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Cronkhite-Canada syndrome: First case report from Egypt and North Africa

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Abstract

BACKGROUND

Gastrointestinal (GI) polyposis isn't a rare one in GI diseases. To date about 500 cases of Cronkhite-Canada syndrome (CCS) have been reported worldwide.

CASE SUMMARY

We report a 60-year-old female patient presented with dyspepsia, abdominal pain, and weight loss of one-year duration. Her physical examination showed alopecia and onychodystrophy. Upper endoscopy revealed diffuse markedly thickened gastric mucosa involving the whole stomach with thickened gastric rugae and numerous polypoidal lesions. Histopathological examination showed marked hyperplasia of the foveolar glands with inflammatory cell infiltration. Endoscopic ultrasound showed significantly hypertrophic mucosa, muscularis mucosa, while the submucosa and the muscularis propria are spared favouring its benign nature. Colonoscopy showed multiple sessile polyps scattered at different parts of the colon. Histopathological examination revealed tubular adenomatous polyps with low-grade dysplasia. Differential diagnoses included: CCS, Menterier disease (MD), other polyposis syndromes, lymphoma, amyloidosis, and gastric malignancies. The presence of alopecia, nail dystrophy, GI polyposis, markedly thickened gastric mucosa and folds, abdominal pain, weight loss, and marked foveolar gland hyperplasia, all were in favour of CCS. Lymphoma was excluded due to sparing the muscularis propria. The presence

of colonic polyps, antral and duodenal infiltration, and the absence of hypoproteinaemia decrease the possibility for MD.

CONCLUSION

The patient was diagnosed as CCS.

Key Words: Gastrointestinal polyposis; Thickened gastric mucosa; Cronkhite-Canada syndrome; Case report

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INTRODUCTION

Cronkhite-Canada syndrome (CCS) is one of the rarest nonhereditary diseases[1] that its exact aetiology is still unknown[2]; with around 500 cases have been described in the literature[3]. Most of CCS were reported from Japan, and for our knowledge, our case is the 1st case reported from Egypt and North Africa.

Patient with CCS usually presents with gastrointestinal (GI) symptoms such as abdominal pain, weight loss, and diarrhea, or with other symptoms such as onychodystrophy, alopecia, hyperpigmentation of the skin, and rarely vitiligo[4]. GI polyposis is the main endoscopic feature in CCS, which is commonly non-neoplastic and rather inflammatory, hyperplastic, hamartomatous, and/or adenomatous polyps in nature[5]. Moreover, some CCS cases may develop gastric and colorectal malignancies during the disease course[4].

CASE PRESENTATION

Chief complaints

A 60-year-old female patient presented with dyspepsia, abdominal pain, and weight loss of one-year duration.

History of present illness

She denied other GI or anaemic symptoms. She was non-smoker and did not drink alcohol.

History of past illness

Her past medical history was free apart from prolonged Proton-pump inhibitor (PPI) intake.

Personal and family history

There was no family history of gastrointestinal polyposis or colorectal malignancy.

Physical examination

Her physical examination was unremarkable apart from alopecia (Figure 1A) and onychodystrophy (Figure 1B).

Laboratory examinations

Her laboratory profile was within normal limits including a full complete blood picture (CBC), chemistry, serum albumin, serum calcium, urine analysis, antinuclear antibody (ANA), and IgG-4.

Imaging examinations

Oesophago-gastro-duodenoscopy (OGD) revealed diffuse markedly thickened gastric mucosa involving the whole stomach (fundus, body, and antrum), with thickened and tortuous gastric rugae, and numerous polypoidal lesions (3-10 mm in diameter), with hyperaemic mucosa, and to lesser extent down to the duodenal bulb and second part of the duodenum (Figure 2A and B). Multiple conventional biopsies were taken, and

polypectomy was done for the large polyps for histopathological examination. Biopsies showed marked hyperplasia and cystic dilation of foveolar glands with inflammatory cell infiltration including eosinophils, hyperplastic polyps, chronic gastritis, and Helicobacter pylori (H. pylori) association with no atypia or malignancy (Figure 3). IgG4-immunohistochemistry showed a very faintly positive signal.

Endoscopic ultrasound (EUS) was done later and showed significantly hypertrophic mucosa, muscularis mucosa, while the submucosa and the muscularis propria are spared favouring its benign nature. Wall thickness is up to 8-10 mm (Normal is up to 4 mm) (Figure 2C).

Colonoscopy showed multiple variable-sized, sessile, and pedunculated polyps, about 15 polyps, scattered at different parts of the colon, snaring of the large polyps was done after submucosal injection (Figure 2D and E), histopathological examination showed typical features of benign juvenile-like and hamartomatous polyps without dysplastic changes, while other polyps pathology revealed tubular adenomatous polyps with low-grade dysplasia.

Both push enteroscopy and terminal ileoscopy showed no polyposis with normal mucosa in the 3rd and 4th portions of the duodenum, the proximal jejunum, and the terminal ileum.

Computerized tomography (CT) scan of the abdomen & pelvis with oral and intravenous (IV) contrast revealed mild circumferential mural thickening of the gastric wall.

FINAL DIAGNOSIS

The patient was diagnosed as CCS.

TREATMENT

The patient started a sequential therapy for *H. pylori* infection with complete eradication, followed by proton pump inhibitors (40 mg once daily), prednisolone (30 mg/d), and mesalazine (500 mg QID) for 6 mo.

DISCUSSION

In our case, the following differential diagnoses were raised and discussed with our gastroenterologists: Cronkhite-Canada Syndrome (CCS), Menterier disease (MD), other polyposis syndromes (such as familiar adenomatous polyposis, Gardner syndrome, juvenile polyposis, Peutz-Jeghers syndrome and Turcot syndrome), lymphoma, amyloidosis, duodenal gastric heterotopia, and gastric malignancies.

The final diagnosis was based on the medical history, physical examination, endoscopic findings, and the histopathological examination. The presence of anomalies of ectodermal tissues (such as alopecia and nail dystrophy), gastrointestinal polyposis (hamartomatous and adenomatous polyps), markedly thickened gastric mucosa and folds, abdominal pain, weight loss and marked foveolar gland hyperplasia, all were in favour of the Cronkhite-Canada syndrome. On the other hand, there was no protein-losing enteropathy, diarrhea, hypoalbuminaemia or skin pigmentation.

Lymphoma was excluded due to sparing the muscularis propria. Furthermore, markedly thickened gastric mucosa and folds and the histopathological examination which revealed marked foveolar gland hyperplasia were consistent with Menterier's disease. In addition, abdominal pain and weight loss are a common presentation of Menterier's disease, but the presence of colonic polyps, antral and duodenal infiltration, and the absence of hypoproteinaemia decrease the possibility for MD.

The patient started a sequential therapy for H pylori infection with complete eradication, followed by proton pump inhibitors (40 mg once daily), prednisolone (30 mg/d), and mesalazine (500 mg QID) for 6 mo.

Common complications of CCS include anemia, intussusception, rectal prolapse, and gastro-intestinal bleeding, other less common as recurrent severe acute pancreatitis, myelodysplastic syndrome, cecal intussusception, portal thrombosis, membranous glomerulonephritis and osteoporotic fractures that may result from malabsorption of calcium or prolonged glucocorticoid therapy or both. The most serious complication is

malignancy; however, the incidence of CCS-related cancer is estimated to be 5%-25%, especially gastric and colon cancer[6].

The follow-up endoscopies (OGD and colonoscopy) after six and twelve months of treatment showed significant remission with a reduced number of gastric and colonic polyps and regression of hypertrophic gastric folds (Figure 4). Consequently, the patient's clinical condition was markedly improved, and the prednisolone dose was reduced gradually to 7.5 mg/d, but the mesalazine dose remained the same.

There is a tendency of malignant transformation or coexistence of gastrointestinal malignancies in patients with CCS. So, Endoscopic documentation of regression in CCS is important despite the lower incidence of CCS-related cancer in remission patients. Therefore, the comprehensive endoscopic annual surveillance either *via* chromoendoscopy or directed biopsy from irregular polyps, to exclude pre-cancer lesions before development of invasive carcinoma is mandatory, however there are still no recommended guidelines to be followed[7].

Nutritional support, electrolytes, mineral and vitamin supplementation remains the cornerstone in treatment of CCS beside antibiotics, and corticosteroids, however the definitive treatment is still unknown[4,7].

Till now, there is still much that needed to know about this syndrome. In this context, the most important issue is to maintain treatment monitoring and provide appropriate measure to prevent relapse[8].

CONCLUSION

CCS is one of the uncommon, acquired polyposis with obscure aetiology. To date around 500 cases have been reported all over the world. Most of CCS cases were reported from Japan, and for our knowledge, our case is the 1st case reported from Egypt and North Africa. CCS is generally characterized by GI symptoms, such as diarrhea and skin changes (*e.g.*, alopecia, skin pigmentation, and onychodystrophy), while GI polyposis is the main endoscopic feature in CCS, which is commonly non-neoplastic and mainly include inflammatory, hyperplastic, hamartomatous, and/or

adenomatous polyps. CCS has a malignant potential, and some cases may develop gastric and colorectal malignancies during the disease course. Till now, there is no uniform standard treatment for CCS.

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Figure Legends

Figure 1 Physical examination. A: Alopecia; B: Onychodystrophy.

Figure 2 Endoscopy. A and B: Upper endoscopy revealed diffuse markedly thickened gastric mucosa with numerous polypoidal lesions; C: Endoscopic ultrasound revealed significantly hypertrophic mucosa, muscularis mucosa, while sparing the submucosa and the muscularis propria; D and E: Colonoscopy showed multiple variable-sized, sessile, and pedunculated polyps, removed by snare polypectomy.

Figure 3 Histopathological examination showed marked hyperplasia and cystic dilation of foveolar glands with inflammatory cell infiltration including eosinophils, chronic gastritis, and Helicobacter pylori association with no atypia or malignancy.

Figure 4 Follow-up endoscopies after 6 mo and 12 mo of treatment showed significant remission with a reduced number of gastric and colonic polyps and regression of hypertrophic gastric folds. A: Upper endoscopy; B: Colonoscopy.

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