1. Background:
- Pseudohypoparathyroidism is a rare endocrine disorder characterized by resistance to the action of parathyroid hormone.
- Albright hereditary osteodystrophy (AHO) is the most common of 5 sub-types, presenting with a characteristic phenotype.

AIM: To describe a case of premature adrenarche with pseudohypoparathyroidism, an as yet unreported combination.

2. Case:
An otherwise well 8 year old girl presented to a Paediatric Endocrine Clinic with early pubic hair development suggestive of Premature Adrenarche.

Blood tests revealed:
- Hypocalcaemia
- Elevated phosphate
- Highly elevated PTH

She had normal stature (height 50th – 75th centile) and no phenotypic features of Albright Hereditary Osteodystrophy were identified on initial presentation (obesity, learning difficulties, brachydactyly, short stature, shortened 4th/5th metacarpals, dental hypoplasia or a rounded face).

3. Treatment:
- Oral calcium carbonate
- Alfacalcidol

Corrected Calcium and phosphate levels normalised with treatment.

4. Outcome:
- Hand & Wrist for Bone Age (non dominant):
  “The fourth and fifth metacarpals appear shortened" - a phenotypical feature of AHO.
- MRI head: No evidence of white matter calcification
- Genetic testing:
  - Microarray Comparative Genetic Hybridization - no abnormality seen
  - Chromosome 20q13.32: GNAS exon A/B, GNASXL, NESPAS + NESP55 methylation – significant loss of maternal methylation
  - No evidence of uniparental disomy

5. Discussion:
- In our case the defect is likely due to an isolated imprinting error
- Recognition of a broader range of phenotypic features and underlying mutations has led to a novel classification system of iPPSD (Inactivating PTH/PTHRP signalling disorders), developed by the EuroPHP network.
- GNAS1 mutations have been identified underlying various pseudohypoparathyroidism subtypes, resulting in reduced function of the G-protein coupled to the PTH receptor.
- G-proteins are also coupled to other hormone receptors; patients with AHO or iPPSD often present with other endocrine disorders, for example hypothyroidism.
- There are cases of individuals with GNAS1 mutations presenting concurrently with precocious puberty and pseudohypoparathyroidism but no reported case of premature adrenarche and pseudohypoparathyroidism.

6. Key Messages:
The underlying causes for PTH-related disorders are highly heterogenous with a variety of demonstrated underlying (epi)genetics; adrenarche is poorly understood; it is unclear if the premature adrenarche and pseudohypoparathyroidism in our case have a linked underlying mechanism.

References:

Image 1: Hand and wrist X-ray for bone age (non dominant) - "The fourth and fifth metacarpals appear shortened.”

Glossary: PTH – parathyroid hormone; AHO – Albright Hereditary Osteodystrophy