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On the Cover

What's the diagnosis?

Details: This patient with progressive CKD had a past medical history of seizures and episodes of tetany and was taking carbamazepine, lamotrigine and calcium and vitamin D supplements. She had an eGFR of 33 mL/min/1.73m2, hypomagnesaemia, hypocalcemia and hypercalciuria with a mildly elevated PTH. Vitamin D levels were sufficient. Renal imaging demonstrated nephrocalcinosis and a renal biopsy demonstrated nephrocalcinosis. The unifying diagnosis is autosomal dominant hypocalcaemia with progressive CKD secondary to nephrocalcinosis. Genetic analysis confirmed a heterozygous c.354C>A, p.(Asn118Lys) missense mutation in CASR, encoding the Calcium-sensing receptor (CaSR).

Description: The three images show:
   a) CT brain scan demonstrating calcium deposition in a symmetrical pattern at the junction of the grey and white matter
   b) CT of kidneys showing bilateral nephrocalcinosis
   c) Renal biopsy stained with Von Kossa demonstrating nephrocalcinosis

Key teaching points: A family history revealed the patient’s mother and sibling were also affected, consistent with autosomal dominant inheritance. The PTH is usually low as activating mutations in CaSR lower the set-point of calcium-responsive parathyroid hormone release, allowing a low serum calcium to be perceived as normal. In this case PTH was mildly elevated in the context of longstanding CKD. Overzealous attempts at correcting hypocalcaemia in patients with autosomal dominant hypocalcaemia result in hypercalciuria and nephrocalcinosis. Brain calcification (typically basal ganglia calcification) is a frequent finding, the mechanism is not known but is likely to be secondary to the CASR mutation itself. Symptomatic and judicious correction of hypocalcaemia is advised.

(Images and text provided by Shahid Abdullah1, Shalabh Srivastava2, Simren Raktra2, Philip Haslam1, and John A. Sayer1,3; 1The Newcastle Upon Tyne Hospitals NHS Foundation Trust, 2City Hospitals Sunderland NHS Foundation Trust; and 3Newcastle University, Institute of Genetic Medicine, Central Parkway, Newcastle NE1 3BZ)