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MALAKOPLAKIA ASSOCIATED WITH DIARRHOEA AND COLONIC LESIONS AFTER RITUXIMAB TREATMENT

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ABSTRACT

Malakoplakia is a rare granulomatous condition that occurs due to defective lysosomal digestion during phagocytosis and can mimic inflammatory bowel disease (IBD) or malignancies, particularly in immunosuppressed patients. We report the case of a 62-year-old male with IgG4-related orbitopathy, who developed persistent diarrhoea and colonic lesions 6 weeks after receiving rituximab therapy for nephrotic syndrome secondary to membranoproliferative glomerulonephritis. Colonoscopy revealed pancolitis with mucosal granularity, loss of vascular pattern, and small nodules, raising initial suspicion for IBD. However, histological analysis of colonic biopsies confirmed malakoplakia with the presence of Michaelis-Gutmann bodies, pathognomonic for this condition. The patient was treated with ciprofloxacin for 2 weeks, and steroids were discontinued, leading to complete symptom resolution and significant histological improvement. During follow-up, the number and size of white lesions decreased, and no Michaelis-Gutmann bodies were detected. This case underscores the importance of maintaining a broad differential diagnosis for gastrointestinal lesions in immunosuppressed patients, as misdiagnosis can result in inappropriate escalation of immunosuppressive therapy. Recognizing the characteristic histopathology of malakoplakia and linking it with clinical findings are critical for timely diagnosis and effective management. This report adds to the limited literature on rituximab-associated malakoplakia, highlighting the unique challenges in its diagnosis and treatment.

KEYWORDS

Rituximab-associated colitis, malakoplakia, immunosuppression, diarrhoea, Michaelis-Gutmann bodies

LEARNING POINTS

- Malakoplakia, though rare, should be considered in immunosuppressed patients with atypical gastrointestinal lesions to prevent misdiagnosis as inflammatory bowel disease.
- Histopathological evidence, such as Michaelis-Gutmann bodies, is essential for diagnosing malakoplakia.
- Prompt discontinuation of immunosuppressants and targeted antibiotic therapy can lead to clinical and histological resolution.

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INTRODUCTION

Malakoplakia is a rare acquired granulomatous disorder characterized by defective lysosomal activity during phagocytosis, leading to the accumulation of macrophages with distinctive intracytoplasmic inclusions known as Michaelis-Gutmann bodies. Although it most commonly affects the urinary tract, malakoplakia can involve other organs, including the gastrointestinal tract, where it may mimic inflammatory bowel disease (IBD) or malignancies. This overlap poses significant diagnostic challenges, particularly in immunosuppressed patients. Immunosuppressive therapies, such as corticosteroids and biologics, have been implicated in predisposing patients to malakoplakia by impairing microbial clearance. Rituximab, an anti-CD20 monoclonal antibody, is increasingly used in autoimmune and lymphoproliferative disorders but has rarely been associated with gastrointestinal toxicities. Reports of rituximab-induced malakoplakia are exceedingly scarce, with only one prior case documented in the literature[1].

Here, we present the case of a 62-year-old male with IgG4-related disease treated with rituximab who developed persistent diarrhoea and colonic lesions that were ultimately diagnosed as malakoplakia. This case underscores the importance of considering malakoplakia in the differential diagnosis of gastrointestinal lesions in immunosuppressed patients. Early recognition and appropriate treatment, including targeted antibiotics, are essential to prevent unnecessary escalation of immunosuppressive therapy and achieve favourable clinical outcomes.

CASE DESCRIPTION

A 62-year-old man with a history of IgG4-related orbitopathy presented with persistent watery diarrhoea, producing five non-bloody stools daily for 2 weeks. He had been diagnosed with IgG4-related orbitopathy in 2021, for which he received corticosteroid therapy, initially at a higher dose, followed by maintenance therapy with 2-5 mg/day of prednisone. By November 2023, the patient developed renal insufficiency and nephrotic syndrome, with a serum IgG4 level of 5.15 g/l. A renal biopsy confirmed membranoproliferative glomerulonephritis. Due to the lack of improvement with corticosteroids, he was treated with rituximab (375 mg/m^2 weekly for 4 weeks) in January 2024, and his prednisone dose was tapered to 5 mg/day.

On physical examination, the patient's vital signs were within normal limits. There was no evidence of fever or abdominal tenderness. Laboratory investigations revealed an elevated C-reactive protein (CRP) of 80 mg/l, leukocytosis with a white blood cell count of 11.43 g/l (6.95 g/l neutrophils, 1.79 g/L lymphocytes), and a serum gamma globulin level of 6.8 g/l. Stool cultures were negative for bacterial pathogens, *Clostridium difficile* toxin, and parasites, including cryptosporidia and microsporidia.

A colonoscopy performed to investigate the diarrhoea showed pancolitis with complete loss of vascular pattern, mucosal granularity, and the presence of small nodules measuring 2 mm, as well as raised and flat white lesions with or without hyperaemic halos in the sigmoid colon *(Fig. 1)*. Biopsies revealed diffuse infiltration of the colonic mucosa by histiocytes containing intracytoplasmic inclusions. These inclusions were further characterized as Michaelis-Gutmann bodies using haematoxylin and eosin staining (H&E), confirming the diagnosis of malakoplakia *(Fig. 2)*. There was no evidence of cytomegalovirus infection or IgG4-positive plasma cells.

The patient was treated with ciprofloxacin 500 mg twice daily for 2 weeks, and prednisone was discontinued. By the 6-week follow-up, his diarrhoea had resolved completely, and his renal function and nephrotic syndrome had improved. Follow-up laboratory tests showed normalization of inflammatory markers, with CRP at 8 mg/l, serum gamma globulin at 4 g/l, and IgG4 at 0.59 g/l. A follow-up sigmoidoscopy revealed reduced inflammation, persistent granularity, and the absence of Michaelis-Gutmann bodies in repeat biopsies.

DISCUSSION

Malakoplakia is a rare granulomatous disease that predominantly affects immunocompromised individuals. The underlying pathophysiology involves defective lysosomal degradation during phagocytosis, leading to the accumulation of undigested microbial debris within macrophages. This results in the formation of Michaelis-Gutmann bodies, which are pathognomonic for malakoplakia and critical for its diagnosis. In malakoplakia gastrointestinal involvement is second most common after urinary tract involvement.

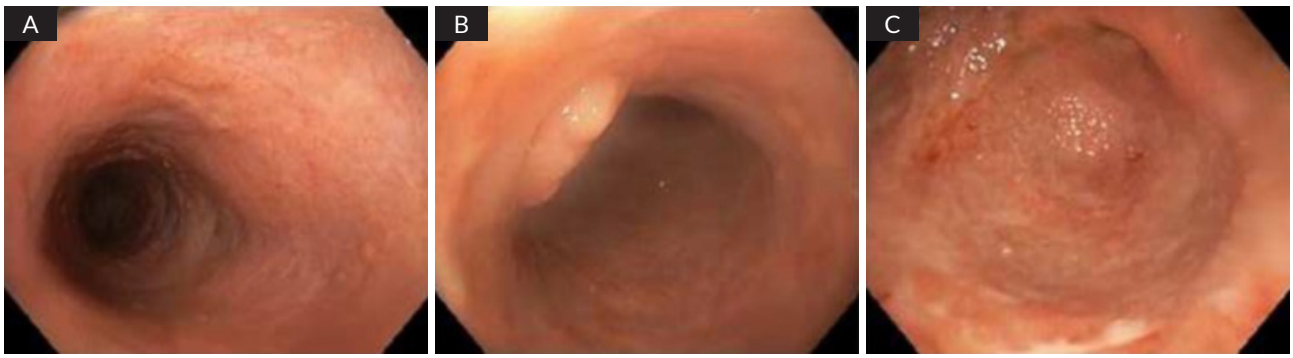


Figure 1. Endoscopic lesions observed during colonoscopy: A) Complete loss of the vascular pattern, mucosal granularity, small nodules (2 mm), B) Raised lesion and C) Flat white lesion with hyperaemic halo in the sigmoid colon.

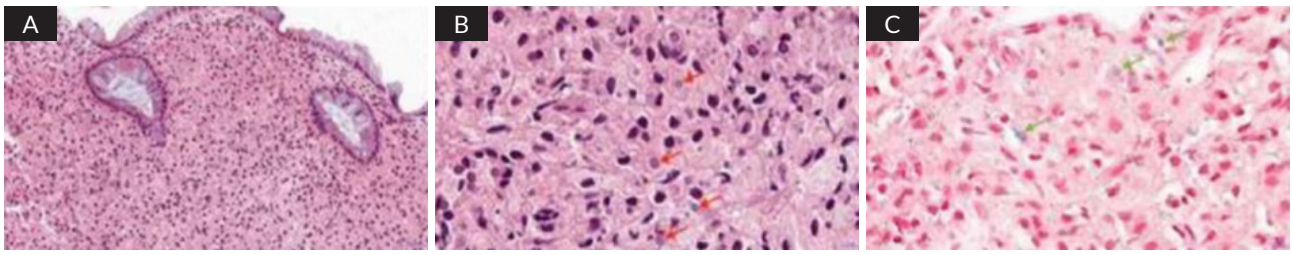


Figure 2. Histological findings of malakoplakia using H&E staining: A) Diffuse infiltration of the colonic mucosa by histiocytes; B) Presence of Michaelis-Gutmann bodies, seen as round, laminated structures with a central dark area, characteristic of malakoplakia; C) Higher magnification showing the intracellular localization of Michaelis-Gutmann bodies within histiocytes.

However, its clinical presentation often overlaps with more common conditions such as inflammatory bowel disease (IBD), malignancy, and infectious colitis, posing significant diagnostic challenges[1].

This case is notable for several reasons. First, the patient developed malakoplakia following rituximab therapy, which is rarely associated with gastrointestinal adverse effects. Rituximab targets CD20-positive B cells, impairing immune regulation and potentially increasing susceptibility to infections. Only one other case of rituximab-associated colonic malakoplakia has been documented[1], underscoring the rarity of this association and the need for increased clinical awareness.

Clinically, the patient's symptoms of persistent watery diarrhoea and the colonoscopic findings of pancolitis with nodular lesions mimicked IBD. The initial presentation could have led to inappropriate escalation of immunosuppressive therapy, which would have exacerbated the underlying condition. However, histological examination, revealing the hallmark Michaelis-Gutmann bodies, confirmed the diagnosis of malakoplakia[2]. This emphasizes the importance of biopsy and histological analysis in distinguishing malakoplakia from other gastrointestinal disorders.

Management of malakoplakia involves targeted antibiotic therapy, primarily with agents like ciprofloxacin or trimethoprim-sulfamethoxazole, which achieve high intracellular concentrations. In this case, a 2-week course of ciprofloxacin and the discontinuation of steroids resulted in symptom resolution and marked histological improvement. Follow-up sigmoidoscopy revealed reduced inflammation and the absence of Michaelis-Gutmann bodies, reflecting effective treatment. These findings highlight the importance of early diagnosis and appropriate therapy in achieving favourable clinical outcomes[3,4].

This case also highlights key considerations for clinicians managing immunosuppressed patients. The rarity of malakoplakia, combined with its clinical overlap with IBD and malignancies, necessitates a broad differential diagnosis for gastrointestinal lesions in this population. Failure to recognize malakoplakia can lead to over-treatment with immunosuppressants, worsening the condition and delaying recovery. By contrast, timely recognition and treatment with antibiotics can lead to resolution and avoid unnecessary complications[4,5].

Finally, this report adds to the limited literature on rituximab-associated gastrointestinal complications, particularly malakoplakia. It underscores the need for clinicians to remain vigilant for rare adverse events in patients receiving immunosuppressive therapy and highlights the value of multidisciplinary collaboration in managing complex cases. Further research is warranted to better understand the mechanisms underlying rituximab-associated malakoplakia and to guide optimal management strategies.

CONCLUSION

This case illustrates the importance of considering malakoplakia as a differential diagnosis in immunosuppressed patients with atypical gastrointestinal lesions. Prompt recognition through histological confirmation and appropriate treatment with targeted antibiotics can lead to favourable outcomes while avoiding unnecessary escalation of immunosuppressive therapy. Greater awareness of rituximab-associated gastrointestinal complications is essential for timely and effective patient care.

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