ine 50 mcg in the morning). First hormonal studies conducted in the early 2000s. There was revealed a high level of TSH, but replacement therapy was continued despite the manifestations of thyrotoxicosis. Free T4 Episodic study revealed increased rates of medical and regarded as thyrotoxicosis. Clinically, the patient had symptoms of hyperthyroidism DC with lesions predominantly cardiovascular system, since 2007 atrial fibrillation, mitral and tricuspid insufficiency, replacement of heart valves. The first pair of hormones (TSH and FT4) on a clean background was investigated in 2016. In the repeated trial (which excluded a laboratory error) at the same time an elevated level of TSH (20.8 mMe/ml) and FT4 (34 pmol/l). The differential diagnosis with resistance to thyroid hormone. The study of the brain and pituitary MRI with dynamic contrast. Pituitary adenoma was found 0.2 cm in diameter. Exhibited a clinical diagnosis of TSH-producing pituitary adenoma. The patient was operated in neurosurgical center of Far Eastern federal university's medical centre. Performed transnasal transsphenoidal adenomectomy with endoscopic video navigation in January 2017. According to the results of immunohistochemistry. According to the results of immunohistochemistry: Ki-67, Alpha ingiban — negative expression. Chromogranin — weak expression in 10—20% of the cells. TSH — strong expression in 90—100% of the cells, prolactin expression severe 80—90% of the cells. **Conclusion.** IHC tumor profile best fits multigormonalnoy pituitary adenoma with minimal formation of proliferative activity of cells. When hormonal study TSH decreased to 3.45 mMe/l, retained a higher level of St. T4 30.4 pmol/l. The patient was recommended treatment with somatostatin analogues (octreotide Long 40 mg of p 1 to 28 days/m) and dopamine agonists (cabergoline 0.5 mg 2 p per week) - on 6 months follow-up examination. The patient entered into the register of entities gipotalyamo pituitary region of Primorsky Krai. This case is the second in the coastal region.

KEYWORDS: pituitary adenoma, endocrine pathology, prolactinoma, somatotropinoma.

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SECONDARY AND TERTIARY HYPERPARATHYROIDISM: CASE REPORT

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Introduction. In the treatment of secondary hyperparathyroidism of chronic kidney disease, allosteric modulators of the calcium-sensing receptor — inhibit glandular hyperplasia, reduce parathyroid hormone (PTH) levels, impact on bone turnover and mineral density (BMD). But the use of calcimimetic did not reduce the need for parathyroidectomy for refractory hyperparathyroidism. Tertiary hyperparathyroidism is a state of excessive secretion of PTH after a long period of secondary hyperparathyroidism and renal transplantation. **Case report.** We present the case of a 43-year-old caucasian male undergoing chronic hemodialysis since 2006. Laboratory investigations showed elevated levels of phosphorus 1.95 mmol/l, calcium 2.6 mmol/l, CaxP 5.07 mmol2/l2, iPTH 817 pg/ml, CTx 3.1 ng/ml, OC >300 ng/ml, ALP 469.6 U/L, vitamin D deficiency 7.9 ng/ml. Ultrasound revealed multiple enlarged parathyroid glands: right superior 1.08 cm3; right inferior 0.04 cm^3; left superior 0.3 cm^3 and left inferior d=0.6 sm. DEXA revealed osteoporosis (Z-sc): Rad 33% –4.0; L2—L4 —1.1; total femur —2.2 SD. We have recommended dialysis with low calcium (1.25 mmol/L) and cinacalcet 30 mg/day. Laboratory investigations were done during the treatment. After normalization of serum calcium and phosphorous concentrations we have added cholecalciferol. Six months later mean iPTH and Ca×P levels decreased by 60.2 and 20.4%. Bone markers decreased by CTx 19.4%; OC 1.4%; ALP 16.8%. 25-D levels increased by 123.4%. The dynamics of BMD from baseline: L2—L4 +5.4%; Rad 33%: +9.3; total femur +6.4%. On ultrasound 3 parathyroid glands (right inferior, left superior and inferior) involute to normal size, but right superior enlarged 1.9 cm^3 (+75%). Patient underwent renal transplantation in 2010 (CKD stages 1—2). After successful kidney transplantation right superior parathyroid gland did not involute. One months later he developed the tertiary hyperparathyroidism with an iPTH 815 pg/ml, calcium 3.4 mmol/l. Was recommended cinacalcet initially in dose 30 mg, then was dose-increased to 180 mg/day in 2011 (calcium 2.4 mmol/l, iPTH 634 pg/ml), added alfacalcidol 6 mcg/week, but did not control hyperparathyroidism. In 2011 performed a right superior-gland parathyroidectomy to treat severe hyperparathyroidism refractory to cinacalcet and alfacalcidol treatment. **Conclusion.** Our case study shows that cinacalcet treatment is an effective therapy of hyperparathyroidism. But enlarged gland (larger than 0.5 cm^3 or 1 cm in diameter) became refractory to medical therapy and patient need for parathyroidectomy.

KEYWORDS: hyperparathyroidism, mineral density, bone, chronic hemodialysis, chronic kidney disease, parathyroid hormone.

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LONG-TERM MANAGEMENT OF RESISTANT ACROMEGALY WITH PASIREOTIDE LAR IN A PATIENT FROM AN AIP MUTATION POSITIVE FIPA FAMILY

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Introduction. AIP-related somatotropinoma patients with active acromegaly after surgery tend to be resistant to adjuvant medical therapy with somatostatin receptor

(SSTR) subtype 2 specific somatostatin analogues (SSA). Pasireotide is a newer multiple SSTR binding SSA with actviity primarily at SSTR5 and SSTR2, which has not been widely studied in AIP mutated patients. **Clinical case and results.** A male patient was diagnosed aged 29 with a GH-producing pituitary macroadenoma (25×18×23 mm); he was from a FIPA kindred and his sister also had acromegaly due to a pituitary macroadenoma (25 mm) at age of 24 and was cured by neurosurgery. A familial AIP mutation p.Gln217X was revealed in the index patient, his sister and an unaffected nephew. The patient underwent transsphenoidal surgery, with partial resection of a GH and prolactin positive adenoma. He was treated for post-operative corticotroph, thyrotroph and gonadotroph deficiencies but GH hypersecretion by the residual tumor required adjuvant medical treatment. He was treated with SSTR2 specific agents (lanreotide autogel and octreotide LAR), but without hormonal control. Addition of cabergoline did not improve hormonal suppression. An increase of tumor residue size was observed on SSA treatment and the residual tumor approximated the chiasma, which precluded safe surgery and pegvisomant therapy, while the patient declined radiotherapy. The patient began pasireotide LAR and was uptitrated to 60 mg/month. The clinical signs of acromegaly improved, GH/IGF-1 was controlled and tumor size was stable. Pasireotide was associated with worsening of existing impaired glucose control and treatment with metformin, gliclazide and liraglutide was required. After 2 years of treatment the dose of paseriotide was decreased to 40 mg/4 weeks and further follow-up showed tumor shrinkage and an empty sella. However, glucose metabolism worsened over time despite existing therapy and exogenous insulin treatment was required. **Conclusion.** In this patient from an AIP-mutation positive FIPA family, resistance to surgery, SSTR2-spcific SSA and cabergoline was seen. Pasireotide permitted clinical, hormonal and tumoral improvement, albeit at the cost of long-term worsening of hyperglycemia requiring increasing antidiabetic therapy.

KEYWORDS: somatotropinoma, acromegaly, AIP, FIPA family, pasireotide LAR.

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CARBOHYDRATE METABOLISM IN PATIENTS WITH CUSHING DISEASE AND ACROMEGALY: A GLANCE AT THE INCRETIN SYSTEM

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Introduction. The relevance of carbohydrate metabolism studying in patients with Cushing disease (CD) and acromegaly can be explained by frequent occurrence of glucose metabolism disturbances on the one hand, and difficulties in glucose-lowering therapy in these patients on the other. The effectiveness of hyperglycaemia treatment may be reduced due to difficulties in remission/cure of the underlying disease, as well as to the use of specific drug-therapy, leading to hyperglycaemia. There is a growing interest in research aimed at studying the role of incretin system in the pathogenesis of secondary hyperglycemia associated with neuroendocrine diseases recently. **Aim of the study.** To analyze the rhythm and levels of incretins and neuropeptides secretion in patients with CD and acromegaly and therefore to specify the pathogenesis of carbohydrate metabolism disturbances. **Material and methods.** 42 patients with Cushing disease and acromegaly were included; the mean age was 37.5 years. All of the patients were newly diagnosed with Cushing disease (using urinary free cortisol levels, evening saliva cortisol levels and low-dose dexamethasone suppression test) and acromegaly (in absence of GH suppression during OGTT and high IGF-1 levels); none of them had a history of previous drug therapy, radiotherapy or pituitary surgery. All patients underwent OGTT, during which glucose, glucagon, GLP1, GLP2, GIP, ghrelin were measured at 0, 30 and 120 min respectively. **Results.** During OGTT glucose levels were not significantly different in all groups. The mean HbA_{1c} level was 5.8% (5.3—6.2). However the relevance of prediabetes was higher in CD patients. In CD patients glucagon levels were significantly higher at all cut off points compared to controls (p=0.001). In acromegaly patients, no significant differences were found. GIP secretion was slightly lower in CD patients; in acromegaly patients, no differences were found. Acromegaly group was characterized by inverse rhythm of GIP secretion, with no peak level at 30': GIP 0 min — 194.2 pg/ml, GIP 30 min — 178.8 pg/ml/. GLP-1 levels were significantly higher in CD patients (p=0.047). In acromegaly group, no significant differences in GLP-1 secretion were found. GLP-2 levels were significantly higher in CD patients compared to acromegaly and controls (p=0.001). Ghrelin levels were significantly higher in CD (p=0.013) and acromegaly (p=0.023) patients. **Conclusion.** More pleotropic actions of glucocorticoids can possibly explain higher relevance of carbohydrate metabolism disturbances in CD patients. This can be also explained by higher levels of glucagon secretion, which does not depend on type of carbohydrate metabolism disorder and is stimulated by a direct action of glucocorticoids on glucagon receptor. GIP and GLP-1 secretion in CD and acromegaly patients are characterized by inverse rhythm with no peak levels which means that these hormones are not playing the crucial role in carbohydrate disturbances development in these patients. On the contrary, GLP-2 and ghrelin seem to influence and potentially regulate glucose homeostasis in CD and acromegaly patients.

KEYWORDS: Cushing disease, acromegaly, glucose metabolism disturbances, hyperglycemia, incretin system.

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