Transient congenital hyperinsulinism and renal Fanconi syndrome

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Background

Congenital hyperinsulinism is the most common cause of persistent hypoglycemia in early infancy. Mutations in the *HNF4A* gene lead to transient hyperinsulinism in early infancy and maturity-onset diabetes of youth (MODY1), later in life.

Fanconi syndrome is a generalised dysfunction of the renal proximal tubule with a loss of glucose, amino acids, phosphate, low molecular weight proteins, bicarbonate and urate, causing growth failure and rickets in childhood.

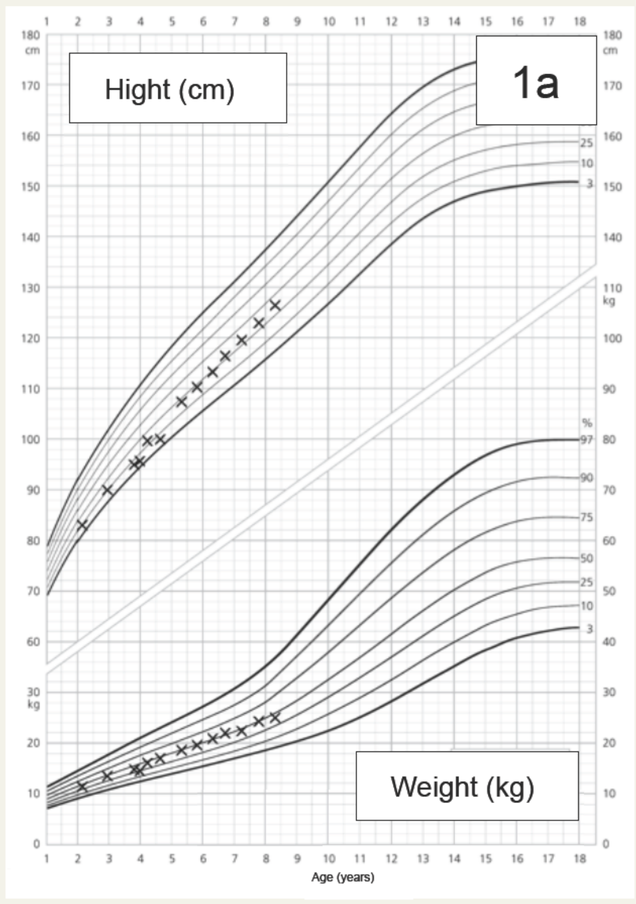
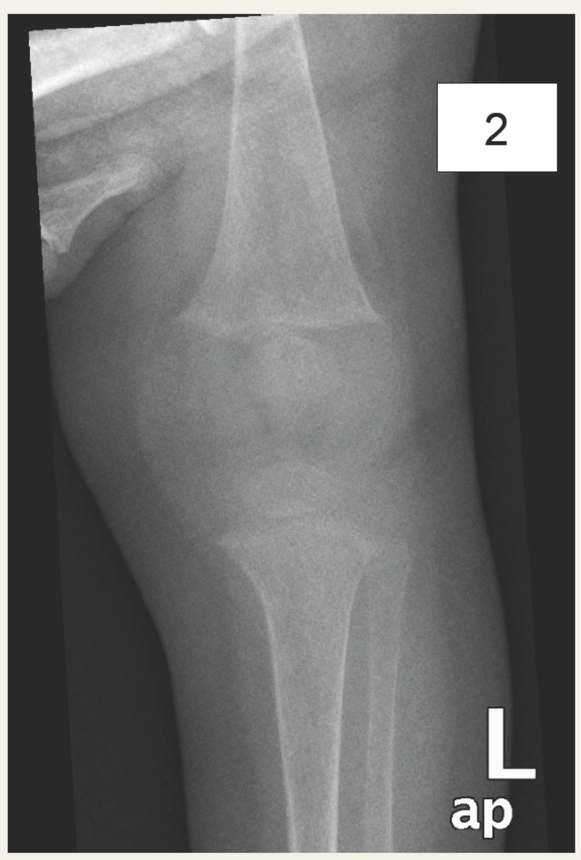


Fig.1 a + b: Growth charts for patient 1 (1a, age in years) and patient 2 (1b, age in months)

Conclusion: The clinical presentation of transient neonatal hyperinsulinism and renal Fanconi syndrome is highly suggestive for a *HNF4A* R76W mutation[I,II,III]. This disease entity seems to be a further differential diagnosis of congenital hyperinsulinism.



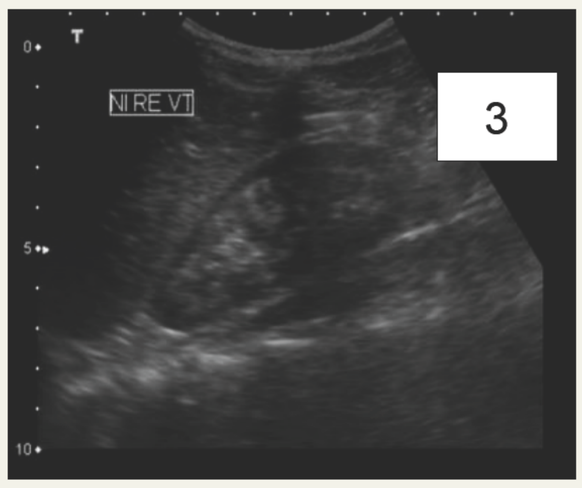


Fig. 2: X-ray of the left knee of patient 2: Cupping and frays of metaphysis
Fig. 3: Ultrasound of the right kidney of patient 1: Nephrocalcinosis °IIa

Case reports

	Patient 1	Patient 2
General characteristics		
Age; sex	10 years; female	16 months; male
Gestational age	Full term (40 + 0/7)	Pre term (35 + 6/7)
Birth weight	3750 g	3960 g (LGA)
Development	Good thriving	Failure to thrive
Metabolism		
Hypoglycemia (minimal)	0 mg/dl	13 mg/dl
Insuline at hypoglycemia	18 pmol/l	1460 pmol/l
Therapy of hypoglycemia	Glucose iv, Maltodextrin po, Diazoxid po (5-7 mg/kg/d)	Glucose iv, Maltodextrin po, Diazoxid po (4-7 mg/kg/d), Somatostatin sc
	HbA1c 4,6 %	-
Nephrology		
Age at clinical manifestation	6 months	6 months
Urine	Glucosuria, proteinuria, hyperaminoaziduria, hyperphosphaturia	
Blood	Hypophosphatemia, alcaline phosphatase ↑	Hypophosphatemia, alcaline phosphatase ↑, metabolic acidosis
Nephrocalcinosis	Grade IIa	Increased echodensity
Phosphopenic rickets	Craniotabes (6 months), radiological evidence and genua valga (3 years)	Radiological evidence
Therapy of Fanconi syndrome	Calcitriol, Cholecalciferol Phosphate	Calcitriol, Cholecalciferol Phosphate, Bicarbonate
Genetics	***HNF4A* R76W**	***HNF4A* R76W**

[I]Hamilton AJ, et al. *J Mol Genet* 2014:51:165-169. [II]Stanescu E, et al. *J Clin Endocrinol Metab* 2012: 97: E2026-E2030. [III]Numakura et al. *Diabes Res Clin Pract* 2015: 108: E53-E55

ESPE 2015
1060--P3
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DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: ESPE 2015 BARCELONA
PosterSessionOnline.com