.9% and 85.3±2.7%, respectively ($p<0.001$). Phagocytic number and phagocytic index was also decreased in those with type 1 diabetes compared to controls — 39.4±1.7% and 7.1±0.4% vs 48.8±1.3% and 8.7±0.3%, respectively ($p<0.05$). The levels of mitochondrial activity SDH and LDH in patients with type 1 diabetes were 12.4±0.9 and 11.5±0.9 standard units and in the control group — 19.8±0.7 and 23.6±1.1 standard units ($p<0,01$). In subjects with diabetes it was the negative correlation between the activity of SDH and LDH of the cellular elements of the respiratory system and hyperglycemia and of index endobronchitis activity, with $r = -0.39$ ($p=0.003$) and $r=-0.29$ ($p=0.03$) and $r=-0.53$ ($p=0.02$) and $r = -0.39$ ($p=0.01$), respectively. We can speculate that the level of dehydrogenase activity may serve as a diagnos-