

First and foremost, I would like to express my sincere gratitude to the reviewers and editors of the journal for your professional and constructive feedback on the article. After thorough review of the literature and careful consideration, I have diligently made revisions to the article and provided detailed responses to each of the review comments.

Reviewer #1:

Specific Comments to Authors: The authors report a rare presentation of CCS with hypothyroidism and summarize specifics relative to this presentation quite well. They then take it a step further by describing a different case of CCS where they delineate the importance of hormonal therapy.

1. Please modify the manuscript title to reflect the real nature of your report with regards to hypothyroidism.

The original title "Cronkhite–Canada syndrome: Report of Two Cases and Literature Review," does not adequately reflect the distinctive features of the case reports. Case 1 involves a CCS patient combined with hypothyroidism, which, upon literature review, has only been reported in one case in China and seven cases worldwide, making it an exceptionally rare presentation. Case 2 is about a CCS patient treated with EMR, offering valuable clinical insights into the current comprehensive treatment trends. The final title of the article, taking into account the content and highlighting the unique aspects, is revised as follows: "Case reports of Cronkhite–Canada syndrome: A rare hypothyroidism presentation and comprehensive treatment."

2. Please ensure proper formatting of the core tip paragraph.

- ① Explanation of the abbreviation "CCS" has been provided.
- ② Comparison and modifications have been made according to the formatting requirements.
- ③ Appropriate modifications have been made to the core tip content.

3. The current structure of the case presentation section detailing both cases is confusing to the reader. Please ensure that case presentation is entirely presented

for each case. Example: Case 1 describe the whole case including lab , imaging, surgical path etc. and then move on to case 2.

Each journal has different formatting requirements. Because this article is a resubmission, the formatting requested by the previous journal's reviewers is different from that of this journal. Therefore, I have revised and polished the article to align with the formatting requirements of this journal. As a result, the article has become more concise and the logic is clearer.

4. Discussion is excellently written. Current case reports are nicely summarized and findings are compared with presenting cases quite well.

Thanks for your praise. During the article revision process, I supplemented the latest research findings by reading the most recent literature. You can find the specific additions highlighted in yellow within the article.

5. Please re-write the conclusion. It seems a bit repetitive.

After revising the content of the article, I have rewritten the conclusion section following the logical order of concepts, etiology, clinical presentation, treatment, and prognosis. The conclusion section succinctly summarizes the content of the article while ensuring there is no repetition of information from earlier in the text.

Key points:

- ①The strongest likelihood of an association between CCS and autoimmunity is suggested.
- ② Clinical manifestations of CCS are diverse, including hypothyroidism, as demonstrated in this study.
- ③Early polyp resection through endoscopic EMR surgery plays a crucial role in preventing malignancy and is an integral part of comprehensive treatment.
- ④Early diagnosis, timely intervention, and long-term follow-up are paramount in managing this condition.

Reviewer #2:

Specific Comments to Authors: Lv et al. presented two cases of Cronkheite-Canada syndrome. The topic is interested, the syndrome is rare, not-fully understood.

1、 The presentations of cases are in helter-skelter manner and English need to be polished, too.

Thank you for the reviewer's feedback regarding the structure of the article. I have restructured the case report section accordingly and, after the revisions, submitted the article for another round of proofreading. The final article has greatly improved in terms of structure, language, and grammar.

2、 The results of administered Levo-thyroxine treatment are missing.

Thanks for pointing out this issue. Indeed, we had overlooked the result of the thyroid function test during the follow-up of patient 1. We will pay close attention to this aspect in future clinical disease management.

The patient initially visited our hospital in 2016, where she was diagnosed with hypothyroidism during their hospitalization. At that time, the endocrinology department recommended oral sodium levothyroxine, with a follow-up scheduled for three weeks later. The patient was discharged after an 8-day hospital stay and returned to the local area. It was only during a follow-up appointment six months later that we learned the patient had self-adjusted her medication dosage and had not complied with the prescribed laboratory tests in the local area.

The patient developed intestinal obstruction four months after discharge and subsequently passed away due to multi-organ failure. Unfortunately, we have lost contact with the patient's family, making it impossible to obtain the results from that time.

The absence of thyroid function treatment results was a limitation of this article. I have now supplemented the explanation in the article to make it more accurate and objective.

3、 In the Discussion section, when comparing presented cases with literature data, very questionable assertion about Graves disease and negative ATG i

ATPOAbs. It is expected to have negative aforementioned antibodies negative, especially in surgically treated patients, but the main clue are TSH receptor antibodies. The text of the manuscript must be improved aiming to be published.

Thank you for the reviewer's feedback on the errors in the article. After re-reading the literature, I have found that in the fourth article summarized in the table regarding CCS and concomitant hypothyroidism, there is no mention of any autoimmune antibody test results for patients who developed hypothyroidism after hyperthyroidism surgery. It was an error in my literature summary, and the original text has been corrected.

Further discussion on this matter is warranted. Hyperthyroidism is an autoimmune disorder typically characterized by the presence of positive autoantibodies. While the original text did not mention the results of autoantibody testing, it can be reasonably assumed that patients with hyperthyroidism had underlying autoimmune abnormalities. Therefore, this can be used to support the association between CCS and autoimmune anomalies. Additionally, in the third article summarized in the literature review, the original text indicated that ATG and A-TPO were negative. Therefore, this case can be added as a second example. In conclusion, there is a correlation between autoimmune dysfunction and CCS, but the research results are still not conclusive, and a significant amount of clinical reporting and research is needed.

Company editor-in-chief:

I recommend the manuscript to be published in the World Journal of Gastrointestinal Surgery. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords

entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Thank you for pointing out the issues, and indeed, this paper lacks coverage of cutting-edge results in CCS research. Through the use of Reference Citation Analysis (RCA), I have gathered several recent and relevant publications. I have made the following improvements to the original manuscript:

1. We have replaced some of the cited references with more recent publications. However, it is challenging to entirely avoid citing older literature in CCS research, given that it primarily relies on case reports with longer publication timelines.

2. We have incorporated several cutting-edge findings related to CCS:

- This paper reports the second case of CCS combined with hypothyroidism in China.

- We have added "fractures" as a symptom of CCS.

- Gut microbiota has been a recent research hotspot, and we have supplemented the discussion with information from the literature mentioning FMT (Fecal Microbiota Transplantation) as a potential treatment for CCS.

- We have included references regarding CCS combined with membranous nephropathy and TNF- α treatment.

Thank you once again for your valuable feedback on the manuscript. I sincerely hope that the revised article meets the requirements for publication in the journal and that our responses to the review comments satisfy both the reviewers and the editors.

Best regards!

