Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 54879

Title: Gitelman syndrome caused by a rare homozygous mutation in the SL 2 gene: a new case report and review of literature

Reviewer's code: 00742368
Position: Peer Reviewer
Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-02-25

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2020-06-17 13:21

Reviewer performed review: 2020-06-21 11:53

Review time: 3 Days and 22 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes 3 Key words. Do the key words reflect the focus of the manuscript? Yes 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Not applicable-case report 6 Results. What are the contributions that the study has made for research progress in this field? The only new information is description of the rare mutation, although the authors mention that they have previously reported it-need reference here. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Can improve the discussion Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Mostly Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Table should be improved (see comments below) 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? not applicable 10 Units. Does the manuscript meet the requirements of use of SI units? yes 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections-one additional reference is suggested Does the author self-cite, omit, incorrectly cite and/or over-cite references? OK 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Can improve 13 Research methods and

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? OK 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? The patient consented Comments: Introduction -Start with Gitelman syndrome not hypokalemia. Describe all associated symptoms to clarify the whole picture to the reader Suggest "Gitelman's syndrome (GS), an autosomal recessive disorder caused by a defect of the thiazide-sensitive Na-Cl cotransporter (TSC) at the distal tubule, is characterized by hyperreninemic hyperaldosteronism with normal or low blood pressure, hypokalemia, metabolic alkalosis, hypomagnesemia and hypocalciuria. It is usually diagnosed in late childhood or adulthood. Symptoms of hypokalemia include fatigue, leg cramps and constipation, but, most critically, the slowing of the heart rhythm and even cardiac arrest. Affected individuals may experience episodes of fatigue, dizziness, fainting due to hypotension, muscle weakness, muscle aches, cramps and spasms or even tetany. Symptomatic episodes may also be accompanied by abdominal pain, vomiting, diarrhea or constipation, and fever. Seizures may also occur and in some people may be the initial reason they seek medical assistance. Facial paresthesia characterized by numbness or tingling is common. Less often, tingling or numbness may affect the hands. Affected individuals may or may not experience polydipsia, polyuria including nocturia. When these symptoms do occur

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

they are usually mild. Affected individuals often crave salt or high-salt foods. Some affected adults develop chondrocalcinosis which is thought to be related to hypomagnesemia. Affected joints may be swollen, tender, reddened, and warm to the touch." -Suggest adding the reference: Blanchard et al. Gitelman syndrome: consensus and guidance from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney International 2017; 91: 24–33. Case -In the discussion, seizures were mentioned, though not in the case presentation - The choice of a case with hepatitis B is actually confusing the message. Suggest attempting to divide the studies relating to hep B from those related to GS. Start with GS findings (Mention low K, mag to stress the findings in text) and mention "In addition, etc. Alternatively just mention GS findings in text and divide table into GS and Hep B studies with the available normograms to help in the interpretation of increased, deccreased, or normal. - a missense mutation affecting gene function, and one novel SLC12A3 pathogenic mutation was reported in a cohort of Chinese patients with GS previously-need to put reference Treatment Dosage should be mentioned clearly: "He was maintained on potassium 1 g/d and spironolactone 20 mg twice daily" Discussion -A better description of Bartter syndrome is warranted: "Some researchers believe it is better to consider the Bartter syndrome and Gitelman syndrome as a spectrum of disease rather than distinct disorders. The defect in GS involves the distal convoluted tubule while in Bartter it is in the thick ascending limb. Renal salt wasting is more severe and begins earlier in life in Bartter syndrome than in Gitelman syndrome with manifestations occurring rarely in the newborn (neonatal) period". -Cl-superaturization ---clarify?? - aldosterone receptor antagonists, ACEI/ARB and other drugs. Add precautions against the use of these drugs from Blanchard et al -Add a few sentences on the pathogenesis of proteinuria. Suggest " Proteinuria might develop due to abnormalities of the glomerular basement membrane. Chronic kidney disease might develop in GS patients due to either chronic hypokalemia, which is associated with

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

tubulointerstitial nephritis, tubule vacuolization, and cystic changes, or volume depletion and increased reninangiotensin-aldosterone, which may contribute to renal damage and fibrosis"

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 54879

Title: Gitelman syndrome caused by a rare homozygous mutation in the SL 2 gene: a new case report and review of literature

Reviewer's code: 00742368
Position: Peer Reviewer
Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-02-25

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-07-24 16:57

Reviewer performed review: 2020-07-26 16:13

Review time: 1 Day and 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

The authors have answered the reviewer's concerns appropriately with marked improvement in the content and coherence of the paper. I have the following suggestions: Line 29-delete up to know and replace with: To date Line 29-delete there are and add have been discovered: many kinds of mutations in the SLC12A3 gene have been discovered that trigger different Line 36: This study reports a rare homozygous mutation in SLC12A3 gene in Lines 38-39: Genetic studies may improve the accuracy of diagnosis of Giltelman syndrome and improve genetic counseling for individuals and their families with these types of genetic disorders Line 51-56: In this manuscript, we report a case of a patient presenting with severe hypokalemia wh was diagnosed with Gitelman syndrome by genome sequencing. We identified a relatively unusual homozygous mutation in the SLC12A3 gene, which had been rarely reported previously. Besides, unlike GS patients, this patient had elevated creatinine suggesting some factors, including this kind of mutation, might cause renal impairment. This case gives us new insights into the pathogenesis of Gitelman syndrome. Line 59: caused by a defect in the gene coding for the thiazide-sensitive Line 77: anti-inflammatory drugs for these patients to remain asymptomatic[3]. Change to: anti-inflammatory drugs to control the symptoms of these patients Line 82: His serum chemistry revealed severe hypokalemia for a potassium, change for a potassium to with a potassium Line 85: He had been also diagnosed with hepatitis B virus Line 91: delete perhaps Line 92: were elevated to 18.331ng/ml per hour and 244.6pg/ml; respectively Line 93: Urinalysis revealed Line 102: Val to Asp substitution, causing a missense mutation affecting gene function. A similar novel Line 110: After discharge, the patient reported relief of symptoms of numbness in his hands and fatigue and his serum potassium level remained in a normal range. Line 120: as classic Bartter Syndrome (BS) with analogous clinical features. Line 124: in the neonatal period Line 130: showed no obvious correlation Line 138: and reduced levels of urinary calcium as in our case. Line 148: found that blood potassium of patients with normal

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

magnesium Line 152: It is very important to facilitate patient education-move this sentence to line 160 Line 1532: delete - and management in terms of treatment of GS Line 152: GS treatment mainly involves correcting Line 154: better efficacy, the potassium-delete the Line 158: ACEI/ARBs could also aggravate Line 160 should read: It is very important to facilitate patient education which is an essential component of management. Patients are encouraged to eat more Line 161: It is necessary to teach patients to pay attention to the adverse reactions-change to: It is imperative that patients are aware of the adverse reactions of Line 163: what to do in case of an emergency Line 168: Laboratory examination showed Line 171: identified in the study patient which supported our diagnosis of GS. This type of mutation is relatively rare. At present Line 179: so the cause and progress of renal dysfunction need further investigation. Line 180: Excluding other causes of renal impairment From table delete last line