

# Small Bowel Malakoplakia Associated with Crohn's Disease: A Novel Association

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## Abstract

Malakoplakia is an uncommon chronic granulomatous inflammatory disease with a distinctive microscopic pattern. It rarely affects the gastrointestinal system and has rarely been reported involving the ileum. No association with Crohn's disease has been documented to date. We report the case of an asymptomatic 70-year-old woman with Crohn's disease in remission and de novo Malakoplakia developing in the last centimeters of the terminal ileum. Follow-up colonoscopy after withdrawal of mercaptopurine therapy and prolonged ciprofloxacin with vitamin C treatment revealed endoscopic and histological improvement.

## INTRODUCTION

Malakoplakia is an uncommon chronic granulomatous inflammatory disease with typical microscopic features, described originally by Michaelis and Gutmann a century ago. (1) The designation derives from the Greek words malakos (connotation soft) and plakos (connotation plaque).

Gastrointestinal malakoplakia has been considered rather unusual, mainly reported in the literature in association to colonic involvement, particularly in the recto-sigmoid area.

(1,3) Pure small bowel involvement is extremely rare, with two cases published to date. (4,5) It usually appears in the background of a systemic disease. (1,3,6) In the digestive tract, it has been linked to bacterial and fungal infections, colonic tumors, ulcerative colitis and several immunocompromising conditions. (1,2,3,6) However an association with Crohn's disease has not been previously documented in the literature.

We report the case of an asymptomatic 70-year-old woman with a novel association of Crohn's disease in remission and malakoplakia restricted to the last centimeters of the terminal ileum.

## CASE REPORT

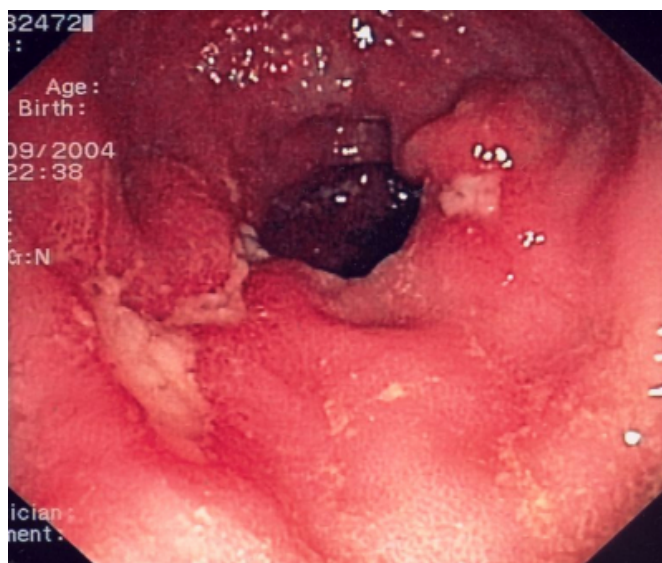
A 70-year-old woman with a history of Crohn's disease diagnosed in the nineties with initial radiologic, endoscopic and histopathologic involvement of the small and large bowel was scheduled for a surveillance colonoscopy in

April, 2004. The patient had been in remission since 2001 on 6 mercaptopurine therapy (1 mg/kg/day). No other treatment (i.e. steroids, mesalamine or infliximab) had been used during the last five years prior to the examination.

Colonoscopy demonstrated quiescent patchy areas of erythema in the right colon. Biopsies were consistent with mild chronic focal inflammation and no dysplasia. Ileoscopy revealed discrete nodular lesions and aphthous ulcers in the last cm of the terminal ileum (Figure 1).

## Figure 1

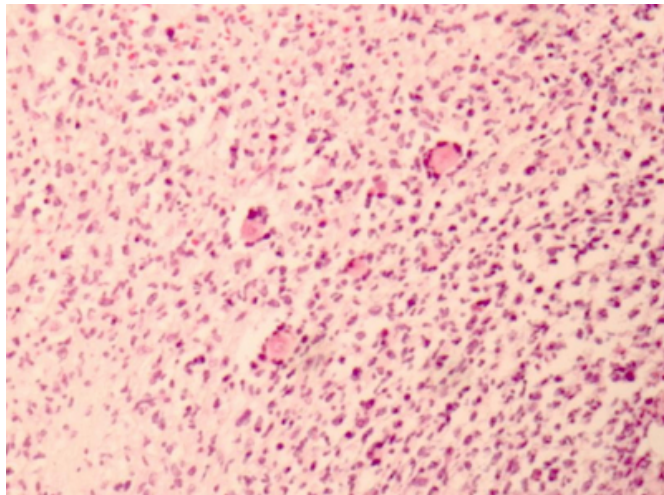
Figure 1: Ileoscopy showing discrete plaques and ulcers in the last cm of the terminal ileum.



Microscopic examination of the biopsy specimens taken from these lesions disclosed a dense cellular infiltrate composed of histiocytes with granular cytoplasm, containing round and targetoid bodies, stained positively for both periodic acid-Schiff (PAS) (Figure 2) and von Kossa's stains (Figure 3).

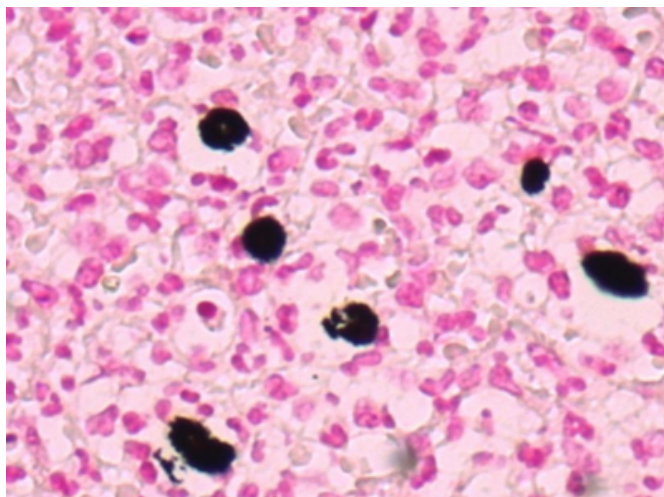
### Figure 2

Figure 2: Presence of multiple von Hanseman cells and Michaelis-Gutmann bodies in the ileum plaques biopsy (PAS stain, original magnification, x 100).



### Figure 3

Figure 3: Michaelis-Gutmann bodies are positive for calcium (von Kossa stain, original magnification, x 200).



Prussian blue stain for iron also highlighted these inclusions bodies. A Ziehl-Neelsen stain was negative. There was no evidence of *Yersinia enterocolitica* or *Yersinia pseudotuberculosis* in the specimens. A diagnosis of small bowel malakoplakia was established based on the presence of these von Hanseman cells and Michaelis-Gutmann

bodies.

Mercaptopurine treatment was stopped. Follow-up colonoscopy and abdominal computed tomography were normal, six months later. Ileoscopy showed partial regression of the ileal plaques; however no major histological improvement was manifest.

After a year with no immunosuppressive treatment, the patient started a trial of oral ciprofloxacin 500 mg twice daily and Vitamin C 1000 mg daily, both for three weeks. Significant endoscopic and histological improvements were evident on ileoscopy with follow-up biopsies.

As this patient has been asymptomatic during the follow-up period, no other antibiotic or surgical treatment has been suggested.

## DISCUSSION

The diagnosis of Malakoplakia is confirmed by the presence of von Hanseman histiocytes and Michaelis-Gutmann calcospherites. <sup>(1,2,3)</sup> Patients with gastrointestinal malakoplakia can be asymptomatic or present with fever, abdominal pain, diarrhea and hematochezia. <sup>(2,3)</sup> Several patterns of endoscopic presentation have been described, including diffuse colonic involvement with polyps or nodular lesions, large widespread masses and the classic focal mucosal plaques, <sup>(2,3)</sup> which in our case were concomitant with aphthous ulcers in the distal ileum. To the best of our knowledge, there have been only two reported cases of malakoplakia involvement of the small intestine. <sup>(4,5)</sup> While, both of them presented with a diffuse, transmural pattern and enterocutaneous fistulas, our patient was unique with an isolated mucosal prototype restricted to the last centimeters of the terminal ileum segment.

The etiology and pathogenesis of malakoplakia have been somewhat obscure since its original discovery. The most important implicated hypothesis is based on a defective immunoregulatory system, resulting in an impairment of mononuclear phagocytosis and lysosomal hydrolysis function. <sup>(2,3,6)</sup>

Hence, we suspect that mercaptopurine treatment was the most reasonable trigger for the development of this complication in our case. It is unclear what role Crohn's disease plays in the etiology of isolated terminal ileum malakoplakia in this patient, as it has been suggested that an abnormal mucosal immune system or specific defects in cellular immunity could be the basis for these disorders.

Since no association between both diseases has been documented to date, we would be hesitant to suggest it.

Our treatment strategy was based on anecdotal available reports since gastrointestinal malakoplakia is a quite rare disease. Because immunosuppression is one of the common associated factors to this situation, <sup>(6,7)</sup> mercaptopurine was stopped. The subsequent management was based on the reliable intracellular penetration of quinolones antibiotics into the macrophages and the hypothetic capability of ascorbic acid of improving the macrophage function by increasing the cyclic guanosine monophosphate. <sup>(8,9)</sup> Indeed, the withdrawal of mercaptopurine and prolonged ciprofloxacin and vitamin C treatment resulted in an endoscopic regression of this form of malakoplakia restrained to the terminal ileum.

In summary we have drawn attention to a novel association between Crohn's disease and malakoplakia confined to a rare location, in the setting of an asymptomatic patient. Follow-up colonoscopy revealed significant improvement with the above mentioned approach.

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