An unusual case of hamartomatous polyposis with malignancy complication in a patient with ulcerative colitis treated with golimumab

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Abstract

We report an unusual case of hamartomatous polyposis with malignant complications in a patient with ulcerative colitis on golimumab and previous thiopurine therapy. This patient was evaluated for iron deficiency anemia and underwent hemicolectomy for extensive right-side predominant inflammatory pseudopolyps. Anemia persisted post-colectomy and subsequent gastroscopy showed a fungating polypoid lesion along with numerous carpet-like strawberry appearing polyps in the stomach extending from the gastro-esophageal junction to the distal part of the antrum, necessitating a gastrectomy. Histology showed extensive hamartomatous-like polyps with adenocarcinoma and nodal metastases. Presence of alopecia totalis and hamartomas in this patient raise the possibility of Cronkhite-Canada Syndrome although this may also represent an undescribed hamartomatous polyposis associated with ulcerative colitis. Even though thiopurine analogue and anti-tumor necrosis factor agents have not been associated with increased risk of solid tumors, immunosuppression in patients with extensive polyposis should be cautiously used due to the potential accelerated malignancy risk. This case also highlights the importance of performing additional imaging of the gastrointestinal tract, in inflammatory bowel disease patients with anemia, particularly if the severity is incongruent with disease activity. (Acta gastroenterol. belg., **2017**, 80, **530-532**).

Key words : Hamartomatous polyposis, ulcerative colitis, iron deficiency anemia, golimumab, gastric adenocarcinoma

Introduction

Anemia is the most common extraintestinal manifestation found in inflammatory bowel disease (IBD) resulting from multiple potential causes (1). Prompt evaluation and management are pertinent in order to minimize associated detrimental outcomes. Benign mucosal polyps, including inflammatory pseudopolyps are uncommon causes of anemia that may complicate the management of IBD patients. We report an unusual case of iron deficiency anemia in an ulcerative colitis (UC) patient with extensive hamartomatous and inflammatory polyposis.

Case report

A 49-year-old man was referred to our institution for the management of UC. This was diagnosed in 2008 and was treated with golimumab following failure of 5-aminosalicylate and thiopurines for approximately two years. At the time of diagnosis, he also underwent an esophagogastroduodenoscopy (EGD) that was normal. Physical examination only revealed features of alopecia totalis. The patient was subsequently found to have iron deficiency anemia (IDA, hemoglobin of 80 g/L, ferritin of 3.7 ug/L, and serum iron of 2.5 umol/L), 5 years after his UC diagnosis. Colonoscopy showed extensive inflammatory pseudopolyps with white exudate cap from the ascending to the transverse colon with relative sparing distally and his UC was in endoscopic remission. Given the difficulty to perform neoplasia surveillance and the presumed polyp-induced IDA, the patient elected for right hemicolectomy with primary ileocolic anastomosis. His IDA (hemoglobin of 75 g/L, ferritin of 2.9 ug/L and serum iron of 3.5 umol/L) persisted post colectomy despite intravenous iron supplementation. A repeat colonoscopy showed no active disease with few scattered pseudopolyps and he subsequently underwent a gastroscopy that showed a large fungating friable polypoid lesion with a central purple discoloration in

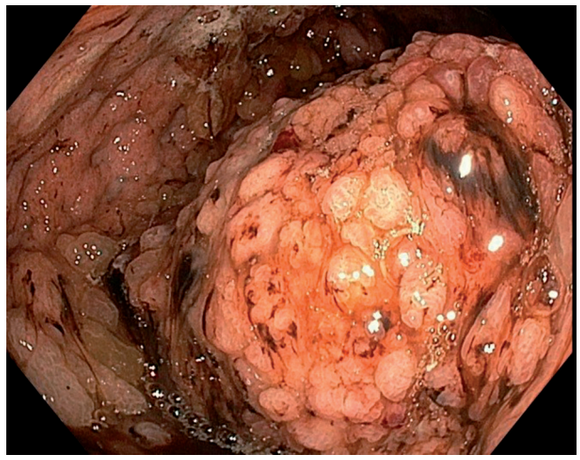

Fig. 1. — Endoscopic findings in the stomach showing a large fungating friable polypoid lesion with a central purple discoloration along with numerous carpet-like strawberry appearing polyps.

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Submission date : 06/02/2016
Acceptance date : 12/04/2016

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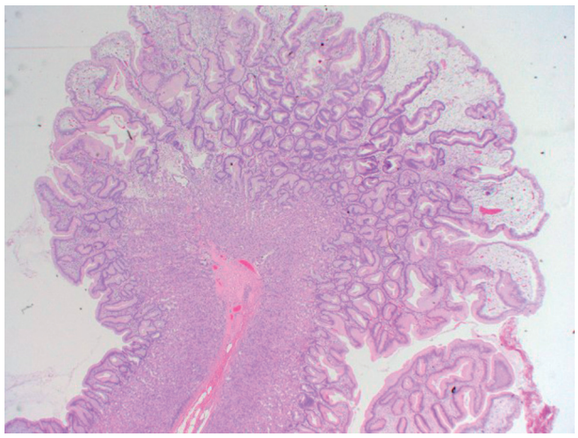

Fig. 2. — Histological examination showing feature of hyperplastic epithelium with inflamed and edematous stroma consistent with hamartomatous polyps.

addition to numerous extensive carpet-like strawberry appearing polyps in the stomach extending from the gastro-esophageal junction to the distal part of the antrum (Fig. 1). Biopsies showed polypoid gastric mucosa with foveolar cell hyperplasia and low grade dysplasia. Upper endoscopic ultrasound revealed marked hyperechoic thickening of the mucosal layer without overt features of invasive malignancy (Fig. 2). Capsule endoscopy showed no evidence of polyps in the small intestine. The patient underwent a total gastrectomy and his golimumab was withdrawn. Gross examination of the surgical specimen revealed an exophytic fungating lesion measuring 27 x 15 x 6.3 cm along with numerous smaller polyps throughout the stomach. However, after cut sectioning, no obvious malignant invasion was noted. Histology showed extensive hamartomatous-like polyps complicated by a small focus of well-differentiated adenocarcinoma with nodal metastases (pT1bN1) (Fig. 2). He then received subsequent adjuvant chemotherapy. This case represents a rare case of gastric hamartomatous polyposis (HP) complicating the management of ulcerative colitis.

Discussion

There have not been any reports of HP associated with UC. The presence of alopecia and extensive hamartomas raises the possibility of Cronkhite-Canada Syndrome (CCS). This is a rare, non-hereditary gastrointestinal (GI) hamartomatous polyposis syndrome and typically associated with ectodermal changes of alopecia, onychodystrophic nail changes and skin pigmentation. Around 500 cases of CCS have been reported worldwide predominantly of Japanese origin (2). CCS is usually diagnosed in middle-aged to older adults with men being slightly more affected than women (ratio of 3:2). The etiology is unknown although an autoimmune process has been suggested. It has been reported previously that positive immune staining for IgG4 plasma cells are increased in the CCS polyps as well as tumor necrosis factor (TNF) expression (3-4). Furthermore, there have been associations between CCS and high antinuclear antibodies (ANA), as well as some autoimmune disease like hypothyroidism, rheumatoid arthritis, and systemic lupus erythematous (5).

Patients often present with diarrhea, dysgeusia, weight loss, abdominal pain or protein losing enteropathy. Endoscopically, the typical findings are multiple mucosal polyps with appearances akin to strawberries found diffusely distributed throughout the GI tract, only sparing the esophagus. Histologically, they are usually harmatomatous or juvenile-like polyps characterized by cystic gland dilation, expanded edematous lamina propria, hyperplasia of foveolar epithelium and mild infiltration of inflammatory cells including eosinophils (6). Traditional serrated and conventional adenomas have also been found in the colon of patients with CCS. Numerous complications can rise from CCS, including the development of malignancy arising in approximately 15% of patients with CCS (2). Due to the rarity of this disease, optimal screening strategies have not been developed. To date, there is no specific and effective treatment although corticosteroids, nutritional optimization and immunosuppressant, including thiopurine analogue and anti-TNF, has been utilized previously (7).

Other differentials include juvenile polyposis syndrome although the lack of family history and older age of diagnosis would be unusual (8). Similarly, this patient also lacks the pathognomonic mucocutaneous changes and multi-organ polyposis typically seen in CCS, Cowden and other phosphatase and tensin homolog (PTEN) related HP syndromes (9). Peutz-Jeghers syndrome is also unlikely in light of the lack of small bowel involvement and absence of mucocutaneous pigmentations (10). The development of these hamartomatous changes may also be sporadic in nature and non-syndromic or related to an undescribed isolated gastric HP associated with UC.

Multiple observational and post-market surveillance studies have not shown a significant increase risk of solid tumors in patients treated with anti-TNFα agents, including golimumab (11). Similarly, the use of thiopurine agents in the setting of inflammatory bowel disease also is not associated with development of solid tumors in patients without prior history of malignancy. This case however highlights an important issue with the use immunosuppression in harmatomatous syndrome that has not been reported previously. Although the malignant complication in this case may be related purely with known cancer association in HPS, the potential contribution by golimumab and thiopurine analogue cannot be excluded. Furthermore, published reports suggest the malignant association in CCS is predominantly colonic with gastric cancer being <10% of the case. Majority of these patients were Japanese, which is of a higher risk population for gastric cancer, therefore some have argued the true risk of gastric

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cancer in CCS may not be significant. Consequently, gastric neoplastic transformation in this case may have been enhanced in the setting of immunosuppressant. Moreover, the underlying malignancy risk is even higher in other hamartomatous syndromes. For example, up to 29% of Peutz-Jeghers patients may develop gastric cancer and the lifetime risk in juvenile polyposis is around 20 to 30%. Once again the risk modification in these syndromes with immunosuppression is not defined. Clear estimates of malignant risk in sporadic gastric hamartoma are not reported in the literature due to its rareness. Only few case reports have been published to date which highlighted the potential, albeit uncommon risk (12). Therefore, in light of the paucity of scientific data and variable underlying malignancy risks, use of immunosuppression in syndromic or sporadic hamartomatous polyposis needs to be cautiously considered. Further studies are needed to guide our use of immunosuppression in these situations.

Interestingly, CCS has been reported to present with colitis mimicking symptoms along with similar endoscopic and histological findings prior to the development of typical polypoid changes in the colon (13). This patient nevertheless had a definitive histological diagnosis of UC and predominant burden of hamartoma in this patient resides in the upper GI tract. It is also important to know that often histological changes in hamartomatous polyps cannot be conclusively distinguished from inflammatory pseudopolyps as there are multiple overlapping non-specific features. Therefore, one could also wonder if this patient's extensive colonic polyps are partly related to HP particularly in light of the right sided predominance which is unusual if these were driven purely by previous UC activity.

Finally, this case also illustrates the importance of performing additional imaging of the GI tract, including EGD and small bowel imaging, in inflammatory bowel disease patients with IDA, particularly if the severity of IDA is not consistent with disease activity and the early identification of contributing pathologies could minimize associated complications.

In summary, this is a first case of HP complicating the management of a patient with established UC. Immunosuppressive therapy should be used cautiously in HP in light of potential acceleration of malignant transformation. Appropriate evaluation of the GI tract should be performed in patients with anemia incongruent to disease activity.

Funding

No funding was received for the preparation of this manuscript.

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