Severe Hypocalcaemia in Propionic Acidaemia caused by Parathyroid Hormone Resistance and treated with Alfacalcidol.

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What is known?

- Propionic Acidaemia (PA), an organic acidaemia, is characterized by episodes of decompensation with severe metabolic acidosis and hyperammonaemia
- This condition has been associated with low bone mineral density and osteoporosis
- Hypocalcaemia occurs in 35-65% of decompensation events, the underlying pathophysiology of this is unknown
- One previous case report suggests this may be due to PTH resistance occurring transiently during decompensation

What this poster adds?

- This case confirms PTH resistance as likely pathophysiology behind severe hypocalcaemia in PA decompensation
- Demonstrates the first use of alfacalcidol in the management of hypocalcaemia due to PTH resistance in PA

What questions does it raise?

- Why and when does transient PTH resistance occur in PA?
- Does alfacalcidol have a role in prevention of hypocalcaemia and hypercalciuria in intermittent PTH resistance?
- Does intermittent hypocalcaemia due to PTH resistance affect bone health in children with PA?

Case:

Day 3: The initial diagnosis of PA

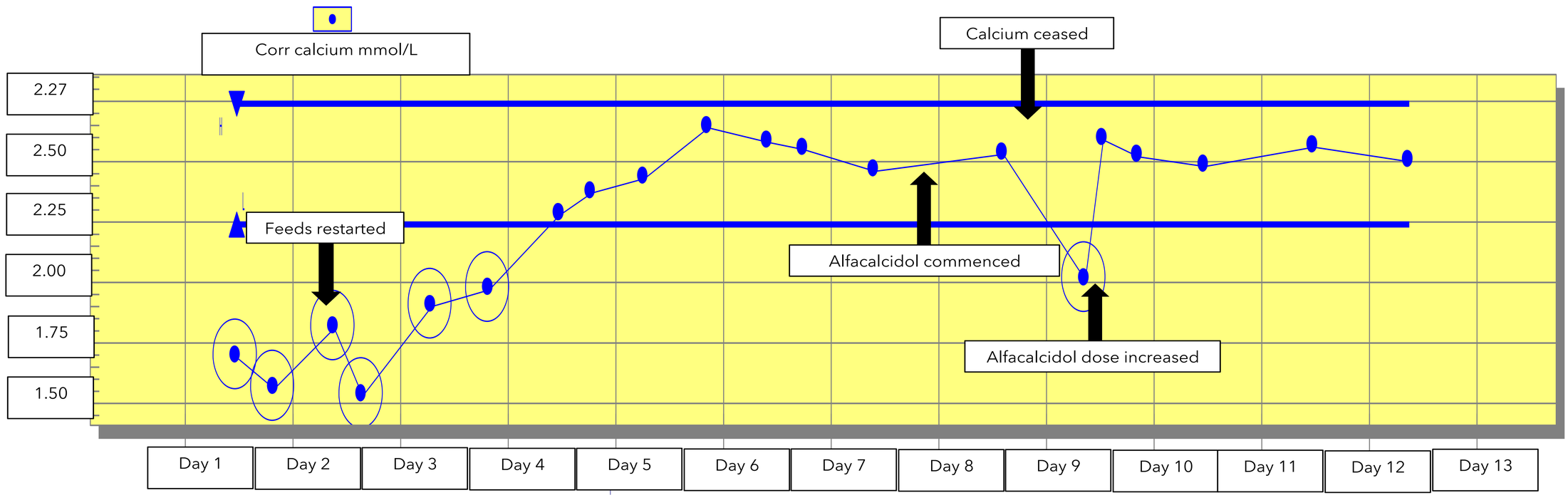
- Presented with grunting, acidosis, hyperammonaemia
- Term, no medical/family history, non-consanguineous parents
- Rapid testing and later genetic confirmation of PA
- Hypocalcaemic at the time of presentation with profile suggestive of PTH resistance
- Serum calcium normalized with IV calcium & oral cholecalciferol

Investigation	Result	Normal Range
Calcium Corrected	**1.32 ↓**	**2.19-2.69mmol/L**
Phosphate	1.8	1.0-1.9mmol/L
Magnesium	0.78	0.65-1.05mmol/L
Alkaline Phosphatase	**77 ↓**	**187-429IU/L**
Parathyroid Hormone	**115 ↑**	**10-65ng/L**
Vitamin D	**29 ↓**	**>50nmol/L**

2.5 months: Second presentation

- Presented with decompensation due to gastroenteritis with acidosis and hyperammonaemia
- Hypocalcaemia with profile again suggestive of PTH resistance

Investigation	Result	Normal Range
Calcium Corrected	**1.56 ↓**	**2.19-2.69mmol/L**
Phosphate	1.6	1.0-1.9mmol/L
Magnesium	0.68	0.65-1.05mmol/L
Alkaline Phosphatase	227	187-429IU/L
Parathyroid Hormone	**297 ↑**	**10-65ng/L**
Vitamin D	91	>50nmol/L
Urine Calcium:Creatinine	**2.75 ↑**	**0.05-0.60**
Urine Phosphate	**<1.1 ↓**	**nmol/L**
Renal/Liver profile Normal	Renal Ultrasound: no nephrocalcinosis	
Wrist X-ray: no signs of rickets		



Management (of second presentation):

- Calcium normalised after treatment with oral calcium (1.25mmol/kg/day) and cholecalciferol (3000 units/day)
- Alfacalcidol started (30ng/kg/day)
- Oral calcium/cholecalciferol reduced
- Calcium fell (2.5 to 2.01mmol/L) after cessation of calcium supplements (inadequate calcium in diet)
- Alfacalcidol increased (60ng/kg/d) and calcium normalised

Follow-up at 6 months: *remains stable on alfacalcidol, no episodes of hypocalcaemia with decompensations*

Discussion and conclusions:

- **PTH resistance** appears to be the mechanism for **hypocalcaemia** during episodes of **PA decompensation**.
- **Acute management of PTH resistance** includes **active vitamin D** (calcitriol or alfacalcidol) and adequate **calcium** intake.
- A retrospective chart review of our unit showed that 4 of 6 children with PA had hypocalcaemic episodes (range 1.19-2.01mmol/L) associated with decompensation. Out of a total of 25 episodes of decompensation with hyperammonaemia, 9 were associated with hypocalcaemia with normal or low ALP. No hypocalcaemia was recorded when patients were well, however routine monitoring was not undertaken. Only in our case was PTH measured and only our case was treated with alfacalcidol.
- We propose that **intermittent hypocalcaemia secondary to PTH resistance** may contribute to **bone demineralisation** in PA.
- Further studies assessing the mechanism of this and potential utility of **ongoing treatment with alfacalcidol** would be valuable in guiding long-term management.

References:Griffith et al. Parathyroid hormone resiatance and B cell lyniphopenia in propionic acidemia. Acta Pediatr.1996;85:875

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Bone, growth plate and mineral metabolism

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