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Esophageal Mucosal Calcinosis: A Rare Site of Gastrointestinal Mucosal Calcinosis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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None declared

Patient: Male, 68
Final Diagnosis: Esophageal mucosal calcinosis
Symptoms: Dysphagia
Medication: —
Clinical Procedure: Esophagogastroduodenoscopy
Specialty: Gastroenterology and Hepatology

Objective: Rare co-existence of disease or pathology
Background: Gastrointestinal tract mucosal calcinosis (MC) tends to affect the gastric mucosa, while esophageal involvement is rare. Gastric MC may be seen with solid organ transplantation, use of aluminum-containing antacids or sucralfate, malignancy, and chronic renal failure. While the incidence of gastric MC in renal transplant patients undergoing gastric biopsy is common (between 15–29%), to our knowledge esophageal MC has only been previously reported 3 times.
Case Report: A 68-year-old male dialysis-dependent end stage renal disease status-post deceased donor kidney transplant underwent an esophagogastroduodenoscopy (EGD) for dysphagia and diffuse esophageal wall thickening seen on imaging studies. EGD demonstrated diffuse, circumferential thick white esophageal plaques and mucosal friability. Esophageal biopsies demonstrated erosive esophagitis with basophilic calcium deposits within the fibrinopurulent exudate and squamous mucosa. Stains for fungal organisms and viruses were negative. A diagnosis of esophageal MC was made. Although the patient had a protracted postoperative course after transplantation, he had improvement of the esophageal wall thickening on imaging after transplantation.
Conclusions: Esophageal MC is a rare phenomenon and all of the previously reported cases of esophageal MC, including our case, have been in patients with end stage renal disease who were on dialysis. Although prolonged hypercalcemia and hyperphosphatemia, an elevated calcium-phosphorus product, and associated underlying inflammation are likely key etiologic factors, the pathogenesis of esophageal MC is not fully understood and is likely due to multiple collective etiologies. Likewise, more reported cases are likely to increase our understanding of the clinical significance and management of this rare disorder.

MeSH Keywords: Calcinosis • Calciophylaxis • Esophageal Diseases

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Background

When mucosal calcinosis (MC) occurs in the gastrointestinal tract it most commonly affects the gastric mucosa, while esophageal involvement is rare [1–7]. There are numerous associated conditions identified for gastric MC including solid organ transplantation, use of aluminum-containing antacids or sucralfate, malignancy, and chronic renal failure. Rarely some cases of gastric MC may be idiopathic in etiology [1–7]. The reported cases of esophageal MC have been in patients with similar associated conditions, especially end stage renal disease which was present in all 3 previously reported cases [4–6]. The reported incidence of gastric MC in renal transplant patients undergoing gastric biopsy is relatively high (between 15–29%) [2,3] but esophageal MC has only been previously reported 3 times [4–6]. The most common presenting symptom of esophageal MC appears to be dysphagia. It may also be a rare cause of an episode of upper gastrointestinal tract bleeding [4–6]. Given the limited experience with this disease, the treatment is not entirely clear; however, some of the reported cases have utilized intravenous sodium thiosulfate in an attempt to improve the condition [4–6].

Case Report

A 68-year-old male with dialysis-dependent end stage renal disease due to type 2 diabetes mellitus recently status-post deceased donor kidney transplant underwent an esophagogastroduodenoscopy (EGD) for dysphagia and diffuse esophageal wall thickening seen on computed tomography (CT) scan (Figure 1). Prior to transplantation, the patient had been dialysis dependent for 5 years (hemodialysis). EGD demonstrated diffuse,

Figure 1. Endoscopic photo demonstrating white plaques in the esophagus.

Figure 2. Esophageal wall thickening on CT scan.

Figure 3. Biopsies demonstrating ulcerated and active esophagitis with basophilic calcium deposits within the squamous mucosa and fibrinopurulent exudate (H&E, original magnification 100×).

circumferential thick white esophageal plaques (Figure 2) and mucosal friability. Esophageal biopsies demonstrated erosive esophagitis with active (neutrophilic) inflammation and fragments of fibrinopurulent debris. There were extensive basophilic deposits within the squamous mucosa and fibrinopurulent debris (Figure 3). A stain for fungal organisms (Gomori methenamine silver) and immunohistochemical stains for herpes simplex virus and cytomegalovirus were all negative. A von Kossa stain for calcium was positive highlighting the basophilic deposits within the squamous mucosa and the fibrinopurulent exudate, confirming that the mucosal deposits were calcium (Figure 4). Review of medications revealed use of sucralfate and the patient was noted to have an elevated calcium-phosphorus product. The patient had a prolonged hospital course after transplantation and was ultimately discharged home. There was some improvement in the esophageal wall thickening seen on CT scan but not complete resolution. The

Figure 4. Von Kossa stain demonstrating numerous black calcium deposits within the squamous mucosa and fibrinopurulent exudate (von Kossa stain, original magnification 200×).

patient was alive 12 months post diagnosis of esophageal MC and his calcium and phosphorus levels normalized after transplantation. He did not receive specific pharmacotherapeutic interventions (i.e., sodium thiosulfate) targeting solely the esophageal MC while hospitalized.

Discussion

Gastrointestinal tract mucosal calcinosis (MC) may be dystrophic, metastatic, iatrogenic, or idiopathic in etiology. The most frequent of these is metastatic calcification in normal tissue secondary to hypercalcemia or hyperphosphatemia. Dystrophic calcification refers to calcium deposition in damaged tissues without hypercalcemia or hyperphosphatemia. Iatrogenic calcification occurs secondary to pharmacotherapeutic intervention (i.e., sucralfate or calcium therapy). Idiopathic calcification occurs in normal tissues without hypercalcemia or hyperphosphatemia [1,5]. Rarely, gastric MC has been reported without an associated condition in which case it may be considered idiopathic in etiology [7]. MC may be secondary to multiple factors including renal transplantation, sucralfate therapy, an elevated calcium-phosphorus product, and/or dystrophic calcification in inflamed/eroded mucosa [1–5]. All of the reported cases of esophageal MC, including our case, have been in patients with end stage renal disease and it seems that the most important etiologic factor in these cases was hypercalcemia or hyperphosphatemia in renal disease (i.e., metastatic calcification) [4–6].

Of the few reported cases, esophageal MC typically presents most commonly with dysphagia and/or upper gastrointestinal tract bleeding [4–6]. The endoscopic findings range from plaque-like areas to nodules and/or ulceration, similar to our

case which demonstrated diffuse white plaque-like areas and ulceration [4–6]. Endoscopically, these deposits may resemble candidiasis or eosinophilic abscesses [1]. Histologically, there are basophilic intraepithelial deposits of calcium within the squamous mucosa often associated with erosions/ulcerated mucosa. There is also associated active (neutrophilic) inflammation in the squamous mucosa [5]. The calcium deposits are positive on von Kossa stain. The histologic differential diagnosis mainly includes other mucosal deposits especially iron deposition. Iron deposits tend to be yellow-brown in color and will be positive on iron staining. Another consideration, particularly in renal failure patients, is sevelamer or kayexalate crystal deposition. Sevelamer is an ion exchange resin used to lower phosphate levels in chronic kidney disease. Histologically, the crystals demonstrate a broad, curved “fish scale” appearance and usually a 2-toned bright pink and rusty yellow background appearance. Kayexalate is another ion exchange resin used to lower potassium levels in chronic kidney disease. Kayexalate crystals demonstrate a narrower “fish scale” pattern and the crystals are violet on hematoxylin and eosin stained slides [8].

In all 3 of the previously reported cases of esophageal MC, the patients also had calcific uremic arteriolopathy (CUA) or calciphylaxis which has a mortality rate approaching 60–80% and in 2 of these cases the patients died [4–6]. The patient in the current case did not have evidence of calciphylaxis. Calciphylaxis is usually associated with painful, violaceous skin lesions and has only rarely been reported in the gastrointestinal tract, once in the rectum and twice in the esophagus [5,6,9]. Histologically, there is concentric calcification of vessel walls [5,6,9]. Therefore, if esophageal MC is associated with calciphylaxis, it may be a harbinger of a poor outcome. Attempts to treat the dysphagia and esophageal calcium deposits with intravenous sodium thiosulfate do not appear to alter the esophageal deposits, the endoscopic findings, or, in the cases with calciphylaxis, the course of the disease [4–6]. Currently the appropriate treatment of esophageal MC is unclear and there is no definitive pharmacotherapeutic management that appears to clear or lessen the calcium deposits within the esophageal mucosa [4–6]. However, in one of the reported cases there was “modest improvement” in symptoms with the use of sodium thiosulfate and cinacalcet (a calcium mimetic agent) [4].

Conclusions

In summary, esophageal MC is a rare phenomenon or at least the paucity of reports in the literature would suggest as much. Gastrointestinal tract MC may be associated with numerous conditions and the etiology and the pathogenesis is likely multifactorial. From the cases in the literature and our current case, it appears that dialysis-dependent end stage renal disease is

the largest risk factor for esophageal MC. More reported cases are needed to truly understand the etiology, treatment, and outcome of esophageal MC.

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Conflict of interest

None.