

Mar 17, 2014

Dear Editor,

Title: Cronkhite-Canada syndrome: report of 6 cases and review

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) New findings of the syndrome should be better addressed? From our experience and review of the literature, comprehensive treatment led by glucocorticoids, is the most effective option at present. It could improve prognosis and quality of life.

(2) Figure 3: The hyperplastic and juvenile polyps should be better illustrated.?Yes,we have showed the hyperplastic and juvenile polyps in figure 3.

(3) Given the rarity of this disease the authors need to begin with the accepted rigorous clinical and pathological diagnostic criteria?CCS diagnosed by history, physical examination, endoscopic findings of gastrointestinal polyposis, and histology, including diffuse polyposis of the gastrointestinal tract; ectodermal dysplasia, cutaneous hyperpigmentation, dystrophic changes of fingernails, and alopecia; diarrhoea, weight loss, abdominal pain. There are four histological types of polyps: hyperplastic polyps, tubular adenomas, juvenile polyps and inflammatory.

(4) The authors introduction should include a brief review of currently accepted diagnostic algorithms and etiological theory?Cronkhite-Canada syndrome (CCS) is a rare non-congenital gastrointestinal polyposis syndrome, characterized by skin hyperpigmentation, hair loss and nail atrophy.Its etiology is still unknown.

(5) Discussion of the correct diagnosis of these patients. Demonstrating exclusion criteria and why these patients were included?Peutz-Jeghers syndrome, juvenile polyps, familial polyposis of the colon, Gardner syndrome, Turcot syndrome; Menetriers disease were excluded. The six patients met the diagnostic criteria..

(6) Since the authors are trying to make the point of autoimmune etiology, it may be helpful to graph each of the autoimmune markers discussed (ASCA, ANA, and response to steroids). This would provide support to their argument?All 6 cases in this study showed positive immune parameters, with 2 cases showing antibody markers (ASCA) as positive and 1 case with ANA

positive. Hormonal therapy was effective for all three patients, especially in a significant short time for the ANA positive patient.

(7) Cronkhite-Canada syndrome is a rare non-congenital gastrointestinal polyposis syndrome. However, this study is a retrospective study. Some limitations might be occurred? Some limitations might be occurred, as this is a retrospective study, Cronkhite-Canada syndrome is a rare disease, so there are no prospective randomized controlled studies.

(8) How do the authors do to diagnose Cronkhite-Canada syndrome? Are there any diagnostic tools to confirm the diagnosis? How about the sensitivity and specificity of these tools? Please add these issues in the text? Cronkhite-Canada syndrome is a syndrome, it consists of a group of symptoms. Diagnosis is based on history, physical examination, endoscopic findings of gastrointestinal polyposis, and histology, without a clear diagnosis tool, but one group of diseases must be excluded.

(9) What is the clinical impact of this report? CCS is a rare and serious disease with a high mortality rate. Improvement of the approach with complex medical therapy and increased knowledge of the disease can lead to better prognosis of patients in comparison with former case reports.

(10) The clinical application of the study is very important. The authors should be recommended to apply this knowledge into routine clinical practice? Comprehensive treatment based on prednisone therapy with higher clinical remission rate is recommended.

(11) Information provided in Table 1 is difficult to read and requires revision? Therapy and prognosis in detail for each six patients

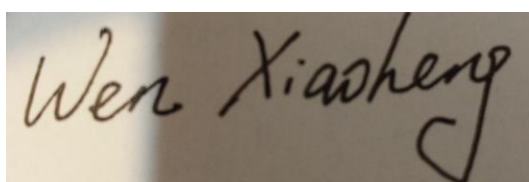
(12) The meaning of the lines in Figure 4 is ambiguous. Do they represent frequencies, episodes, severity, or what else? Thanks a lot, The meaning of the lines in Figure 4 is ambiguous, I have deleted the figure 4 from this paper.

(13) Discussion should be more concise, referenced, shortened, and relevant to the reported cases since more extensive reviews can be found elsewhere? I have modified some part of the discussion.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink on a light-colored background. The signature is written in a cursive, flowing style and appears to read 'Wen Xiaoheng'.

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