Case Presentation A 6.4 year old girl presented with acne, pubic hair and body odour.

Diagnosis of CPP was performed on the basis of clinical signs of central puberty (breast Tanner 2 and pubic hair Tanner 2), increased basal gonadotrophine hormones (LH 4.6 IU/L, FSH 3.7 IU/L, E2 109 pmol/L) and growth spurt (height on 1.6 SDS). Her bone age was assessed to be 7 years.

Brain Magnetic Resonance (MRI) did not disclose any abnormality. Treatment with GnRHα was given subcutaneously once a month (triptorelin in a dose 3.75 mg). Girl’s dyzogenic twin sister developed signs of puberty at the age of 8 years. At presentation, she had breast Tanner 3 and pubic hair Tanner 1. Her bone age was 8.6 years, her height was on 0.8 SDS. Laboratory assessment confirmed CPP (LH 1.07 IU/L, FSH 3.9 IU/L, E2 187 pmol/L) and after additional endocrinological and neuroradiological work-up, suppression of CPP started. Precocious puberty was well controlled by pharmacological therapy and both sisters reached their final height (163.8 and 159.1 cm) in accordance with midparental height (MPH 165 cm, 0.6 SDS).

As CPP was diagnosed in both dyzogenic twin sisters, we sought for a genetic cause.

Coding regions of the MKRN3 gene and exon-intron boundaries were analyzed using Sanger sequencing. Pathologic heterozygous variant NM_005664.3:c.475_476insC (NP_005655.1:p.Ala162Glyfs) of MKRN3 gene was identified in both siblings.

Conclusion We want to highlight the importance of genetic analysis in cases od familial CPP, providing grounds for genetic counseling in later life.

204
CASE REPORT OF RESISTANCE TO THYROID HORMONE WITH MUTATION TO THE THYROID β RECEPTOR GENE
Lizaveta Collins*, Saadia Rao, Helen Shing, Beth McLean. East Suffolk And North Essex NHS Foundation Trust Colchester Hospital

Background Thyroid hormones are important for energy metabolism, the metabolism of nutrients and inorganic ions, thermogenesis, and for stimulation of growth and development of various tissues Case The baby girl, was born at 39/40 uncomplicated pregnancy, presented to prolong jaundice clinic at 19th days old, Newborn bloodspot screening at 5 days was normal. She sleeps a lot and often cries when tired.

Developmentally appropriate The blood test showed the TSH (35.7 mIU/L) and FT4 (2.87 mIU/L). Her thyroid function was monitors and remained the same for 3 months However at 4 months of age she had TSH 1.2mIU/L and T4 25.4mIU/L, Free T3 16.3 mIU/L. She had the fluorescent DNA analysis which showed Thyroid hormone resistance (RTH). Heterozygous mutation in TR beta – c.1286G>A (p.Arg429Gln). The diagnosis helps to provide the genetic counselling for the family.

Conclusion Resistance to thyroid hormone (RTH) 1:40,000 live births is a rare inherited syndrome characterized by diminished response of the target tissue to thyroid hormone caused, in the majority of cases, by mutation of the thyroid hormone receptor beta (THRB) gene. The diagnosis of RTH is challenging for the clinician. It should be considered in a patient presenting with unexplained elevated serum free T4 (T4), unsuppressed TSH levels and decreased serum free T4/T3 ratio. The treatment decision depends on the individual characteristics of each patient. Patients with hypothyroid and hyperthyroid symptoms may require treatment with thyroid hormone and with agents such as beta blockers, antithyroid drugs and thyroid hormone analogues