Colonic malakoplakia in a cardiac transplant recipient

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INTRODUCTION

Malakoplakia is derived from the Greek word “malakos” which means soft and “plax” meaning plaque. It was first described by Michaelis and Gutmann in 1902.[1] It is a rare chronic inflammatory disease associated with Gram-negative bacterial infection most frequently Escherichia coli.[2] It occurs most commonly in the genitourinary tract, but has been reported in the gastrointestinal tract,[3,4] the lung,[5] and skin.[6] Gastrointestinal malakoplakia is observed in association with a variety of conditions such as ulcerative colitis, diverticular disease, adenomatous polyp, carcinoma and immunodeficiency.[7] Malakoplakia has been rarely reported in the setting of liver and kidney transplantation.

CASE REPORT

A 38-year-old male had received a cardiac transplant 4 years previously for severe heart failure due to dilated cardiomyopathy. He had been on treatment with triple immunosuppression for 6 months with prednisolone, tacrolimus and mycophenolate, followed by dual immunosuppression with tacrolimus and CellCept. He was on regular follow up for 5 years until he presented with a 6 month history of diarrhea associated with fecal incontinence. Upper gastrointestinal endoscopy was normal and a deep duodenal biopsy done to exclude protozoal and helminthic infections was also normal. Ileocolonoscopic examination was done and the mucosa of ileum and colon were endoscopically normal. Rectal biopsies were taken to exclude microscopic pathology.

Gross examination showed three grey brown fragments of soft tissue each measuring 0.3 cm. Microscopy revealed an unremarkable epithelium. The lamina propria showed infiltration by histiocytes with granular eosinophilic cytoplasm admixed with a few lymphocytes and plasma cells [Figures 1 and 2]. Many histiocytes had several rounded basophilic structures of approximately 1 to 10 micron in size with the characteristic morphology of Michaelis-Gutmann bodies showing a laminated dense central core with a targetoid appearance [Figure 3]. These Michaelis-Gutmann bodies were diagnostic for malakoplakia. Although rare, malakoplakia may be associated with chronic diarrhea even if there are no macroscopic lesions seen during colonoscopy. The patient’s symptoms resolved with long-term ciprofloxacin therapy.

Key words: Cardiac transplantation, immunosuppression, malakoplakia, rectum

Malakoplakia is a rare inflammatory condition which is usually seen in the urogenital tract and less commonly in the gastrointestinal tract. Gastrointestinal malakoplakia may be associated with organ transplantation. There are previously only three reported cases of malakoplakia in cardiac transplant recipient. We report a case of colonic malakoplakia in a 38-year-old male who underwent cardiac transplantation for dilated cardiomyopathy 4 years previously and who had been on tacrolimus and mycophenolate. The patient presented with history of diarrhea associated with fecal incontinence for the past 6 months. Ileocolonoscopic examination was within normal limits. A rectal biopsy was done to exclude microscopic pathology. Microscopy revealed expansion of the lamina propria by histiocytes admixed with a few lymphocytes. The histiocytes showed granular eosinophilic cytoplasm with intracytoplasmic presence of Michaelis-Gutmann bodies, rounded basophilic laminated structures having central core with a targetoid appearance. These stained positively for Von kossa stain for calcium and were diagnostic for malakoplakia. Although rare, malakoplakia may be associated with chronic diarrhea even if there are no macroscopic lesions seen during colonoscopy. The patient’s symptoms resolved with long-term ciprofloxacin therapy.

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stained with Periodic acid Schiff’s stain (PAS) [Figure 4a] and were resistant to diastase (PAS-D). They also stained for calcium on Von kossa stain [Figure 4b]. There was no intranuclear cytoplasmic inclusion suggestive of viral cytopathy. Gram stain, acid fast stain and Perl’s Prussian blue stain for iron were all negative. A diagnosis of malakoplakia was considered and the patient was treated with ciprofloxacin. At review 1 month later the patient did not have diarrhea.

DISCUSSION

Malakoplakia is a chronic inflammatory disease frequently involving the genitourinary tract. The gastrointestinal tract is the second most commonly involved system by malakoplakia and in most cases the disease involves the colon and rectum. Colorectal malakoplakia was first described by Terner and Lattes in 1965.[8] Malakoplakia of the gastrointestinal tract may be clinically silent or may present with diarrhea, abdominal pain, hemorrhage and obstruction.[9] Malakoplakia has a distinct gross and microscopic appearance. Colonic involvement can be segmental or diffuse. In the early stages the lesions appear soft, flat and tan colored. Later they can develop into raised, tan grey and hyperemic lesions.[9] Three patterns of involvement have been identified: (1) Unifocal mucosal tan to yellow nodules or plaques (the most common), (2) multinodular polypoidal lesions or (3) large mass lesions.[10]

Histologically malakoplakia is characterized by aggregates of large histiocytes (known as Von Hansemann cells) with intracellular and extracellular inclusions known as Michaelis-Gutmann bodies which are phagolysosomes containing incompletely destroyed bacteria that have become encrusted with calcium and iron salts intermingled with lymphocytes and plasma cells and are diagnostic of malakoplakia. They vary in size from 2 to 10 micron and have a targetoid appearance due to concentric lamination and stain with PAS resistant to diastase and Von kossa (calcium). These findings are pathognomonic and establish the diagnosis of malakoplakia.[11]

Microscopically malakoplakia of the gastrointestinal tract must be differentiated from Whipple’s disease, tuberculosis especially atypical mycobacteria, other infectious and non-infectious granulomas and fungal infections especially histoplasmosis. The negativity for Gram stain, acid fast stain and fungal stain (GMS) ruled out the possibility of Whipples disease, atypical mycobacteriosis and fungal infection. The positivity for PAS, PAS diastase and Von kossa confirmed the
diagnosis of malakoplakia. Perl’s Prussian blue stain may show variable positivity.[23]

Escherichia coli is the most commonly associated bacterial pathogen and is found in over 90% of affected patients.[18] The likely mechanism of malakoplakia is defective lysosomal processing of microorganisms by macrophages with the accumulation of debris in lysosomes and subsequent mineralization. Abdou et al.[18] reported a patient with rectal and colonic malakoplakia and have documented that in such patients the monocytes had decreased bactericidal activity against E. coli, abnormally large lysosomal granules, low levels of cytoplasmic mononuclear cell phosphatase in mononuclear cells and poor release of beta glucuronidase in a bactericidal assay. Studies have suggested that decreased intracellular cytoplasmic mononuclear phosphatase level may interfere with adequate microtubular function and lysosomal activity leading to incomplete elimination of bacteria from macrophages and monocytes. The potential contributing factor is an impaired immune response (e.g., immunosuppression used to prevent rejection in organ transplant patients). Approximately 40% of malakoplakia involving the anatomic sites other than the urinary tract have been associated with immunosuppression.[14]

Malakoplakia of colon has been described in post transplant patients. Review of the literature revealed only four cases previously reported in kidney transplant recipients from 1994 to 2010.[15] Other transplant associated colonic malakoplakia included three cases with liver transplants[16] and three cases of colonic malakoplakia in cardiac transplant patients.[17] All patients in the reported cases presented with diarrhea, abdominal pain, fever and/or intestinal perforation. Colonoscopic examination revealed polyoid nodules, mass forming and depressed lesions, edematous mucosa with loss of vascular pattern and patchy erythema. Our case was unique in showing a normal colonoscopic mucosal examination.

Attempts at treatment of malakoplakia have included two main approaches, the administration of cholinergic agonist to improve the macrophage function and long term antibiotic therapy. A dramatic reduction of immunosuppressive medication is often a necessary component of medical treatment of malakoplakia in this setting.[6] We present this case to sensitize readers to the possibility of malakoplakia as a cause of post-transplant diarrhea even if the mucosal appearance is normal.

CONCLUSION

Malakoplakia is a rare chronic inflammatory disease that occurs in a variety of anatomic sites. Only a few cases of colonic malakoplakia have been reported in patients in association with organ transplantation and with varied appearances on colonoscopy. Our case is unique in its presentation in view of its normal colonoscopic examination. Although rare, malakoplakia is one of the potential causes of diarrhea in patients with organ transplantation. It is a benign self limited condition that responds to antibiotic therapy and to reduction of immunosuppression. Our case may serve as a reminder of the clinical significance of malakoplakia with a normal colonoscopic pattern in a cardiac transplant patient.

REFERENCES


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