Reviewer's report

Title: Gitelman's syndrome after cisplatin therapy: a case report and literature review.

Version: 1 Date: 27 March 2006

Reviewer: margaret bia

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General

The authors present a patient treated with chemotherapy, which included cisplatin, for ovarian cancer in 1986 who subsequently developed the characteristic phenotype of Gitelman's syndrome. They conclude that there is a causal relationship between the onset of disease and cisplatin therapy and that this defect may persist long term. Although this phenomenon has been reported previously (see Table 2), none have had the follow up of 20 years reported here. While offering little in terms of medical innovation, this report is the first to provide such long-term follow-up and suggests that the electrolyte disturbances induced by cisplatin and identical to those in Gitelman's syndrome may be permanent. The report also raises the question as to definition of Gitelman's syndrome. The definition, described by Gitelman and present in all the text books describes a phenotype present because of an inherited genetic mutation. Should similar phenotypes, acquired by drug toxicity, also be called Gitelman's syndrome? The apparent lack of metabolic alkalosis in this patient (according to the data presented) as well as the frequency of high serum K+ values from overcorrection (which is rarely, if ever seen in true Gitelman's) would lead me to believe the phenotypes are not identical. A term Gitelman-like syndrome seems more appropriate.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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.

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 3.5mEq/L).

3. The phrase Gitelman-like syndrome (or some phrase other than Gitelman syndrome) should be utilized as stated in general comments.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the...
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”.
2. Would add patient's BMI (29.6--overweight) to her morphometrics.
3. Would report the patient's weight in kilograms (74.1).
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.
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%.
6. In table 1, please provide a normal reference range for urinary Ca/Cr molar ratio
7. Aldo/rennin levels, if ever performed, should be presented