Serum glucose level normalized 20 hours after treatment started. The diagnosis of T1DM was made based on elevated blood antibodies against islet cells (ICA) and islet antigen 2 (IA-2) antibodies. He was discharged after 10 days without any complications related to HHS and is being regularly followed up. Since HHS has high mortality rate, early recognition and proper management are necessary for a better outcome.

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NEUROENDOCRINE TUMOURS OF THE APPENDIX

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Introduction Neuroendocrine tumours (NETs) are rare tumours in paediatric population. They are most often located at appendix and are usually diagnosed accidentally, as a result of pathohistological evaluation after appendectomy, following acute appendicitis. They are found in 0.3% appendectomies in children, more often in girls (56%), with median age of 12 years at the time of diagnosis. The prognosis is usually favourable and depends on the size and location of the tumour, protrusion into the mesoappendix, metastatic potential (Ki-67 index) and possible local metastasis. NET of the appendix can rarely be found as a part of some genetic diseases, such as multiple endocrine neoplasia (MEN) type 1 and 2, neurofibromatosis, tuberous sclerosis and von Hippel-Lindau disease. Due to the small number of individuals affected, there are no standardised diagnostic and therapeutic guidelines in paediatric population.

Case Report Here we report two cases of boys in whom pathohistological evaluation following appendectomies performed due to acute appendicitis revealed appendiceal NETs in both patients. The appendectomy upon the first patient was performed at 12.4 years of age. The tumour was located at the apex of the appendix, it was up to 0.5 cm in diameter, well differentiated, with low mitotic index (Ki-67 around 1%) and with clear resection margins. Family history revealed that the boy's grandfather was treated for appendiceal tumour at the age of 17 years. The other patient was operated at 12.8 years of age. The tumour was located at the apex of the appendix, in its muscular layer, with the length of 0.6 cm and Ki67 4% – grade 2 NET. During the follow-up (6 years and 2 months) neither relapse nor other tumours occurred. The additional diagnostic procedure revealed elevated parathormone levels (7.7...7.3...7.46 pmol/L, norm. 1.0-6.0 pmol/L), while blood calcium levels were at the upper limit of normal range (up to 2.57 mmol/L, norm. up to 2.53 mmol/L), blood phosphate levels were normal, vitamin D levels periodically lowered (60...51 nmol/L, norm. >75 nmol/L), despite the peroral substitution therapy, and the US examination of the neck was normal. Molecular genetic analysis did not reveal mutations characteristic for multiple endocrine neoplasia type 1.

Discussion Neuroendocrine tumours of the appendix have an excellent prognosis, particularly tumours smaller than 1 cm, with low mitotic index, located in the apex of the appendix and with clear resection margins. When such cases occur (as described here in two of our patients), appendectomy is considered a therapeutic method of choice. Our patients did not experience a relapse of the tumour. Furthermore, there were no signs of associated diseases during the follow-up (6.2 years

and 1 year), which is consistent with the data published in literature (a 100% survival rate and no evidence of relapse occurrence). Even though aforementioned tumours are described for the most part in girls, both of our patients are boys. Reports on patients with this rare form of appendiceal tumour will contribute to accumulation of data regarding the course and prognosis of the disease and will contribute to development of guidelines for treatment and monitoring of paediatric patients, which are currently insufficient.

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ADRENAL SUPPRESSION WITH GROWTH RETARDATION IN AN INFANT TREATED WITH TOPICAL OCULAR GLUCOCORTICOIDS

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Introduction Corticosteroid therapy can lead to severe iatrogenic adrenal insufficiency (IAI) and Cushing syndrome. These side-effects are common with systematic corticosteroid treatment and are less common with topical treatment modalities, even though it has been described with corticosteroid inhalation, trans- or intradermal use, intranasal and intraarticular corticosteroid application. Although ocular administration was thought to rarely lead to the development of IAI, recent studies have shown that more than two-thirds of children develop some degree of adrenal suppression, and patients who have developed an adrenal crisis during anaesthesia have been described.

Case Report We present a female infant who developed post-operative glaucoma following the surgery for congenital cataract. The therapy with topical corticosteroid eye preparations was started at the age of 5.5 months [Maxitrol drops (dexamethasone 0,1%), Tobradex ointment (dexamethasone 1 mg/g)], at an average dose of 1.5 mg/day dexamethasone. At the age of 8.7 months, 3 months after the initiation of corticosteroid use, she was examined by a paediatric endocrinologist for growth retardation [BW 6190 g (<3 ct, -2.1 SDS), BH 63 cm (<3 ct, -2.4 SDS)]. There were no other clinical signs of Cushing syndrome or other growth hormone deficiency associated syndromes. Laboratory finding revealed low ACTH levels with suppressed cortisol secretion (ACTH 1,1 pmol/L; norm 1,6-13,9; cortisol <3 nmol/L, norm 138-690). Further investigation ruled out other endocrine causes of reduced growth and congenital malformations of other organ systems. A normal female karyotype was found by classical karyotyping, 46, XX. Analysis of a panel of genes whose mutations are associated with congenital cataracts found no pathogenic variants. The girl was of normal intellectual development, and the result of pharmacogenetic analysis showed normal metabolism of corticosteroid drugs. Despite the recommendation to gradually reduce the dose of corticosteroids, local therapy was abruptly discontinued and at the age of 9 months the girl was hospitalized due to the development of an adrenal crisis. Hydrocortisone replacement therapy was initiated (10 mg/m²/day) and topical ocular corticosteroids (dexamethasone 0,1%) were continued in the dose of 2-5 drops daily. Adrenal function recovered after 10 months (ACTH short test 250 µg/m²; cortisol 60' 523,7 nmol/L), followed by growth spurt. At the age of 3 years and 4 months, the girl reached 25-50 centile in high-for-age curve (-0.15 SDS) which is in accordance with

her genetic potential (mother's height 159.5 cm, father's height 176 cm, mid parental height 162.5 cm)

Conclusion Topical ocular administration of corticosteroid preparations, although rarely, may lead to the development of IAI. Growth suppression due to corticosteroid administration may occur in children without other symptoms of Cushing syndrome. Growth monitoring is required in all children receiving long-term topical corticosteroid therapy, and discontinuation of therapy should be gradual due to the possibility of developing of an adrenal crisis.

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46,XY DISORDER OF SEX DEVELOPMENT – PARTIAL GONADAL DYSGENESIS – CASE REPORT

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Introduction 46, XY partial gonadal dysgenesis (PGD) is a disorder of sex development characterised by an incomplete testicular development (dysgenetic gonad) which results in incomplete virilisation of external genitalia in utero and partial involution of Müllerian ducts in individuals whose karyotype is 46,XY.

Case Report A 14-year old girl was admitted due to primary amenorrhea. A physical examination showed: BW 66 kg (88. c.), BH 156.7 cm (22.c.), BMI 24.9 kg/m² (94.c.), axillary and pubic hair (Tanner stage 4), the lack of breast development (Tanner stage 1), clitoromegaly/micropenis (length of 3 cm) with the urethral opening at its tip, labial fusion, no palpable gonads; the rest of the physical examination was without abnormalities. She referred to herself as a female.

The results of the diagnostic evaluation: high gonadotropin levels – LH (11.6 IU/L) and FSH (58.6 IU/L), low levels of sex hormones – testosterone (0.6 nmol/L) and oestradiol (<32 nmol/L), low AMH (<0.21 nmol/L) and normal androstenedione (4.3 nmol/L) and 17-OHP (2.1 nmol/L). Karyotype was 46,XY with partial duplication Xp ((46,XY dupl(X) (p11.4p22.1)). There was no increase in plasma testosterone following hCG administration. Pelvic MRI showed no uterus, vagina was positioned commonly with blind ending, structures resembling dysgenetic gonads were found bilaterally at the level of internal inguinal rings. Cystovaginoscopy revealed an opening of the short urogenital sinus beneath the hyperplastic clitoris/hypoplastic penis, with the upper part opening at the urinary bladder and the normoposition of the orifice; at the lower part there was a vagina which measured 8.5 cm in length, closed at the end. Surgical exploration and gonadectomy were performed. Pathohistological evaluation of the gonads showed structures of incompletely developed testis – clusters of incompletely developed convoluted seminiferous tubules with the absence of germinative cells, single cell atrophy and sclerosis of tubules, with hyperplasia of Leydig cells and persevered tubules of rete testis, as well as all efferent ductules of the testis; there was no tumour tissue. Karyotype of the gonads matched the one from the peripheral blood – 46,XY dupl(X)(p11.4p22.1). Oestrogen substitution was initiated.

Discussion Patients with 46, XY PGD generally have their diagnosis established shortly after birth during evaluation of the ambiguous genitalia. In a smaller number of girls, as was in our patient, it is revealed during puberty due to the lack

of anticipated sex development. Even though it is indisputable, genetic background is unknown in more than 30% of patients. Alongside with 46,XY karyotype, our patient had duplication of Xp(p11.4p22.1). Duplicated region contains

NR0B1 gene, which has an important role in the process of sex differentiation; furthermore, changes in the number of its copies are described in some of the patients with 46,XY gonadal dysgenesis. On the subject of patients with 46,XY PGD, it is important to establish the diagnosis as soon as possible regarding the malignant potential of the dysgenetic gonads and the need of prophylactic gonadectomy.

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PRECOCIOUS PUBERTY CAUSED BY GERM CELL TUMOR OF THE CENTRAL NERVOUS SYSTEM – CASE REPORT

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We present a boy with peripheral precocious puberty caused by germ cell tumor of the central nervous system. Our patient presented at the age of 10.5 years with accelerated growth and progressive virilization in the preceding 6 months (he gained about 11 cm in height, his muscle mass increased significantly, accelerated genital development was noticed, as well as acne occurrence and greasy hair). There were no headaches or visual disturbances, and he did not complain of frequent urination. Physical examination: BW 52 kg (96th ct.), BH 152 cm (93rd ct.), prominent muscles, genitals stage 4 on Tanner scale. Laboratory findings: increased concentrations of βhCG (811 IU/L; ref. <5) and total testosterone (82.2 nmol/L; ref. 0.8-1.3), normal concentrations of alpha-fetoprotein, DHEAS, androstenedione and 17-OHP, immeasurably low concentrations of LH and FSH. Bone age assessment by Greulich-Pyle atlas was 13.5 years. Brain MRI: expansive lesion in the pineal region with radio-morphological characteristics of non-germinomatous germ cell tumor (NGGCT) – choriocarcinoma (according to laboratory findings). After chemo and radiotherapy remnants of the tumor were surgically removed (histopathology of previously irradiated tissue was noninformative). Most cases of precocious puberty are seen in girls, in whom it is usually idiopathic. In boys, however, it is often caused by an underlying disease which is why it should always be taken seriously and investigated in a timely manner.

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VAN WYK-GRUMBACH SYNDROME – A RARE MANIFESTATION OF UNTREATED PRIMARY HYPOTHYROIDISM

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Introduction Hypothyroidism in children causes growth retardation and delayed puberty, but in some cases long-lasting and severe, untreated primary hypothyroidism can cause precocious puberty and hyperprolactinemia with or without galactorrhea – Van Wyk-Grumbach syndrome (VWGS). It is hypothesized that 'hormonal overlap' of TSH and gonadotropins who