Cronkhite-Canada syndrome (CCS) is a rare but serious protein-losing enteropathy, but little is known about the mechanism. Furthermore, misdiagnosis is common due to non-familiarity of its clinical manifestation. A 40-year-old male patient was admitted to our hospital because of diarrhea and hypogeusia associated with weight loss for 4 mo. On physical examination, skin pigmentation, dystrophic nail changes and alopecia were noted. He had no alike family history. Laboratory results revealed low levels of serum albumin (30.1 g/L, range: 35.0-55.0 g/L), serum potassium (2.61 mmol/L, range: 3.5-5.5 mmol/L) and blood glucose (2.6 mmol/L, range: 3.9-6.1 mmol/L). The erythrocyte sedimentation rate was elevated to 17 mm/h (range: 0-15 mm/h). X-ray of chest and mandible was normal. The endoscopic examination showed multiple sessile polyps in the stomach, small bowel and colorectum. Histopathologic examination of biopsies obtained from those polyps showed hyperplastic change, cystic dilatation and distortion of glands with inflammatory infiltration, eosinophilic predominance and stromal edema. Immune staining for IgG4 plasma cells was positive in polyps of stomach and colon. The patient was diagnosed of CCS and treated with steroid, he had a good response to steroid. Both histologic findings and treatment response suggested an autoimmune mechanism underlying CCS.

Key words: Gastrointestinal polyposis; Cronkhite-Canada syndrome; IgG4 plasma cells; Autoimmune mechanism

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diagnosis can improve prognosis of the patients, but delay in diagnosis is common due to non-familiarity of its clinical manifestation. Here we report a case of a patient with CCS, in this report showed the patient’s clinical characteristics and response to treatment.

INTRODUCTION

Cronkhite-Canada syndrome (CCS) is a rare, non-hereditary condition characterized by gastrointestinal polyposis associated with diarrhea and epidermal manifestations, such as cutaneous hyperpigmentation, alopecia and onychodystrophy\cite{1}. So far, the pathogenesis of CCS is still not fully understood\cite{2}, and autoimmune mechanism is probably involved. We here report a case of CCS in a male patient whose polyps presented with IgG4 - positive plasma cells. This finding is consistent with the autoimmune mechanism underlying CCS.

CASE REPORT

A 40-year-old male patient with a 4-mo history of non-bloody watery diarrhea and hypogeusia associated with weight loss was admitted to our hospital in October of 2015. He defecated 6 to 10 times daily. No blood, mucosa, fat or oil was observed in the stool. He had no fever and abdominal pain. Family history was negative. In the past 4 mo, the patient experienced a weight loss of 17 kg.

Vital signs on physical examination were normal. His nutritional status was poor. Systemic skin pigmentation, dystrophic nail changes (Figure 1A and B) and alopecia (Figure 1C) were noted, but there was no pigmentation within oral cavity. The rest of the physical examination was non-contributory.

Laboratory results revealed low levels of serum albumin (30.1 g/L, range: 35.0-55.0 g/L), serum potassium (2.61 mmol/L, range: 3.5-5.5 mmol/L) and blood glucose (2.6 mmol/L, range: 3.9-6.1 mmol/L). The erythrocyte sedimentation rate was elevated to 17 mm/h (range: 0-15 mm/h). The C reaction protein was within normal ranges. Both serum IgG4 (0.42 g/L, range: 0.08-1.4 g/L), and serum total IgG were normal (6.16 g/L, range: 6.0-16.0 g/L). Antinuclear antibody, anti-mitochondrial antibody, and smooth muscle antibody were all negative. There were no abnormal findings in X-ray of chest and mandible. The patient underwent electron esophagogastroduodenal endoscopy, capsule endoscopy and electronic colonoscopy, respectively, after admission. The endoscopic evaluation revealed multiple sessile polyps in the stomach (Figure 2A), small bowel (Figure 2B), and colon and rectum (Figure 2C). Histopathologic examination of biopsies obtained from those polyps showed hyperplastic change, cystic dilatation and distortion of glands with inflammatory infiltration, eosinophilic predominance and stromal edema (Figure 3A and B). The histopathology of his rectal polyp showed a serrated adenoma. Mild chronic inflammation was found in the rectal mucosa which appeared normal under endoscope. Esophago-gastroduodenal endoscopy revealed an esophageal papilloma, but did not show polyp of the esophageal mucosa.

Immune staining for IgG4 plasma cells was positive in polyps of stomach (Figure 3C) and colon (Figure 3D), and IgG4 positive cell count of each high power field was 0-3 and 10-18 in gastric and colonic polyps, respectively. Cronkhite-Canada syndrome was diagnosed based on a
combination of clinical features, endoscopic findings and histopathology of polyps. The patient was given nutrition support and symptomatic treatment, and his symptom of diarrhea improved. The patient refused steroid treatment and was discharged.

After a month, he was admitted to our hospital again because of severe diarrhea. By consent, he started on steroid treatment, and was administered methylprednisolone 40 mg/d intravenously for 6 d. His condition became much better, and was discharged. The patient was then treated with prednisone 30 mg/d orally for 4 wk, tapered by 2.5-5 mg/d every 1-2 wk. Follow-up was carried out at 8 wk after discharge, his diarrhea was improved, taste returned to normal and weight gain was 5.0 kg.

**DISCUSSION**

CCS was first described in 1955 by Leonard W. Cronkhite, and Wilma J. Canada[1]. It occurs most frequently in middle-aged or older adults, with a slight male predominance, and a male-to-female ratio of 3:2[3]. CCS is a rare but serious protein-losing enteropathy, classically characterized by gastrointestinal polyposis and ectodermal features. Gastrointestinal polyposis is closely related to the malabsorption which...
induced these ectodermal changes\cite{41}. There is no strong evidence to suggest a familial aggregation and genetic predisposition. The etiology remains obscure but immune dysregulation may be important, given the increased IgG4 mononuclear cell staining in CCS polyps\cite{15,16}. In this case, IgG4 immunostaining was positive in polyps of stomach and colon. This histologic finding further supports that autoimmune mechanism may be involved in CCS.

Differential diagnosis of CCS includes a number of polyposis syndromes, such as familial adenomatous polyposis, Peutz-Jeghers syndrome, Cowden disease, Turcot syndrome and juvenile polyposis. These can be distinguished based on the polyp histology, polyp distribution, clinical presentations, family history, and molecular genetic testing\cite{7}. Polyps in CCS patients can develop throughout the gastrointestinal tract (except the esophagus) and are usually non-neoplastic hamartomas\cite{5}. But polyps of CCS also displayed hyperplastic, inflammatory, or adenomatous features\cite{8}. Watanabe et al\cite{8} demonstrated common features typical of CCS polyps, such as focal dilated cystic glands, some filled with proteinaceous fluid or inspissated mucus, the polyp and interpolyp area was edematous, with congestion and chronic inflammation of the lamina propria and submucosa, even though endoscopically the mucosa appeared normal. These findings are consistent with our case.

Optimum therapy for CCS is not known because of the rarity of the disorder and the poor understanding of the etiology. Combination therapy based on nutritional support and corticosteroids appears to lessen symptoms. The total treatment period is also not evidence-based, some recommended a range from 6 to 12 mo\cite{10,11}. Relapse was common with steroid tapering. For some patients with CCS who initially responded to corticosteroids, long-term maintenance therapy by for the patient with Cronkhite-Canada syndrome, early diagnosis and follow-up is important to improve the prognosis. Immune staining for IgG4 plasma cells in the polyps is helpful for exploring the mechanism underlying chronicle-Canada syndrome.

**COMMENTS**

**Case characteristics**

A 40-year-old male patient with a 4-mo history of diarrhea and hypoguesia associated with weight loss.

**Clinical diagnosis**

Cronkhite-Canada syndrome.

**Differential diagnosis**

Familial adenomatous polyposis, Peutz-Jeghers syndrome, Cowden disease, Turcot syndrome, juvenile polyposis.

**Laboratory diagnosis**

Low levels of serum albumin (30.1 g/L) and serum potassium (2.61 mmol/L).

**Imaging diagnosis**

The endoscopic evaluation revealed multiple sessile polyps in the stomach, small bowel and colorectum.

**Treatment**

The patient was treated with steroid.

**Related reports**

Cronkhite-Canada syndrome is a rare and serious disease, but few report is related to the mechanism.

**Experiences and lessons**

For the patient with Cronkhite-Canada syndrome, early diagnosis and follow-up is important to improve the prognosis. Immune staining for IgG4 plasma cells in the polyps is helpful for exploring the mechanism underlying chronicle-Canada syndrome.

**Peer-review**

In this manuscript, the authors demonstrated interesting Cronkhite-Canada syndrome case.

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