ADENINE PHOSPHORIBOSYLTRANSFERASE DEFICIENCY: TWO NOVEL GENETIC MUTATIONS AND UNITED KINGDOM EXPERIENCE

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INTRODUCTION: Adenine phosphoribosyltransferase (APRT) deficiency causes 2,8-dihydroxyadenine (2,8-DHA) crystals and renal failure. We present three cases with two novel mutations from a single centre. UK data of APRT is limited; we undertook a cross-sectional survey of patients identified at the Purine Research Laboratory.

METHODS: An 18-year old man of presented with a history of recurrent nephrolithiasis. 2,8-DHA stones were identified by UV spectrophotometry. 11 years after his initial symptoms, he re-presented with chronic kidney disease stage (CKD) 4. His younger brother presented with loin pain and acute kidney injury. Kidney biopsy showed acute tubulointerstitial nephritis with crystalline deposits.

A 48-year man with a history diabetes and hypertension presented with an acute on chronic kidney injury. Renal biopsy showed minimal diabetic features but chronic tubulointerstitial nephritis with crystalline deposits.

We sent questionnaires to obtain outcome information of the identified cases from 1979-2013 at the purine research laboratory.

RESULTS: All three cases had 2,8-dihydroxadenine in urine and complete APRT deficiency. Genetic studies identified a homozygous novel mutation in the APRT gene from Case 1 and 2; APRTc.543 A>T, p.181X>C, and case 3 APRTc.380a>G, p.127D>G.

We identified only 17 patients (12 M) from 14 families. Mean age at diagnosis was 26 (range 2-70). Clinical information was not available in 2 patients (1 had ESRD) and 3 patients were deceased (1 had ESRD). The commonest reason for testing was nephrolithiasis (11/17). 8/12 had normal renal function and 4/12 had CKD.

CONCLUSION: APRT is a rare disease with varied presentation. It is under-diagnosed in the United Kingdom. Stone analysis and family screening are important ways to identify cases. The finding of unexplained crystalline deposits on renal biopsy should prompt a possible diagnosis of APRT deficiency. It is easily treatable and a more concerted approach should be undertaken to diagnose patients in the UK. This would be feasible with the National Renal Rare Disease Registry (RaDaR).