Reviewer's report

Title: Gorlin syndrome associated with small bowel carcinoma and neuroleiomyomatosis of the gastrointestinal tract: Is two-hit mutational inactivation of PTCH a rare pathomechanism in GI malignancies? Case report and review of literature

Version: 1 Date: 30 December 2009

Reviewer: Mariana Cajaiba

Reviewer's report:

REVIEWER’S COMMENTS

In this manuscript, the authors describe an exceptional association of Gorlin syndrome and gastrointestinal neoplasms. Although interesting, this case study lacks many additional details to make it worth being published. In addition, the text is often confusing. I suggest this manuscript should undergo substantial changes and then re-submitted before being considered for publication.

A major issue in this paper is the histopathological diagnosis of neuroleiomyomatosis; it is not a well-recognized pathological entity, and the authors do not provide bibliographical evidence to support their diagnosis. The authors should also provide more detailed clinical and pathological information to better delineate this interesting case study.

Additional suggestions that may help to improve the quality of the manuscript:

1. The stromal nodules found in this patient's small bowel should be further characterized, and possible differential diagnoses explored. The proposed diagnosis should be justified by appropriate literature and other ancillary techniques. Additional smooth muscle stains should be performed, including smooth muscle actin and calponin, and more detailed morphological description and illustration added. Ultrastructural studies, even performed in paraffin-embedded tissue, could provide some additional useful information.

2. Was the patient submitted to endoscopic evaluation of the remaining gastrointestinal tract (other than stomach)? With >100 nodules in the terminal ileum, it would be interesting to know about the possible involvement of other bowel segments.

3. Were the small bowel mucosal nodules similar to the gastric lesions? Were any of them polypoid?

4. When was the diagnosis of GS first suspected? At age 49, when multiple BCCs were excised, or at the time of his gastrointestinal manifestations? When was it confirmed by molecular studies? It should be clarified in the manuscript, and the text should be rearranged in the following order: first, all clinical data including physical examination and past medical history that led to suspicion of
GS; second, surgical and other therapeutic procedures; third, pathological
description; fourth, patient’s follow-up, if indicated.

5. Was the PATCH mutation a missense alteration leading to a stop codon? If so,
was there a 2 nucleotide change (AC>GA)? Are sequencing results available for
publishing? Has this mutation been previously described?

6. Line 6 of “Case presentation”: were the colon, ileum, duodenum and stomach
biopsy endoscopic mucosal biopsies, or they represented serosal/full-thickness
biopsies obtained during the laparotomy procedure?

7. What is the relevance of the MIB-1 proliferative index in the ileal
adenocarcinoma? It is not part of routine diagnostic work up of gastrointestinal
carcinomas.

8. Line 3 of “Discussion”: “Endoscopic examination provided evidence that the
stomach was involved too…”. “Provided evidence” should be replaced for
“suggested”, as the diagnosis was not confirmed by histological examination.

9. The last paragraph of “Discussion” should be re-drafted, as it contains
redundant information already explored in the previous paragraph.

10. Figure 1B is irrelevant; the “lumpy-bumpy” appearance of the mucosa could
just represent chronic gastritis and there is no microscopic correlation with the
disease being described. Gross pictures of the small bowel irregularities,
however, would be very useful.

11. If possible, Figure 2B should be magnified to better illustrate the palmar pits.

12. The manuscript should be carefully reviewed for correction of several English
grammar and typographical errors.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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.