SHORT REPORT

Microcarcinoids associated with diversion colitis in a patient with Crohn's disease

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Abstract

Diversion colitis is an iatrogenic disorder related to surgical diversion of the faecal stream from the colorectal mucosa, first described by Morson in 1972. Inflammation of the defunctioned mucosa seems to be related to deprivation of luminal nutrients, in particular short chain fatty acids. Histologic abnormalities include damage of the epithelium and reparative changes with crypt distortion and branching, a mixed acute and chronic inflammatory infiltrate with crypt abscesses and lymphoid hyperplasia, Paneth cell metaplasia and thickening of the muscularis mucosae. We report a case of diversion colitis in a 51-year-old female with Crohn's disease with multiple submucosal microcarcinoids in the rectal stump 17 years after diversion and discuss the hypothesis that hyperplastic and neoplastic lesions of neuroendocrine cells can result from proliferative response to chronic inflammation and repair, as well as epithelial neoplasms.

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KEYWORDS: Diversion colitis; Crohn's disease; Microcarcinoids

1. Introduction

Diversion colitis is an iatrogenic disorder related to surgical diversion of the faecal stream from the colorectal mucosa, first described by Morson in 1972. It is an inflammatory process that develops in a substantial proportion of patients following intestinal diversion for the treatment of tumours, diverticular disease, trauma or inflammatory conditions of the colorectum. Inflammation of the defunctioned mucosa seems to be related to deprivation of luminal nutrients, in particular short chain fatty acids. Changes in bacterial flora may also play a role in the pathogenesis of diversion colitis. The macroscopic and microscopic appearances of this condition vary widely and overlap with idiopathic inflammatory bowel disease and infectious colitis, although the degree of histological changes may be influenced by the nature of the underlying disease. Histologic abnormalities include superficial ulcers and damage of the superficial epithelium, crypt distortion and branching, atrophy, a mixed acute and chronic inflammatory infiltrate with crypt abscesses and lymphoid hyperplasia, Paneth cell metaplasia, thickening and splaying of the muscularis mucosae.

We report a case of diversion colitis in a patient with Crohn's disease submitted to subtotal colectomy and ileostomy, with multiple submucosal microcarcinoids in the rectal stump.
2. Case report

The patient was a 51-year-old Caucasian female who had a diagnosis of Crohn’s disease of the ileum and colon at the age of nineteen years. Six years after the diagnosis she had a subtotal colectomy and ileostomy following perforation of the sigmoid colon, due to severe pancolitis. She maintained clinical remission afterwards and refused reconstruction surgery.

After 17 years the patient presented with complains of persistent rectal mucus discharge and bleeding. Rectosigmoidoscopy revealed a rectal stump of 15 cm with erythema and friability of the mucosa. Endoscopic biopsies showed moderate architectural distortion and lymphoplasmacytic infiltrates in the lamina propria, consistent with diversion colitis. A perianal fistula was found, requiring a fistulotomy and the prescription of azathioprine and metronidazole, with fistula healing and good clinical response.

She was well until last year when she started complaining of proctalgia and intermittent rectal bloody discharge with normal ESR, CRP and blood count. The endoscopy revealed severe proctitis with areas of hyperemia and multiple erosions of the rectal stump mucosa and a tight stenosis at 10 cm from the anal verge. Random biopsies were taken and the histological aspects of the mucosa were strongly suggestive of diversion colitis, with severe crypt distortion, intense inflammatory infiltrate that was limited to the lamina propria, a few crypt abscesses and lymphoid hyperplasia. The muscularis mucosae was thickened, focally permeated by inflammatory cells (Fig. 2a,b). The submucosa was totally infiltrated by adipose tissue. On the distal third of the specimen, there were numerous trabeculae and small nests of large uniform cells with round nuclei with speckled chromatin, infiltrating the mucosa and within the upper third of the muscularis mucosae. This picture was diagnostic of microcarcinoids in the context of hyperplasia of neuroendocrine cells.

The confirmation of the neuroendocrine nature of the cells was obtained by immunohistochemistry, which showed intense positive staining for synaptophysin and chromogranin (Fig. 2c).

2.1. Pathology

The resected protectomy specimen consisted in a segment measuring 18 cm, with the lumen progressively narrowing towards the proximal end. Macroscopic examination revealed a granular mucosa with a thickened lipomatous submucosa.

On histological examination, the mucosa showed the typical features of intense diversion colitis: erosions, severe crypt distortion with focal atrophy, mixed inflammatory infiltrate that was limited to the lamina propria, a few crypt abscesses and lymphoid hyperplasia. The muscularis mucosae was thickened, focally permeated by inflammatory cells (Fig. 2a,b). The submucosa was totally infiltrated by adipose tissue. On the distal third of the specimen, there were numerous trabeculae and small nests of large uniform cells with round nuclei with speckled chromatin, infiltrating the mucosa and within the upper third of the muscularis mucosae. This picture was diagnostic of microcarcinoids in the context of hyperplasia of neuroendocrine cells.

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3. Discussion

Carcinoid tumours are neoplasms that arise from mature neuroendocrine cells or their stem cells. The most commonly affected site in the large intestine is the rectum, where the disease activity, unknown nature of the stenosis and the existence of a segment of the colon unavailable to endoscopy. The procedure was performed without complications, with an uneventful recovery.
neuroendocrine cells are more numerous. Although these tumours usually occur singly, in a minority of patients multiple carcinoids may occur as micronodules, particularly in the rectum.

In 1979, Hay and Curt reported the first case of a carcinoid tumour complicating ulcerative colitis. Since then, several cases have been described in ulcerative colitis and Crohn’s disease. Although the association could be coincidental, Kortbeek et al. calculated that by chance only, the probability of developing one carcinoid tumour in the inflammatory bowel disease population studied should be as high as one case every 200 years, in contrast with the finding of three carcinoids in a 2-year period reported by these authors. West and collaborators reported four cases and concluded that the incidence found in their series of Crohn’s patients was significantly increased compared to non-IBD patients. These authors used as control appendectomy specimens from non-IBD patients (which could bias the study as the frequency of carcinoid tumours is organ-specific) and theorized that the development of carcinoid tumours may be secondary to distant mediators rather than a local inflammatory effect.

The gut neuroendocrine cells have been noted to undergo proliferative changes in response to mucosal injury. Such changes have been well documented in patients with chronic autoimmune atrophic gastritis, were neuroendocrine cells can be hyperplastic, suffer dysplastic transformation with enlarging micronodules and give rise to microcarcinoids with infiltration of the endocrine cells into the submucosa. In the bowel, hyperplasia of endocrine cells has also been described in a variety of other chronic inflammatory conditions, including celiac disease and chronic cholecystitis. In the context of chronic inflammatory bowel disease, the link between longstanding chronic inflammatory process and increased neoplastic risk for epithelial tumors is substantiated by several studies. The same mechanism could be responsible for hyperplasia and neoplasia of neuroendocrine cells in the gut.

To our knowledge, there is only one previous report of microcarcinoid tumour associated with diversion colitis described by Griffiths and Dixon in a patient with the colon defunctioned for 18 years. As well as inflammatory bowel disease, diversion colitis represents a condition characterized by chronic inflammation, with regenerative changes of the colonic epithelium and lymphoid follicular hyperplasia. The associated hyperplasia of endocrine cells and microcarcinoid formation could be explained by the production of trophic factors by the sustained chronic inflammatory cell response. Neuroendocrine cells seem to share with epithelial cells the potentiality to proliferate in response to chronic inflammatory injury or evolve from multipotential cells.

Our case is, to our knowledge, the second report of neuroendocrine cell hyperplasia and microcarcinoid associated with diversion colitis. This association reinforces the hypothesis that hyperplastic and neoplastic lesions of neuroendocrine cells can also result from proliferative response to chronic injury in colorectal mucosa.

Although in our case the pathological aspects strongly favour diversions colitis, it is impossible to affirm with no
doubt that Crohn’s disease isn’t partially responsible for the chronic inflammatory state that underlies neuroendocrine hyperplasia and microcarcinoid tumour. Either way, it is a rare case that raises our attention to the possible increased risk of carcinoid tumour in this group of patients.

References