Reviewer's report

Title: Recurrent exercise-induced acute renal failure in a young Pakistani man with severe renal hypouricemia and SLC2A9 compound heterozygosity

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Reviewer: Blanka Stiburkova

Reviewer's report:

The purpose of the article is to detail case report of renal hypouricemia. The data are convincing and the discussion appropriate. The methods are sound and the results presented are reliable. The work is comprehensive and well described. However, the conclusions provided are largely confirmatory and do not add significantly novel concept to this research field.

Comments to the Author

2. Page 3, line 9. The sentence about RHUC2 is not correct. In RHUC2 there are two clinical distinctions with important differences: values found in heterozygous renal hypouricemia patients are similar to those with URAT1 mutations; values found in homozygous or compound heterozygous patients are much lower (serum uric acid levels near 0) and renal excretion is markedly higher (>100%).
3. Authors discussed the pathogenic hypothesis based on the powerful antioxidant activity of UA. However, extremely low hypouricemia is also a characteristic of xantine dehydrogenase (XDH, E.C. 1.1.1.204) deficiency (OMIM #278300, OMIM 603592). Probands with xanthinuria had not AKI in their medical history. It suggests, that hypouricemia alone, probably, could not contribute to renal failure in patients with primary renal hypouricemia. This discrepancy should be discussed.
4. Not all readers will be familiar with the units mg/dL. For this reason, the reference ranges for uric acid, creatinine and FE-UA should be given, these will of course vary with age and sex.
5. Use CKD classification, state creatinine and rate of decline of renal function.

Minor points

1. Page 2, line 12. "harboring" should be "harbouring".
2. Several sentences are not clear and need editing, for example: lines 4-5, page 2; lines 3-4, page 4.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.