# Polyps! Polyps! And More Polyps! - The First Case of Cronkhite-Canada Syndrome in Malaysia

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## SUMMARY

**Cronkhite-Canada Syndrome (CCS) is a syndrome characterised by a constellation of signs including but not limited to onychodystrophy of the finger and toe nails, skin hyperpigmentation and alopecia. Endoscopic features showed hamartomatous polyps involving all segments of the gastrointestinal tract with the characteristic exception of being oesophageal sparring. These polyps show confirmation by the presence of eosinophils and mast cells at the lamina propria upon histological studies.**

## INTRODUCTION

Cronkhite-Canada Syndrome (CCS), first documented in 1955 is a rare disease with only 450 cases reported in the literature[1,2] and distinguishable by clinical characteristics, gastrointestinal endoscopic and histologic findings. To our knowledge, this is the first reported case of CCS in Malaysia.

## CASE REPORT

A 63-year-old gentleman presented with chronic history of diarrhoea; occasional blood stained with mucous. Multiple previous presentations to many medical institutions resulted in treatments as infective diarrhoea and possible ulcerative colitis. He had received courses of combination of antibiotics and steroids therapy.

Upon presentation to our institution, history revealed poor appetite, weight loss of 20 kilograms and anasarca. No fever, night-sweats or abdominal pain were noted. No family history of colorectal cancer or polyposis reported.

Physical examination revealed pallor, alopecia, palmar skin hyperpigmentation and global dystrophic nail changes and glossitic tongue. Peripheral and sacral oedema showed pitting characteristics. Cardiovascular, respiratory and abdominal examinations were unremarkable.

Laboratory investigations revealed microcytic anaemia, hypokalaemia, severe hypoalbuminaemia, hypoprotenaemia, hypocalcaemia and depressed serum levels of iron, zinc and magnesium. Serum levels of vitamin B12, folate, immunoglobulins and gastrin were normal and the thyroid status and faecal elastase were within normal range. Both inflammatory markers, CRP and ESR were also moderately increased at 9mg/dL and 61mm/hr respectively. Urine microscopy and protein quantification were unremarkable. Repeated stools for cultures, ova, cyst and clostridium difficile were negative and anti-neutrophil antibody and anti double stranded DNA's were also negative.

Upper endoscopic examination demonstrated a marked erythematous, granular gastric mucosa with thickened folds, multiple semi-pedunculated and sessile polyps in the upper digestive tract with the exception of the oesophagus.

Ileo-colonoscopic examination showed numerous sessile and semi-pedunculated polyps from rectum to distal ileum ranging from few mm up to 2 cm. There was also moderate inflammation of colonic and rectal mucosa, with thickened fold.

Multiple biopsies revealed hamartomatous polyps with histology showing eosinophils and increase in mononuclear cells including mast cells within the lamina propria.

Subsequently, the magnetic resonance enterography was performed and demonstrated numerous polyps in the whole gastrointestinal tract including small bowels but with the exception of the oesophagus.

In light of his symptoms, characteristics clinical features, endoscopic and histology findings, he was diagnosed with Cronkhite-Canada Syndrome (CCS).

He received combination therapy consisting of systemic corticosteroids, proton pump inhibitor (for moderate pan-gastritis) along with elemental diet and hyperalimentation nutritional supplements. Prior to that, a trial of antibiotic was used to correct a possibility of bacterial overgrowth with no response. Further nutritional supplementations were administered and these include oral and intravenous fluids, electrolytes, vitamins, minerals, amino acids, albumin and lipids and the patient responded very well to the above treatment regimen.

## DISCUSSION

Cronkhite-Canada Syndrome (CCS) is characterised by diffuse gastrointestinal polyposis with oesophageal sparring, ectodermal changes, chronic diarrhoea and nutritional disturbances in particular severe hypoalbuminaemia. Typical symptoms include diarrhoea, weight loss, abdominal pain,

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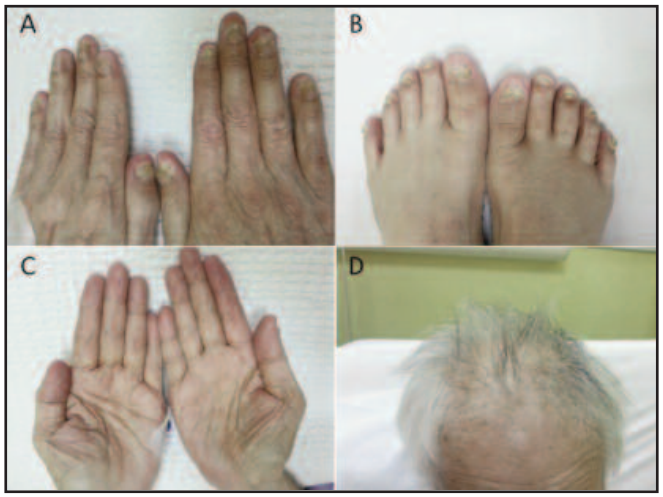


**Fig. 1:** Constellation of signs in Cronkhite-Canada Syndrome. Onychodystrophy of fingernails (A) and toe nails (B), skin hyperpigmentation (C) and alopecia (D).

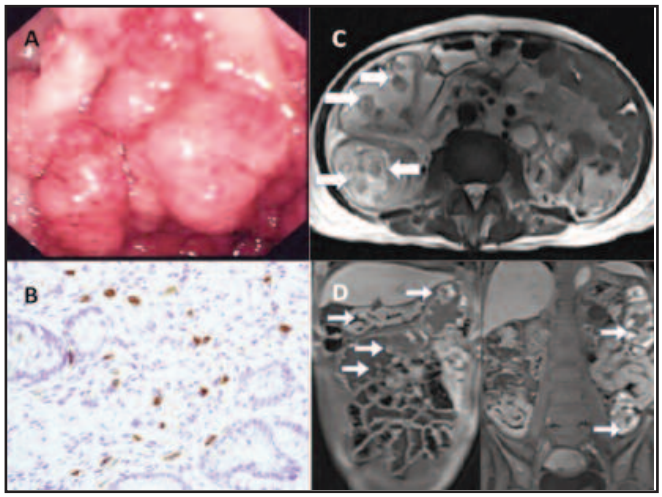


**Fig. 2:** Investigation results in Cronkhite-Canada Syndorme. Hamartamous polyps (A), Mast cell – CD117 40x (B), Axial T2 HASTE – Multiple polyps in the caecum and ascending colon (C), Coronal T1 Post Gadolinium – Multiple enhancing polyps in the the stomach, transverse colon, splenic flexure and descending colon (D).

cutaneous hyperpigmentation, dystrophic nail changes, and alopecia. Hypogeusia and xerostomia have also been described. Protein-losing enteropathy is frequently observed.[2,3]

The polyps are frequently found in the stomach, small and large intestines but do not occur in the oesophagus. CCS is considered as a hamartomatous polyposis syndrome and differentiated by its widespread polyp distribution in the stomach, small bowel and colon with oesophageal sparring. The aetiology is currently unknown. With no evidence to suggest a familial predisposition, current consensus agree on being autoimmune in nature with arguments of an infectious cause considered due to inflammatory cell infiltration with mononuclear cells and eosinophils.[4]

Cases have been associated with elevated antinuclear antibody and levels with association with other autoimmune diseases such as membranous glomerulonephritis, systemic lupus erythematosus, rheumatoid arthritis, and scleroderma.[3,4]

Mental and physical stress ranks among the most important risk factors for this syndrome. The 5 years mortality rate is reported to be 55% with spontaneous regressions were observed in 5-10%.[1]

Potentially fatal complication includes malnutrition, gastrointestinal bleeding and infection with 15% of CCS patients developing gastric and colorectal cancers.[1] Periodic examination of the stomach, colon and rectum with multiple biopsies should be taken in order to identify dysplastic and adenomatous epithelium. However, due to the rarity of the cases, no specific algorithm or screening protocol had been developed. Intervention such as total gastrectomy or pan-colectomy is indicated in the event of dysplastic changes or colorectal carcinoma, with the procedure of choice determined by the lesion location.[1]

Optimal treatment of CCS is currently unknown. Nutritional support in the form of total parenteral nutrition is preferred to allow complete bowel rest. Electrolytes imbalance frequently needs correction. Therapies such as proton pump inhibitors, histamine receptor antagonists and cromolyn sodium have been used in particular patients with degranulating eosinophils and mast cells on biopsies.[1]

In view of autoimmune features, azathioprine and tacrolimus were given in some cases. In a review, Marcela et al recommended omeprazole (20mg twice a day), prednisolone (20mg a day) and azathioprine (2.5 mg/kg/day) for up to 6 to 12 months.

Our patient is currently responded well with the nutritional and supplementation therapy.

## CONCLUSION

This case illustrates the challenges in establishing the diagnosis of the CCS. CCS is a rare and serious disease with high mortality rate. With increased recognition and as our understanding improves, it is hope that prognosis of CCS improves in the near future.

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