Background

- FHHNC is an autosomal recessive disorder, caused by mutations in either claudin 19 or claudin 16.
- A rare disorder of magnesium (Mg) metabolism with fewer than 400 reported cases throughout the literature. Somewhat underdiagnosed disorder, not being commonly observed.

Case presentation

- 2 years old female who was incidentally noted to have nephrocalcinosis as part of evaluation for urinary tract infection.
- Initial workup by renal service revealed elevated PTH, hence prompting a referral to endocrine.
- Labs: 25-OH vitamin D 37ng/ml, 1,25-OH vitamin D 57ng/ml, Alkaline phosphatase 215 U/L, PTH 128 pg/ml, Calcium (Ca) 10.2 mg/dL, Phosphorus 4.3mg/dL, Mg 1.6mg/dL. Urine Ca/Cr 0.6.
- PTH level remained elevated for her Ca level on multiple repeats. A Parathyroid scan did not reveal any adenoma or nodule. On one of follow-up labs, hypomagnesemia (1.4mg/dL) was noted.
- At age 4, she started to have vision problem. An ophthalmology evaluation showed macular scarring. At this time, a suspicion of FHHNC was raised and genetic testing confirmed a C59G mutation in CLDN 19.
- Patient has been on thiazide to decrease Ca excretion and also on Mg supplement.

Discussion

- CLDN16 and CLDN19 encode the tight-junction (TJ) proteins claudin-16 and claudin-19, respectively, which are expressed in the thick ascending limb of Henle’s loop and form an essential complex for the paracellular reabsorption of Mg and Ca.
- Claudin-19 is also expressed in retinal epithelium and peripheral neurons. Defects in CLDN19 are the cause of hypomagnesemia renal with ocular involvement.
- Clinical traits of FHHNC usually occurs early in childhood or before adolescence.
- Patients usually present with recurrent urinary tract infections, nephrolithiasis, polyuria, polydipsia and/or failure to thrive.
- Characterized by primary renal magnesium wasting with hypomagnesemia, hypercalciuria and nephrocalcinosis. Elevated PTH levels observed in FHHNC patients contrast with the normal or reduced PTH levels associated with hypomagnesaeemia.

Conclusion

- FHHNC is a rare disorder of Mg metabolism and often underdiagnosed. In particular, Mg levels are often not checked and there is a spectrum of FHHNC in which the Mg could be normal.
- FHHNC is a progressive disease in both renal and eyes however, the clinical course is not completely clear.
- No known cure, and treatment is largely supportive with thiazide diuretics and Mg supplementation, although whether this helps to slow the rate of progression to end-stage renal disease is not clear at present.
- Multidisciplinary approach is helpful in monitoring and management of this disease.

Reference:
- "Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis: clinical and molecular characteristics. Clinical Kidney Journal, 2015, vol. 8, no. 6, 656–664"