Response to Zhou et al.

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To the editor: We are grateful to Drs. Zhang, Wu, Zhou and Xu for their additional analysis of our data with their well-performed cumulative meta-analysis. With the findings that their analysis confirms our findings, particularly with regard to intestinal metaplasia and dysplasia, it helps us to reinforce the need for careful inspection and sampling of Barrett's mucosa before and early after radiofrequency ablation to rule out the presence of prevalent lesions. This cumulative analysis also notes, however, that clear proof that high grade dysplasia (HGD)/cancer detection within the first year of endoscopic therapy is not equal to or greater than that found in subsequent endoscopies is also important. Nevertheless, the practical point is that, even if the rates of developing HGD/cancer in the first year are close to that of subsequent years, it is more than enough reason to apply the principle that early and careful endoscopic follow-up after ablation is performed to find undetected advanced lesions. Whether our data and this additional analysis will lead to guideline changes merits further exploration.

CONFLICT OF INTEREST

Guarantor of the article: David A. Katzka, MD.

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Chronic Diarrhea Related to Colonic Malakoplakia Successfully Treated with Budesonide in a Kidney Transplant Recipient

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Dear Editor: A 51-year-old female was hospitalized because of chronic recurrent diarrhea with worsening symptoms. She described watery, bloodless diarrhea of 6–12 times per day for two months. The medical history revealed kidney transplant surgery that was performed eleven years earlier and accompanying hypertension. The medications used by the patient on admission were as follows: mycophenolate mofetil (1000 mg/day), tacrolimus (2 mg/day), prednisolone (5 mg/day), losartan (100 mg/day), carvedilol (12.5 mg/day), and lansoprazole (30 mg/day). The vital signs and systemic examination were normal. The laboratory investigations showed; Hemoglobin: 9 g/dL (normal range [NR]: 11.7–15.5), leukocyte: $4.8 \times 10^9/L$ (NR: 4.1–11.2), neutrophil: $3.2 \times 10^9/L$ (NR: 1.8–6.4), platelet: $203 \times 10^9/L$ (NR: 159–388), alanine-transaminase: 9 U/L (NR: 0–50), aspartate-transaminase: 9 U/L (NR: 0–50), creatinine: 1.9 mg/dL (NR: 0.6–1.1), albumin: 3.54 g/dL (NR: 3.5–5.2), C-reactive protein: 0.22 mg/dl (NR: 0–0.8), and fecal calprotectin: < 30 (NR: 0–30). No red blood

cells or polymorphonuclear leukocytes were seen in stool microscopy and the stool culture was negative as well as tests for clostridium difficile and celiac disease. The esophagogastroduodenoscopy was unremarkable except for mild gastritis. Colonoscopy revealed yellowish-white, flat elevated lesions with patchy involvement of the ascending colon (Fig. 1). The histopathological examination of the biopsy of the lesions was consistent with colonic malakoplakia (Fig. 2). In the random biopsies taken of normal-appearing mucosa of the ascending colon, descending colon and rectum, the absence of microscopic colitis or amyloidosis was documented in the histopathological examination. The immunosuppressive medications were modified (Mycophenolate mofetil was stopped, tacrolimus dose was decreased to 1 mg/day, and azathioprine 75 mg/day was initiated), but the diarrhea continued during the subsequent three weeks. Budesonide 9 mg/day was started for diarrhea and the tacrolimus dose was increased to 2 mg/day as ordered by the consultant nephrologist. At the end of the third week of budesonide treatment, the patient had improved dramatically and was symptom-free. Budesonide treatment was continued for three more months and then stopped gradually. The diarrhea symptoms did not recur during the nine-month follow-up after treatment cessation.

Malakoplakia is a chronic inflammatory disorder that can affect various parts of the body, including the urinary tract, gastrointestinal tract, lymph nodes, lung, brain, pancreas, bone, and skin. The gastrointestinal system is the second most common site of involvement of the disease after the urinary tract, and the colon and rectum are predominantly affected. Although the pathogenesis is not completely known, gram-negative bacterial infections, especially *Escherichia coli*, and altered inflammatory activation have been considered responsible in the disease etiology. Malakoplakia is usually encountered with comorbid conditions such as malignancies, organ transplantation, sarcoidosis, tuberculosis, liver diseases, ulcerative colitis, malnutrition, mycotic infections, and immunodeficiency syndromes [1, 2].

Fig. 1 **a, b** Yellowish-white, flat, elevated lesions (arrows) in the ascending colon. 119 × 50 mm (300 × 300 DPI)

Fig. 2 **a** Presence of solid sheets of histiocytes is noted in colonic mucosa. Histiocytes have granular or vacuolated eosinophilic cytoplasm so called as 'Hansemann cell'. A lymphoid aggregate is also seen nearby the lesion (H&E × 100). **b** Marked histiocytic infiltrate admixed with plasma cells, lymphocytes and neutrophils. Michaelis–Gutmann bodies (calcospherites) appears in the cytoplasm of histiocytes (H&E × 400). **c** Histiocytes (von Hansemann cells) with intra and extra cellular tiny basophilic targetoid inclusions (Michaelis–Gutmann bodies) (H&E × 1000). **d** Michaelis–Gutmann bodies (PAS staining). 105 × 104 mm (300 × 300 DPI)

The case is here reported of colonic malakoplakia in a kidney transplant recipient. There are very few reports in literature

of colonic malakoplakia in patients with renal transplantation [3, 4]. The major contributing factor for the development

of malakoplakia could be intense immunosuppressive agent use in this population. The patients can be asymptomatic

or present with fever, diarrhea, vomiting, abdominal pain, constipation, gastrointestinal bleeding, and intestinal obstruction. The diagnosis of colonic malakoplakia can be made from the observation of endoscopic lesions and histopathological examination. Colonoscopic findings may vary from yellowish-white mucosal plaques, as in the current case, to nodular, polypoid, ulcerated, or mass-like lesions. The presence of von Hansemann cells (clusters of histiocytes with abundant eosinophilic cytoplasm) and Michaelis–Gutmann bodies (intracytoplasmic basophilic calcified inclusions) are characteristic findings on histopathological examination [1–3]. Treatment options include the reduction of the immunosuppressive regime, and the use of cholinergic agonists such as bethanechol, and ascorbic acid to improve macrophage function. Long-term use of antibiotics (trimethoprim/sulphamethoxazole, ciprofloxacin, and rifampicin) have also been used with some success, as well as endoscopic or surgical excision of the lesion [1–5]. In the current patient, the diarrhea did not improve with the modification of immunosuppressive agents. Antibiotherapy was not initiated as antibiotics had been used for diarrhea (Metronidazole, ciprofloxacin, and rifaximin) several times before admission. However, the budesonide was used for three months and the diarrhea was completely resolved. To the best of our knowledge, this is the first report of the successful use of budesonide in the treatment of colonic malakoplakia. Budesonide is a synthetic glucocorticoid with local anti-inflammatory effects. The oral form of budesonide has a high first-pass effect with minimum systemic absorption that does not lead to systemic immunosuppression (Systemic immunosuppression is contributory factor for colonic malakoplakia). It converts the active drug form in the distal small intestine and proximal colon and the anti-inflammatory effects of budesonide are especially seen in these localizations [6]. Budesonide was used in the current case due to its local anti-inflammatory activity which may correct malakoplakia, which is related to altered inflammatory activation of the colon, without causing systemic immunosuppression. In addition,

the malakoplakia-related lesions in this case were on the ascending colon, where budesonide is known to have a higher anti-inflammatory effect.

In conclusion, colonic malakoplakia should be considered in the differential diagnosis of chronic diarrhea in immunocompromised patients such as renal transplant recipients and budesonide seems to be an effective treatment choice for this indication. However, further research is needed to clarify the effects of budesonide in the treatment of colonic malakoplakia.

Informed consent was obtained from the patient.

CONFLICT OF INTEREST

Guarantor of the article: Dr. Hayretdin Köklü, MD.

Specific author contributions: HK wrote the text and performed the endoscopic procedures. TK edited the manuscript and reviewed the literature. CS and EI performed the pathological procedures.

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Successful Long-term Treatment of Diversion Colitis with Topical Coconut Oil Application

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To the Editor: We report the case of a 32-year-old Caucasian female patient with fistulizing Crohn's disease complicated by diversion colitis.

Due to therapy-refractory perianal fistulae, diverting sigmoidostomy had been performed in early 2016. Initially, the patient reported good general condition under vedolizumab therapy, although the fistulae persisted. In late 2016, she noticed looser stools, progressive lower abdominal pain, and passage of mucus and blood via the anus.

Suspecting a manifestation of Crohn's disease, treatment was switched to ustekinumab and, due to non-response, intermittent topical hydrocortisone application was needed. Subsequently, combination therapy with infliximab and 6-mercaptopurin was initiated. Again, there were no signs of therapeutic efficacy as clinical disease activity persisted.

Endoscopically, mucosal inflammation was evident in the distal ostomy branch (Fig. 1a), while the proximal branch was unaffected. Histological evaluation revealed edematous mucosa with lymphoplasmacytic lamina propria infiltration and hyperplasia of local lymphatic tissue (Fig. 1b). Together, these findings indicated the presence of diversion colitis [1].

Reversal of sigmoidostomy was not a therapeutic option due to the persisting fistulae. Local therapy with 5-ASA