METHODS

Study population, baseline characteristics and statistical analysis

Three patients from Westmead and Nepean Hospital diagnosed with APRT deficiency on renal biopsy were identified and consented for this report. Clinical and laboratory data from time of diagnosis and during the follow up period were obtained from medical records. Estimate GFR (eGFR) was calculated via the CKD-EPI formula. Patient characteristics are presented in Tables 1 and 2.

Laboratory methods

APRT enzyme activity was measured in erythrocyte lysates (thin layer chromatography on polyethyleneimine-cellulose plates using radiolabelled adenine substrates, Women's and Children's Hospital, South Australia). Serum oxypurinol levels were measured by St Vincents Pathology (SydPath, Sydney, Australia). Transplant patients underwent protocol 3-month measured GFR via standard technetium-99m diethylene-triamine-pentaacetic acid (DTPA) renal scan. Genetic sequencing of the *APRT* gene was done on an Illumina TruSight One next generation sequencing platform. Analysis was limited to coding regions of the *APRT* gene (informed consent for genetic testing was obtained).

Standard processing of both native and transplant renal biopsies included light and polarized light microscopy (haematoxylin and eosine, periodic acid-schiff, masson's trichrome and jones methemamine silver; and in addition for transplant biopsies, immunohistochemistry for C4d and simian virus-40. Transplant biopsies were performed for indication and at protocol intervals (1, 3 and 12 months), and these were scored for rejection in accordance with the revised Banff Criteria 2017[7]. For all available post-transplant biopsies were also assessed for percentage (of the biopsy) affected by crystals; and the overal luminal, epithelial and interstitial distribution on polarized microscopy by an experienced pathologist.

Urine microscopy was performed on all three patients. Where possible, morning urine samples and 10ml of urine were spun down at 3000 rpm for 3 minutes before standard preparation of microscopy slides were performed. One patient was only able to provide 3-5ml/urine over 24 hours (dialysis dependent) and the total volume of this was analyzed.

Supplementary REFERENCES

S1. 10 Kaartinen, K. *et al.* Adenine Phosphoribosyltransferase Deficiency as a Rare Cause of Renal Allograft Dysfunction. *Journal of the American Society of Nephrology : JASN* **25**, 671-674, doi:10.1681/ASN.2013090960 (2014).

S2. 11 Lim, D.-H. *et al.* Febuxostat in Hyperuricemic Patients With Advanced CKD. *American Journal of Kidney Diseases* **68**, 819-821, doi:10.1053/j.ajkd.2016.07.001 (2016).

S3. 12 Akimoto, T. *et al.* Febuxostat for Hyperuricemia in Patients with Advanced Chronic Kidney Disease. *Drug Target Insights* **8**, 39-43, doi:10.4137/DTI.S16524 (2014).

S4. 13 Shibagaki, Y., Ohno, I., Hosoya, T. & Kimura, K. Safety, efficacy and renal effect of febuxostat in patients with moderate-to-severe kidney dysfunction. *Hypertension Research* **37**, 919, doi:10.1038/hr.2014.107 (2014).

S5. 14 Tojimbara, T., Nakajima, I., Yashima, J., Fuchinoue, S. & Teraoka, S. Efficacy and Safety of Febuxostat, a Novel Nonpurine Selective Inhibitor of Xanthine Oxidase for the Treatment of Hyperuricemia in Kidney Transplant Recipients. *Transplantation Proceedings* **46**, 511-513, doi:10.1016/j.transproceed.2013.09.045 (2014).

S6. 15 Stocker, S. L. *et al.* The pharmacokinetics of oxypurinol in people with gout. *British Journal of Clinical Pharmacology* **74**, 477-489, doi:10.1111/j.1365-2125.2012.04207.x (2012).

S7. 16 Dalbeth, N. & Stamp, L. Allopurinol Dosing in Renal Impairment: Walking the Tightrope Between Adequate Urate Lowering and Adverse Events. *Seminars in Dialysis* **20**, 391-395, doi:10.1111/j.1525-139X.2007.00270.x (2007).

S8. 17 Edvardsson, V. O. *et al.* Comparison of the effect of allopurinol and febuxostat on urinary 2,8-dihydroxyadenine excretion in patients with Adenine phosphoribosyltransferase deficiency (APRTd): A clinical trial. *European Journal of Internal Medicine* **48**, 75-79, doi:10.1016/j.ejim.2017.10.007 (2018).

S9. 18 Mulay, S. R. & Anders, H.-J. Crystal nephropathies: mechanisms of crystal-induced kidney injury. *Nature Reviews Nephrology* **13**, 226, doi:10.1038/nrneph.2017.10 (2017).

S10. 19 Nankivell, B. J. & Chapman, J. R. The Significance of Subclinical Rejection and the Value of Protocol Biopsies. *American Journal of Transplantation* **6**, 2006-2012, doi:10.1111/j.1600-6143.2006.01436.x (2006).

S11. 20 Kee, T. Y.-S. C., Jeremy R.,; O'Connell, Philip J.,; Fung, Caroline L.-S.; Allen, Richard D. M.; Kable, Kathryn; Vitalone, Matthew J.; Nankivell, Brian J. Treatment of Subclinical Rejection Diagnosed by Protocol Biopsy of Kidney Transplants. *Transplantation* **82**, 36-42 (2006).

S12. 21 Oyake, C., Ikeda, H., Fuyama, M., Watanabe, T. & Isoyama, K. Minimum allopurinol dose for adenine phosphoribosyl transferase deficiency. *Pediatrics International* **59**, 1097-1098, doi:10.1111/ped.13350 (2017).