Pseudohypoparathyroidism -- Albrights Hereditary Osteodystrophy

Case

9-year-old boy referred by GP with two-month history of intermittent body aches and corrected calcium 1.3mmol/L (2.2-2.6). Long-standing constipation, description of dystonic posturing, unco-ordinated (parents attributed to leg length discrepancy from previous Perthes). No relevant family history – only child on non-consanguineous family.

Examination showed tetanic muscle contractions, leg length discrepancy (left shortening), short 4th metacarpal/tarsal on right, weight 28.1kg and height 121.6cm (-1.9 SDS), otherwise unremarkable systems examination.

ECG QTc prolonged. Calcium low as above, phosphate high at 3.1mmol/L (1.0-2.0), normal vitamin D and ALP, PTH elevated at 71.8pmol/L (1.6-7.0). Urine calcium low, tubular reabsorption PO4 98%. CT head showed basal ganglia calcifications. Xrays showed moderately advanced bone age (12y 5m vs. 9y 2m) and short right metacarpal. Nephrocalcinosis on renal USS.

Acutely managed with a calcium infusion for 36 hours followed by oral calcium and calcitriol with resultant clinical and biochemical improvement.

Further investigations included the following: Genetics; IGF1 generation test; gonadotropins; TFTs

Discussion

Albrights Hereditary osteodystrophy

- Clinical and biochemical features including multi-hormonal resistance
- Genetics

Treatment of short stature with advanced bone age

- Treatment with GH
- GnRH analogues
- Different approach to assessing BA

Other management/monitoring considerations

- PTH resistance
- Ectopic ossifications
- TSH resistance
- Cognitive impairment
- Puberty- sex steroids as indicated
- Decreased insulin sensitivity
- Early onset obesity

Non-autoimmune diabetes due to Wolfram Syndrome

Case

SR (14yrs), NR (8yrs) and FR (8yrs) are three siblings with Wolfram Syndrome (DIDMOAD). SR presented at 4 years of age having been previously well with a 3 month history of polyuria and polydipsia. His BGL was 17.3mmol/L without ketonaemia and he was commenced on subcutaneous insulin. His autoantibodies were negative. He was reviewed at 7 years of age and was noted to have nocturnal enuresis and some behavioural problems. His serum osmolality was 292mmol/kg. He was investigated for Wolfram syndrome and was found to have two pathogenic mutations in the WFS1 gene, one inherited from each parent. At this stage all other children in the family had genetic analysis and twins NR and FR were found to have the same mutation. SR was commenced on DDAVP but has continued to have nocturia and daytime frequency. His initial ophthalmologic review did not demonstrate optic atrophy but he has gone on to develop early changes of optic atrophy with loss of colour vision and he requires glasses. SR has behavioural issues, low mood and history of self harm. He has NDIS funding for psychological support.

NR and FR both developed symptoms of diabetes during a viral illness at 2 years of age. They were both found to be hyperglycaemic (NR = 14mmol/L, SR = 14mmol/L) without ketonaemia and were commenced on subcutaneous insulin. They developed symptoms of diabetes insipidus with increased thirst and wet nappies over the following two years and were commenced on DDAVP at 4 years of age. They had deterioration of colour vision at 5 years of age and both require glasses. They both have behavioural issues and have NDIS funding for psychological support. All siblings have normal audiological reports.

Discussion

- Clinical features and pathophysiology of Wolfram Syndrome
- Insulin management in Wolfram Syndrome
- Potential novel treatment targets for Wolfram Syndrome