6-year old girl with mutation in DNMT3A – a new overgrowth syndrome

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Background:
- Overgrowth disorders are a heterogeneous group of conditions characterized by increased growth and other clinical features
- Overgrowth may be apparent at birth and can be static or progressive
- The increased growth can be seen in combination with an increased weight and/or increased head circumference
- Many of the overgrowth syndromes are associated with an increased risk of malignancy

Methodology:
Standard DNA sequencing of all coding exons and flanking UTR’s of DNMT3A was performed.

Results:
- A de novo mutation (DNMT3A c. 1232dup) was detected
- In 2014, Katrina Tatton_Brown et al reported the detection of 13 different DNMT3A mutations in 152 individuals with overgrowth phenotype
- A consistent phenotype was evident amongst the 13 individuals with DNMT3A mutations: distinctive facial appearance, tall stature and intellectual disability
- DNMT3A mutation is frequently found in acute myeloid leukemia and have also been reported in other hematological malignancies

Objective and hypotheses:
- A 6 year old girl with accelerated growth rate was seen in paediatric outpatient clinic
- She was born at term, and her birth length was 55 cm long (+2.4 SD)
- At 6 years she was 134.4 cm tall (+3.7 SD) with a high growth rate at 8.9 cm/year
- Her growth rate was above the range for her family
- There were no signs of precocious puberty
- She had a bone age more than 3 years advanced
- She had cognitive impairment and slightly retarded motor development
- The only dysmorphic feature was heavy horizontal eyebrows

Conclusions:
- In childhood, the differential diagnosis of increased growth includes normal variants, nutritional obesity, endocrinopathies, connective tissue disorders, sex chromosome abnormalities and overgrowth syndromes
- When assessing a child with tall stature and intellectual disability mutations in DNMT3A is important to consider
- In general, follow-up of children with overgrowth syndrome should be conducted due to the potential malignancy risk
- The DNMT3A related malignancy risk may be linked to a different mechanism and may not be present in patients with truncating mutations

Results: Figure 1. 6 year old girl with accelerated growth rate

Figure 2. The girls height

Figure 3. Growth Velocity

Bibliography:

Disclosure Statement:
None of the authors have any conflicts of interest