We have described clinical course and laboratory data of 4 patients (3 M, 1 F, all Caucasian) with rare genetic syndromes. As complete genetic analysis was not available, clinical data were pitfalls for the diagnosis.

**OBJECTIVES**

Children with rare genetic disorders may have different endocrine problems. We present paediatic patients with different genetic syndromes: Pallister-Hall, Holt-Oram, Ellis-van Creveld and Marshall.

**METHODS**

In the case: the child was born in term to non-consanguineous parents (BW 3400 gr, BH 54 cm, Apag 8 b) with polydactyly on both hands and bithro septal defect. Karyotype 46, XY. At 12 months old: cerebral palsy - motor and mental retardation. First visit to paediatric endocrinologist at 5 y., the main complaint - poor growth and appetite, speech and developmental delay, unexplained mood changes, laughing, aggression. Height 95 cm (3,-4 SDS), weight 13 kg (3 p.c.). MPH 179 cm (0,75 SDS). Postaxial polydactyly on both hands. Tanner st I. Genetic syndrome was suspected. Investigation results: BA was 3 p.c.; Brain MRI – in the floor of the 3rd ventricle polycystic kidney, dysgenesis of the corpus callosum, an isointense mass. 25/20 mm, non-enhancing. Abdominal US – right kidney hypofunction. TFTs and cortisol - normal. Two deficient GH stimulation tests. Insulin test GH peak – 1.1 IU/l; clonidine test GH peak – 14.6 IU/l; NR 0-20 IU/l). Neurorousole consult – hypercalcaemia hamartoma with no need for surgery. Diagnosis: Pallister-Hall syndrome (hypercalcaemia hamartoma, polydactyly, syndactyly, kidney hypofunction, isolated GH deficiency, developmental and behavioral problems). No signs of precocious puberty. No adrenal insufficiency. GH treatment was started at 7 IU y. - 0.025 mg/kg daily. After 5.5 y. of GH treatment his height was 161 cm (1 SDS), weight 61 kg (97 p.c.), BMI 23,4 kg/m² (99 p.c.). Puberty started spontaneously at the age of 12 y. Due to BA progression GH treatment was stopped when pl was 13 y.o. Due to weight gain, insulin resistance signs (HOMA IR 3,6), antipsychotic intake and food behavioral problems metformin 1000 mg daily was prescribed.

At the age of 14 y., BA=14½ y. GV 5,5 cm after 1 y. of GH discontinuation with predicted height 176,5 cm (within target height).

**RESULTS**

**1 Pallister-Hall syndrome (PHS)** - AD inheritance with unknown frequency, mutations/ mosaicism in the GLI3 gene; about 25% are de novo - includes hypocalcemia hamartoma (often gelastic epilepsy and central precocious puberty), postaxial/central polydactyly, syno-dactly, anal atresia, bilateral epiglottis, cephalic dysphagia, cardiac, pulmonary and renal anomalies, behavioral problems. Different degree of hypopituitarism can be present, in neonatal period, adrenal insufficiency may be life-threatening condition.

**2 Holt-Oram syndrome (HOS)** - AD inheritance, the frequency is 1 in 100,000 individuals, mutations in the TBX5 gene, 85% of cases are de novo - is characterized by skeletal abnormalities of the hands and arms (a hypoplastich thumb, malformations or fusions of the carpal bones, partial or complete absence of bones in the forearm) and heart problems (atrial/ventricular septal defects, cardiac conductive disease). No endocrine problems described...

**3 Ellis-van Creveld syndrome (EvCS)** - AR disease, is frequency varies from 1 in 60,000 to 1 in 150,000 live birth, mutations in either EVCL or EVCS genes in about 60% of cases - short/limb disproportionate dwarfism, postaxial polydactyly, ectodermal dysplasia and in 50-60% of cases congenital heart defects. In unique cases renal, pulmonary, ocular, hemopoetic malformations, hypoplasia and cryptorchidism were present. Some EvCS patients may benefit from GH treatment.

**4 Marshall syndrome – AD chondrosioplasia (mutation of COL11A1 gene) - characterized by mid-facial hypoplasia, short stature, hearing damage and ocular defects (cataract, high myopia), bone maturation can be advanced.

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