Case Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(5) 1–5

DOI: 10.1177/0300060520922427
journals.sagepub.com/home/imr
SAGE

Cronkhite–Canada syndrome: report of a rare case and review of the literature

Yuping Liu[1]*, Li Zhang[1]*, Yingshan Yang[2] and Tao Peng[3]

Abstract

Cronkhite–Canada syndrome is rarely encountered in clinical practice. Notably, most patients with Cronkhite–Canada syndrome exhibit hypoalbuminemia. Because the cause of Cronkhite–Canada syndrome is unknown, no specific treatment method has been established. Here, we describe a 59-year-old woman with Cronkhite–Canada syndrome in whom clinical manifestations were considerably relieved after treatment with prednisone.

Keywords

Cronkhite–Canada syndrome, prednisone, hypoalbuminemia, intestinal polyposis, blood protein disorders, metabolic diseases

Date received: 18 November 2019; accepted: 3 April 2020

Introduction

Cronkhite–Canada syndrome is a disease involving multiple gastrointestinal polyps and other manifestations.[1,2] Most patients exhibit hypoalbuminemia (<30 g/L) with reduced total serum protein (<60 g/L).[3] The disease was first reported in 1955,[4] and was named Cronkhite–Canada syndrome by Jarnum and Jensen in 1966;[5] however, the etiology and cause have remained unclear thus far. Therefore, specific treatment methods have not yet been established. The prognosis of patients with

[1]Department of Nephrology, Juye County People's Hospital, Juye, China
[2]Department of Gastroenterology, Juye County People's Hospital, Juye, China
[3]Department of Nephrology, Shandong University Qilu Hospital, Jinan, China

*These authors contributed equally to this work.

Corresponding author:
Tao Peng, Department of Nephrology, Shandong University Qilu Hospital, No. 107, Wenhua Xi Road, Jinan, 250012, China.
Email: sesame_oil@126.com

Cronkhite–Canada syndrome remains poor, with a 5-year mortality rate of 55%.[6]

Here, we describe a 59-year-old woman with Cronkhite–Canada syndrome who had multiple gastrointestinal polyps and severe hypoalbuminemia over a 98-month course of disease. Notably, she required recurrent and prolonged hospitalization related to hypoalbuminemia. After treatment with glucocorticoid, she experienced substantial relief of disease manifestations.

Case report

Patient history

A 59-year-old Chinese woman presented with an 8-year history of chronic gastritis, accompanied by frequent nausea and acid reflux, loss of appetite, abnormal taste, and fatigue. She reported a history of upper gastrointestinal endoscopy 6 years prior, which was unsuccessful. She had an 8-month history of edema in both lower extremities, for which she had previously sought treatment at a local hospital. Tests conducted at the local hospital revealed hypoalbuminemia (20.7 g/L) and trace albuminuria (260 mg/L), but the patient refused further treatment.

Clinical and laboratory findings

On physical examination after admission to our hospital, the patient exhibited edema in bilateral eyelids and lower limbs without bleeding points, purpura, or oral ulcers. She exhibited pigmentation on her back and partial nail dystrophy, particularly involving the second and fifth toenails of the left foot and big toenail of the right foot (Figure 1). Pertinent laboratory findings included hypoalbuminemia (serum albumin, 21.8 g/L) with reduced total protein (46.6 g/L), as well as anemia (serum iron, 74 g/L). Notably, the level of urinary albumin was high (537 mg/L) and serum cancer antigen (CA) 125 was above normal (415 U/mL). Levels of potassium, calcium, phosphorous, carbon dioxide combining power, erythrocyte sedimentation, C-reactive protein, blood urea nitrogen, serum creatinine, alanine aminotransferase, and aspartate aminotransferase were normal. In addition, levels of coagulation-related indicators, D-dimer, rheumatoid factor, antistreptolysin O, antinuclear antibodies, dsDNA, antineutrophil cytoplasmic antibodies, C3, and C4 were normal. Serum immunofixation electrophoresis, blood/urinary light chain, anti-glomerular basement membrane antibody, anti-phospholipase A2 receptor antibody, and IgG4 findings were also normal.

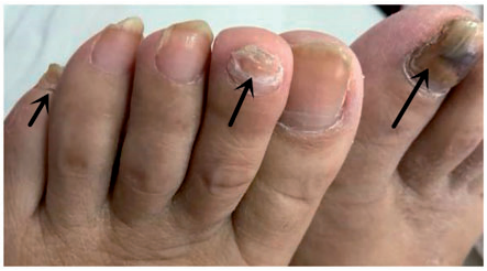

Figure 1. Partial nail dystrophy, particularly involving the second and fifth toenails of the left foot and big toenail of the right foot (indicated by arrows).

Imaging and endoscopic findings

After admission, the patient underwent upper gastrointestinal barium examination and electronic gastrointestinal endoscopy. Radiographic assessment of the barium examination revealed normal peristalsis and thickening of the gastrointestinal mucosa. Endoscopy revealed a large number of polyps covering the gastric mucosa, as well as multiple mucosal bulges, surface hyperemia and edema, and some erosion. The largest polyp constituted a columnar structure with a length of 1.5 cm (Figure 2). Pathological manifestations of polyps comprised acute/chronic inflammation of the

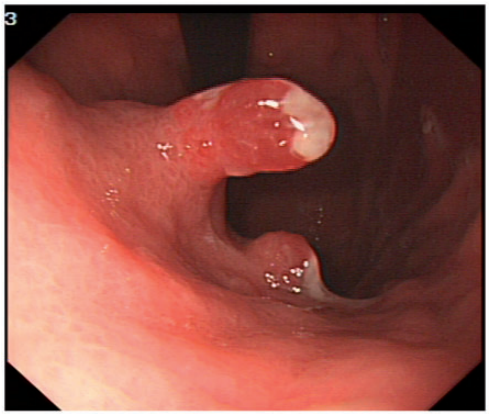

Figure 2. Largest polyp (1.5 cm) of many polyps covering the gastric mucosa; mucosal bulges, hyperemia, and surface edema with erosion are also observed.

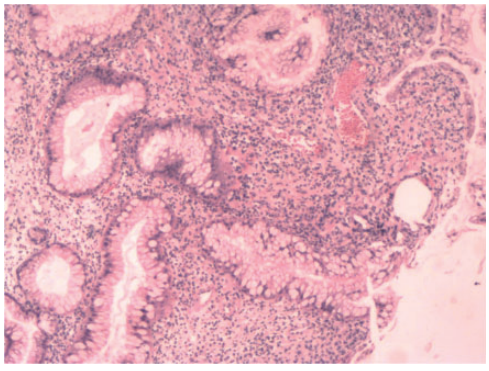

Figure 3. Pathological manifestation of polyps comprises inflammatory cell infiltration in the gastrointestinal tract, particularly involving eosinophil infiltration and small vessel hyperplasia (hematoxylin-eosin stain, ×400).

gastrointestinal tract mucosa, with substantial inflammatory cell infiltration; in particular, eosinophil infiltration and small vessel hyperplasia were observed (Figure 3). Computed tomography examination revealed ascites, pelvic effusion, and a slightly thickened gastrointestinal wall. Because of financial limitations, the patient did not undergo further examination of emission computed tomography and bone density.

Diagnosis and treatment

Clinical manifestations, laboratory findings, and imaging results were suggestive of Cronkhite–Canada syndrome. Therefore, treatment was initiated with methylprednisolone 40 mg intravenously three times per day for 3 days; the patient was then switched to prednisone 50 mg/day (1 mg/kg) with other supportive treatment. Notably, tacrolimus, methicillin, azathioprine, and mycophenolate mofetil were all refused by the patient and her family because of their high costs. Prednisone was reduced to 45 mg/day after 2 weeks, then reduced by 5 mg at approximately 2-week intervals; thus, after 5 months of treatment, it was administered at 10 mg/day. After 5 months of treatment, the dose was modified to prednisone 5 mg daily for 3 months; the patient currently is prescribed prednisone 2.5 mg daily. Repeat gastrointestinal endoscopy showed polyp shrinkage. Serum albumin increased to 28.8 g/L after 1 month of treatment, then to 33.1 g/L after 3 months of treatment. At the 3-month follow-up, CA125 had decreased to 46 U/L, hemoglobin had increased to 91 g/L, and serum albumin had increased to 79.6 g/L. Edema disappeared from the patient's eyelids and lower limbs; nausea and acid reflux, loss of appetite, abnormal taste, and fatigue all gradually resolved during the course of treatment. Furthermore, edema and fullness of the abdomen disappeared. The patient's appetite gradually improved; after 3 months, she returned to her normal (pre-illness) diet, and gained approximately 4.5 kg in weight.

Patient consent

Because this was a retrospective report, we have obtained consent from the patient and her family before publication of relevant data. Additionally, because this was a retrospective report, our group presumed that no registration was necessary; informed

consent from the patient was considered sufficient.

Discussion

Cronkhite–Canada syndrome is an extremely rare clinical disease with multiple gastrointestinal polyps; 88% of affected patients exhibit hypoalbuminemia. In recent years, the incidence of Cronkhite–Canada syndrome has increased.[7] The age at onset ranges from 26 to 85 years (mean age, 61 years).[8] There is no difference in the incidence of disease between men and women in Europe or the United States.[9] Common predisposing factors are mental stimulation, overwork, or surgery. The present patient was a 59-year-old woman from a rural area with a low socioeconomic status. The patient reported that, when she felt fatigued, her symptoms and edema worsened; they were slightly relieved by rest. Before admission to our hospital, she had experienced fatigue for 4 days.

Gastrointestinal symptoms are the main manifestations, including abdominal pain and diarrhea;[10] these are accompanied by frequent nausea and acid reflux, anorexia, parageusia, or fatigue. Some patients exhibit skin pigmentation on the back, back of hands, and feet; some patients have nail dystrophy, which involves one or more digits. Additionally, some patients have edema, especially in the eyelids and extremities.[11] The present patient had an 8-year history of chronic gastritis with frequent nausea and acid reflux, as well as anorexia. She exhibited edema in bilateral eyelids and lower limbs, as well as pigmentation on her back and partial nail dystrophy on her toes.

In laboratory tests, more than 88% of patients exhibit hypoalbuminemia (serum albumin <30 g/L),[12] but few exhibit albuminuria. Clinical manifestations suggest that hypoalbuminemia is not associated with liver or renal dysfunction.[13,14] Our patient exhibited substantial hypoalbuminemia (serum albumin, 21.8 g/L); her urinary albumin level was also high (537 mg/L). She exhibited multiple polyps in the gastrointestinal tract (up to 1.5 cm). The CA125 level can be elevated in patients with serous effusion. After treatment, when effusions are reduced or resolved, the CA125 level can be considerably reduced.[15] Our patient exhibited this elevated level of CA125; other diseases were excluded from the differential diagnosis by computed tomography imaging.

Therapy for Cronkhite–Canada syndrome includes glucocorticoid and supportive treatment.[16] Although the effectiveness of glucocorticoid treatment for Cronkhite–Canada syndrome is uncertain, it has become the first empirical treatment. Glucocorticoid dosage is generally considered to be based on body weight (1 mg/kg); its therapeutic mechanism may involve reduction of gastrointestinal inflammation and inhibition of autoimmune responses.[16] In addition to glucocorticoid therapy, supportive treatment is important. Other immunosuppressive agents, such as tacrolimus, have been shown to exhibit partial effects.[17,18] Our patient accepted glucocorticoid (methylprednisolone and prednisolone) with other supportive treatments; however, the patient and her family refused tacrolimus, methicillin, azathioprine, and mycophenolate mofetil because of their high costs. After treatment, clinical manifestations were considerably ameliorated and all laboratory test indicators showed improvement. The patient's health gradually returned to normal, such that she did not exhibit nausea, acid reflux, or fatigue.

In conclusion, Cronkhite–Canada syndrome is rarely encountered in clinical practice. It is not difficult to diagnose by use of typical clinical and laboratory tests, but patients' symptoms may be atypical. For treatment, glucocorticoid is the first drug of choice. Detailed observation and documentation of Cronkhite–Canada syndrome may contribute to an in-depth understanding

of the mechanism and pathogenesis of the disease, although the specific pathophysiological mechanism remains unknown.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This study was supported by Shandong Province Outstanding Young Scientist Research Award Fund Project, NO. BS2013YY042.

ORCID iD

Tao Peng https://orcid.org/0000-0002-4300-7806

References

1. Vashistha N, Chakravarty S and Singhal D. Cronkhite-Canada syndrome. *Gastrointest Endosc* 2017; 86: 922–923.
2. Safari MT, Shahrokh S, Ebadi S, et al. Cronkhite-Canada syndrome: a case report and review of the literature. *Gastroenterol Hepatol Bed Bench* 2016; 9: 58–63.
3. Yashiro M, Kobayashi H, Kubo N, et al. Cronkhite-Canada syndrome containing colon cancer and serrated adenoma lesions. *Digestion* 2004; 69: 57–62.
4. Cronkhite LW Jr and Canada WJ. Generalized gastrointestinal polyposis: an unusual syndrome of polyposis, pigmentation, alopecia and onychorotrophia. *N Engl J Med* 1955; 252: 1011–1015.
5. Jarnum S and Jensen H. Diffuse gastrointestinal polyposis with ectodermal changes: a case with severe malabsorption and enteric loss of plasma proteins and electrolyte. *Gastroenterology* 1966; 50: 107–118.
6. Watanabe C, Hokari R and Miura S. Other polyposis syndrome—report from Japanese nationwide survey of Cronkhite-Canada syndrome. *Nihon Shokakibyo Gakkai Zasshi* 2017; 114: 431–437.
7. Zhao R, Huang M, Banafea O, et al. Cronkhite-Canada syndrome: a rare case report and literature review. *BMC Gastroenterol* 2016; 16: 23.
8. Wen XH, Wang L, Wang YX, et al. Cronkhite-Canada syndrome: report of six cases and review of literature. *World J Gastroenterol* 2014; 20: 7518–7522.
9. Christensen T and De Muckadell OBS. Two cases of the rare Cronkhite-Canada syndrome. *Ugeskr Laeger* 2017; 179: pii: V02170155.
10. Kronborg C, Mahar P and Howard A. Cronkhite-Canada syndrome: a rare disease presenting with dermatological and gastrointestinal manifestations. *Australas J Dermatol* 2016; 57: e69–e71.
11. Lee SH, Kim CR and Kim KN. Changes in fecal calprotectin after rifaximin treatment in patients with nonconstipated irritable bowel syndrome. *Am J Med Sci* 2019; 357: 23–28.
12. Murata M, Bamba S, Takahashi K, et al. Application of novel magnified single balloon enteroscopy for a patient with Cronkhite-Canada syndrome. *World J Gastroenterol* 2017; 23: 4121–4126.
13. Kim Y, Yang YS, Park SS, et al. Congenital analbuminemia in a Korean male diagnosed with single nucleotide polymorphism in the ALB gene: the first case reported in Korea. *Yonsei Med J* 2019; 60: 700–703.
14. Peng T, Hu Z, Wu L, et al. Correlation between endothelial dysfunction and left ventricular remodeling in patients with chronic kidney disease. *Kidney Blood Press Res* 2014; 39: 420–426.
15. Kalluri M and Judson MA. Sarcoidosis associated with an elevated serum CA125 level: description of a case and a review of the literature. *Am J Med Sci* 2007; 334: 441–443.
16. Fukazawa M, Inoue H, Kawamura H, et al. A high CEA level in a case of Cronkhite-Canada syndrome, showing decrease by prednisolone treatment. *Nihon Shokakibyo Gakkai Zasshi* 1997; 94: 543–548.
17. Chaubal T and Bapat R. Mulberry-shaped gingival overgrowth induced by amlodipine and cyclosporine. *Am J Med Sci* 2017; 354: e13.
18. Ueyama H, Fu KI, Ogura K, et al. Successful treatment for Cronkhite-Canada syndrome with endoscopic mucosal resection and salazosulfapyridine. *Tech Coloproctol* 2014; 18: 503–507.