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# Cronkhite-Canada Syndrome: A Case report of Rare Disease from Nepal

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## ABSTRACT

Cronkhite-Canada syndrome first described in 1955, is a rare clinical syndrome of unknown etiology. Since then, more than 500 cases have been reported worldwide in the literature. The disease is characterized by diffuse gastrointestinal polyposis, dystrophic changes of the fingernails, cutaneous hyperpigmentation, alopecia, diarrhea, weight loss, and abdominal pain. A 84-year-old woman was admitted in our hospital with severe dehydration following diarrhea and epigastric discomforts. She also had dystrophic change of fingernails, and pigmentation of the palm and alopecia, all of which began several months ago. Endoscopy showed numerous, dense, tiny red polyps throughout the stomach, and duodenum. Her clinical manifestations and endoscopy were consistent with Cronkhite-Canada syndrome. We prescribed oral corticosteroids, which dramatically improved her condition. We here report rare case of Cronkhite-Canada syndrome who presented to our hospital.

**Keywords:** Cronkhite-canada syndrome; gastrointestinal polyposis; onychodystrophy nail

## INTRODUCTION

Cronkhite-Canada syndrome(CCS) is a rare non-hereditary disease of unknown etiology, first described in 1955.[1,2]A gastrointestinal hamartomatous polyposis and gastrointestinal symptoms such as diarrhea, other symptoms such as onychodystrophy, alopecia, hyperpigmentation of the skin, and rarely vitiligo[2] are also associated with this condition. Its pathogenesis remains unclear, however, an autoimmune process is suspected due to increased IgG4 levels found in CCS polyps.[3] More than 500 cases have been described in the literature, 75.0% originate from Japan. The average age of onset is 59.0 years with a 3:2 male/female distribution.[4]

Here, we describe a 84 year old woman presented to our hospital with CCS who had gastrointestinal symptoms such as recurrent episodes of diarrhea since last two month of duration associated with multiple gastrointestinal polyps, dystrophic change of fingernails, and pigmentation of the palms and sloes. Notably, she required recurrent and prolonged hospitalization related to severe gastrointestinal symptoms. After treatment with oral glucocorticoid, she experienced substantial relief of disease manifestations.

## CASE REPORT

An 84 year-old woman from western part of Nepal presented to our hospital with severe dehydration following diarrhea and epigastric discomfort. History revealed that she had recurrent episodes of watery diarrhea since last two months associated with decreased appetite with weight loss of around 7.0 kg. However she denied any history of fever, cough, shortness of breath, vomiting, dysphagia, hematemesis or malena. She and her family had no history of Gastrointestinal (GI) diseases in the past.

Patient was admitted for further evaluation. She was afebrile. Her blood pressure was 100/60 mm of Hg. Her pulse rate was 116/min with respiratory rate of 20/min. Sign of severe dehydration was present along with pallor and pedal edema. She had significant thinning and loss of the frontal scalp hairs and dystrophic changes of her fingernails (Figure 1). There was also a localised hyperpigmentation of her palms (Figure 2) and soles.She had no lymphadenopathy and her abdominal exam was unremarkable.

The Initial laboratory work up revealed anemia (hemoglobin 10 g/dL,reference range:12-16 g/dl), leukocytosis (12,400cells/mL, reference range:4,500-11,000 cells/mL), hyponatremia (130mmol/L,reference range:135-145mmol/L), Potassium 4.28mmol/L(reference range:3.6-5.2 mmol/L),hypoalbuminemia (3.2g/dL,reference range:3.4-5.4 g/dL). Her C-reactive protein, adrenocorticotrophic hormones(ACTH), cortisol, Liver function test(LFT), Renal function test(RFT) ,D-dimer, antinuclear

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antibodies(ANA), Anti-double stranded DNA (Anti DsDNA) antibodies) , rheumatoid factor(RF) were normal. Her stool Routine examination show no ova or parasites, negative Helibobacter pylori (H. pylori) antigens test and positive fecal occult blood test.

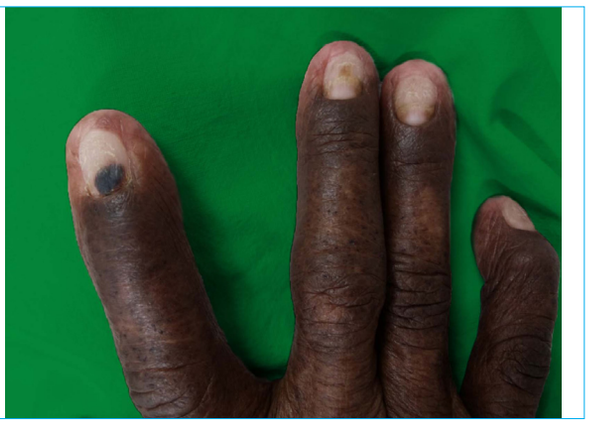

Figure 1. Showing onychodystrophy in fingers nail.

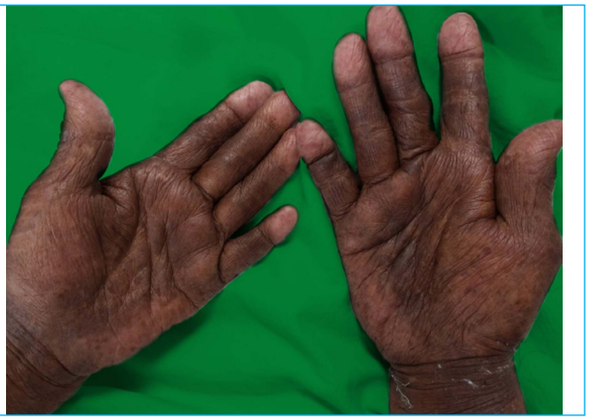

Figure 2. Showing localised hyperpigmentation in Palms of hand.

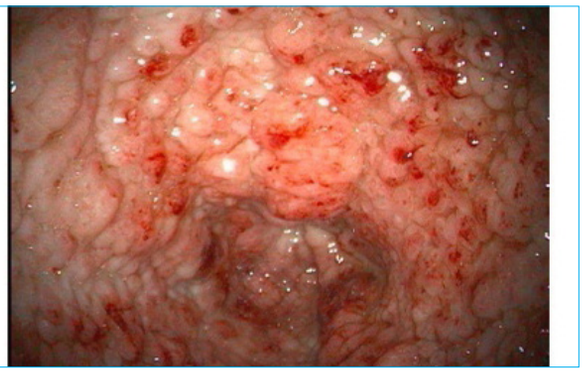

Figure 3. Showing diffuse polyposis in stomach with haemorrhagic spot.

Esophagogastroduodenoscopy revealed diffuse polyps lining the stomach and duodenum with multiple hemorrhagic spot and mucosal edema. There was no clear cut separation of the polyps from the surrounding mucosa (Figure 3). Multiple polyps within the stomach were removed along with normal appearing mucosa and sent to pathology department. The gastric polyp biopsies showed cystic dilated glands, edematous lamina propria with inflammatory infiltration of lymphocytes.

Differential diagnosis(DD) of CCS includes familial adenomatous polyposis, Peutz-Jeghers syndrome, inflammatory bowel disease, Whipple disease, juvenile polyposis, Cowden syndrome and small intestinal lymphoma. In our case, the patient was diagnosed with CCS based on a combination of her symptoms of recurrent episodes of diarrhea, cutaneous localised hyperpigmentation in palm, dystrophic changes of finger nails and endoscopic finding of diffuse gastrointestinal polyposis that excluded other DD.

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. 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 tapered to administered at 10 mg/day. After 5 months of treatment, the dose was modified to prednisone 5 mg daily for 3 months. Diarrhea, loss of appetite and dystrophic nail changes all gradually improved during the course of treatment. Repeat gastrointestinal endoscopy showed polyp shrinkage.

## DISCUSSION

Cronkhite and Canada first described CCS in 1955. CCS is a rare, acquired, nonhereditary syndrome with diffuse GI polyposis associated diarrhea with ectodermal changes, including hyperpigmentation of skin, alopecia and onychodystrophy.[1,2] CCS may occur in all ethnic groups, and the estimated incidence of CCS is extremely rare, approximately one case in a million individuals. At present, more than 500 cases have been described in the literature, 75.0% originate from Japan.[4] CCS affects more men compared with women, with a ratio of 3:2, and commonly occurs in the fifth decade of life. A total of 80% of patients are more than 50 years of age at the time of presentation.[5] According to a previous study, it has been revealed that the mean age of onset of CCS is 63.5 (range,31-86) years.[6]

For patients with CCS, diarrhea is the most common initial symptom, which may develop to substantially watery diarrhea, followed with symptoms of

malabsorption, including weakness, anemia, weight loss, edema and dysgeusia.[7] Histopathological reviews of biopsies obtained from these polyps revealed that these polyps are similar to that of juvenile adenomatous polyps or inflammatory type polyps, however they were additionally marked by striking stromal and lamina propria edematous changes, eosinophilic inflammation, were cystically dilated and had distorted glands with inflammatory infiltration.[6]

Ectodermal changes include alopecia, nail dystrophy and hyperpigmentation. These changes often occur later during the disease progression, usually several weeks or months subsequent to the GI symptoms.[8] Consistent with this, in the present case ,the patient initially experienced diarrhea and abdominal pain followed by onychodystrophy and hyperpigmentation.

Complications of CCS include GI bleeding with anemia, intussusception, hypoproteinemia, rectal prolapse, malabsorption, electrolyte turbulences, enteropathy and hypovitaminosis.[9] Among them, the risk of GI tract tumor types substantially increases. It has been reported that between 1980 and 2011, there were 383 patients diagnosed with CCS in Japan, and of these patients, 10.4% (40 patients) of them were also diagnosed with gastric cancer and 69 lesions (51 patients) were also diagnosed with colon cancer.[10]

The treatments and strategy of CCS currently include corticosteroids, nonsteroidal anti-inflammatory drugs, proton pump inhibitors, H2-receptor antagonists, hyperalimentation, cromolyn sodium, antibiotics, anabolic steroids, surgery, 5-aminosalicylate acid, antitumor necrosis factor α agents and the eradication of H. pylori and combinations of these therapies.[6] Steroids are considered to be the mainstay of medical treatment, however until now, there have been no guidelines for the recommended dose and duration of their use.

The prognosis of CCS is poor, with a 5-year mortality rate of 55% and the majority of mortality being associated with malnutrition, hypoalbuminemia, repetitive infection, sepsis, heart failure and GI bleeding.[8] The natural history of CCS appears to be substantially improved owing to the sufficient dose and duration of corticosteroid therapy accompanied by nutritional support and periodic endoscopic surveillance.[6]

## CONCLUSIONS

CCS is rarely encountered in clinical practice. Delays in diagnosis are common, primarily due to the non-familiarity of physicians with this rare entity, resulting in a poor outcome. Therefore, in order to avoid the misdiagnosis of CCS, physicians are recommended to suspect CCS for any case presented with diarrhea, weight loss, abdomen pain, endoscopic finding of diffuse gastrointestinal polyposis with cutaneous hyperpigmnetation, alopecia and dystrophic changes of the finger and toe nails.

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