Author's response to reviews

Title: Gitelman-like syndrome after cisplatin therapy: a case report and literature review.

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Author's response to reviews: see over
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Re: Revised Manuscript # 9034259818886939

Dear BMC nephrology editors

Thank you for reviewing our manuscript. Below please find an itemized explanation of our responses to the reviewers’ comments:

Reviewer #Kreso Galesic:

1. The plasma renin activity and plasma aldosteron concentration should be given. Increased plasma renin and plasma aldosteron are laboratory characteristics of Gitelman's syndrome.
   i. We did not measure plasma aldosterone and renin level. She has laboratory criteria for Gitelman syndrome suggested by Bettinelli.

2. The kidney concentrating capacity should be given. This laboratory value is the part of laboratory evaluation of Gitelman's syndrome.
   i. Added urine osmolarity in table 1.

3. The renal ultrasonographic findings are necessary in this case presentation because of possible nephrocalcinosis.
   i. Added her ultrasound finding in the case presentation (Page 4, paragraph 1).

4. The authors should discuss prostaglandin excretion in Gitelman's syndrome and eventual association of renal prostaglandin with blood pressure and plasma rennin
   i. Added the association of Gitelman syndrome and prostaglandin, rennin and blood pressure in the discussion (Page 5, paragraph 1).

5. The authors should discuss the findings of juxtaglomerular hyperplasia on kidney biopsy. Although striking is not specific for this disorder and may occur in association with chronic diuretic use and sustained sodium depletion. Renal biopsy generally is not needed to make diagnosis of Gitelman's syndrome.
i. Added the pathology finding of Gitelman syndrome in the discussion (Page 5, paragraph 1).

Reviewer # Margaret Bia:

Major Compulsory Revisions

1. In table 1, the authors provide initial laboratory data from January 2004 when their patient first presented to their clinic for consultation. However, it is clear that the patient's hypokalemic metabolic alkalosis with hypomagnesemia had been present since 1986 (starting several months after cisplatin, adriamycin, and cyclophosphamide for ovarian cancer). In order to conclude that this phenotypic change was related to the antineoplastic therapy, it is essential to show that pre-treatment the patient was phenotypically normal. This would best be accomplished by adding to Table 1 the patient's baseline laboratory data from 1986 (i.e. prior to receiving chemotherapy). In addition, a more representative K+ value other than the initial K of 5.2 should be presented in the table.
   i. The patient’s baseline laboratory data prior to receiving chemotherapy are no longer available, but according to her, they were normal (Case presentation, page 3, paragraph 2).
   ii. Added laboratory data from 1986 after chemotherapy (Table 1).
   iii. Added all K+ values from 2004 (The first year that we saw her) (Table 1).

2. In the case presentation, paragraph #1, sentence #8, the authors indicate that the patient had plasma potassium values which ranged from 1.2 to 7.2 mEq/L. Presumably, the hyperkalemia was a consequence of over supplementation. But, this is worth noting in the text. More importantly, the authors should indicate how many of the 44 measurements between 1986 to 2003 were below normal (less than 3.5 mEq/L).
   i. There are 23 K+ value that ≤ 3.5 mEq/L and 43 Mg++ value that < 2.1 mEq/L.
      Added data (Case presentation, page 3, paragraph 2).

3. The phrase Gitelman-like syndrome (or some phrase other than Gitelman syndrome) should be utilized as stated in general comments
   i. Changed to Gitelman-like syndrome phrase in general comments (Title, abstract, and discussion).

Minor Essential Revisions.

1. In the case presentation, paragraph #2, sentence #3, change the phrase “she was started IV magnesium sulphate” to “she was started on IV magnesium sulphate”.
   i. Edited the sentence (Case presentation, page 3, paragraph 3).

2. Would add patient's BMI (29.6--overweight) to her morphometrics.
   i. Added BMI (Case presentation, page 4, paragraph 1).

3. Would report the patient's weight in kilograms (74.1).
   i. Added weight in kilogram (Case presentation, page 4, paragraph 1).
4. Authors comment that no family members have “kidney disease”. Would state that no family members have the Gitelman's syndrome phenotype if this is also the case.
   i. There was no family history of any electrolyte disorders (Case presentation, page 4, paragraph 1).

5. To strengthen the conclusion that this patient's magnesium wasting is at the level of the DCT, would parenthetically note that proximal tubule and thick ascending limb magnesium wasting generally results in a fractional excretion greater than 10%.
   i. Added this information (Discussion, page 6, paragraph 1).

6. In table 1, please provide a normal reference range for urinary Ca/Cr molar ratio
   i. Added it (Table 1).

7. Aldo/rennin levels, if ever performed, should be presented
   i. We did not do these tests.

Once again, thank you very much for considering our work for publication in Biomed Nephrology. The changes in the text are in bold

Sincerely,

Kenneth Nugent, MD