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CASE REPORT | SMALL BOWEL

Cholesterol Crystal Embolization to the Kidney and to a Duodenal Leiomyoma

Alexander M. Sy, MD[1], Jogarao Vedula, MD[2], Iman Hanna, MD[2], Bhawna Halwan, MD[1], and Patrick Saitta, MD[1]

[1]*Division of Gastroenterology Hepatology and Nutrition, NYU-Winthrop Hospital, Mineola, NY*
[2]*Department of Pathology, NYU-Winthrop Hospital, Mineola, NY*

ABSTRACT

Cholesterol crystal embolism can be spontaneous or iatrogenic, and it can involve any organ of the gastrointestinal tract, presenting with common gastrointestinal symptoms such as bleeding, perforation, obstruction, and inflammation. It is therefore considered the "great masquerader," requiring a high level of suspicion because the condition is associated with increased morbidity and mortality. We present a 69-year-old man who presented with gastrointestinal bleeding and azotemia. He was found to have cholesterol crystal embolization in the kidney and a duodenal leiomyoma, the latter being an uncommon site to embolize.

INTRODUCTION

Cholesterol crystal embolism (CCE) is a condition resulting from a plaque rupture with the release of cholesterol crystals into circulation, which then embolizes in various tissue organs. Involvement of the gastrointestinal (GI) tract can lead to GI bleeding, obstruction, inflammation, and perforation. These protean presentations often mimic other diseases, leading to difficulties and delays in diagnosis, unnecessary diagnostic tests, and suboptimal therapy. For these reasons, CCE has been dubbed the "great masquerader."

CASE REPORT

A 69-year-old man with coronary artery disease, hypertension, gastroesophageal reflux disease, and hyperlipidemia came to the hospital complaining of a 4-day history of melena accompanied by near syncope and exertional dyspnea. He denied abdominal pain, nausea, and vomiting. Two months prior, the patient underwent coronary angioplasty and triple-vessel coronary artery bypass graft. His medications included aspirin, clopidogrel, atorvastatin, metoprolol, amlodipine, and omeprazole. He smoked 2 packs of cigarettes per day for more than 30 years and only stopped after his heart surgery. His blood pressure was 189/90 mm Hg, heart rate 88 beats per minute, respiratory rate 18 breaths per minute, temperature 98.4°F, and oxygen saturation 99% on room air. Physical examination revealed pale palpebral conjunctiva and a healed anterior chest wall scar. The rest of the examinations were unremarkable. Pertinent laboratory results in the emergency department revealed hemoglobin 5.6 g/dL, hematocrit 17.6%, sera blood urea nitrogen (BUN) 67 mg/dL, and creatinine 3.3 mg/dL. His baseline laboratories 2 months prior were hemoglobin 10.7 g/dL, hematocrit 30%, serum BUN 30 mg/dL, and serum creatinine 1.4 mg/dL.

In the emergency department, the patient was started on pantoprazole drip, and a unit of packed red blood cells was transfused. Initial impression was upper GI bleeding, likely due to an ulcer caused by nonsteroidal anti-inflammatory drug use. After stabilization of his hemodynamics, an esophagogastroduodenoscopy revealed a large, subepithelial mass lesion with an ulcerated center arising from the second portion of the duodenum just opposite the

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Correspondence: Alexander M. Sy, MD, Division of Gastroenterology, Hepatology and Nutrition, NYU-Winthrop Hospital, 259 First St, Mineola, New York 11501 (asy@nyuwinthrop.org).

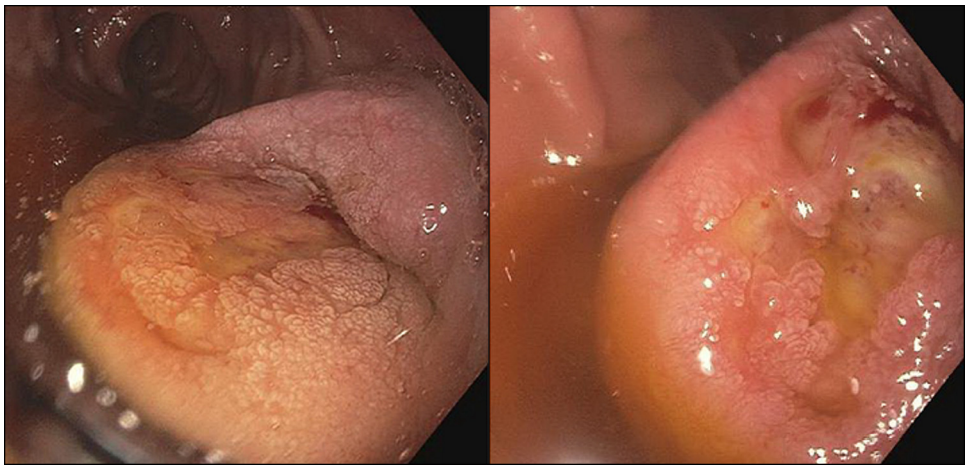

Figure 1. A large, subepithelial mass lesion with an ulcerated center arising from the second portion of the duodenum just opposite the normal-appearing major papilla.

normal-appearing major papilla (Figure 1). Endoscopic ultrasound revealed an exophytic solid mass arising from the muscularis propria of the duodenum (Figure 2). Fine-needle aspiration biopsy revealed a spindle-cell neoplasm. Immunohistochemical stains were positive for smooth muscle actin and desmin, compatible with leiomyoma. The patient's hemoglobin was maintained at 9 g/dL after transfusion of 3 units of packed red cells. A pancreaticoduodenectomy was deferred due to increasing serum creatinine, with a peak value of 5.4 mg/dL despite adequate hydration. Work-up for the acute kidney injury did not show any etiology, and a renal biopsy revealed multiple intraluminal clefts and spaces within the glomerulus consistent with an atheroemboli, indicative of renal atheroembolic disease (Figure 3). The cardiology department recommended controlling the patient's metabolic risk factors. His creatinine eventually stabilized, and surgery was performed.

An open exploration confirmed the large tumor to be mostly exophytic to the duodenum and was easily identifiable and mobilized. A local excision was carried out. Gross pathology revealed a tan-pink irregular ovoid mass measuring 9 cm in its greatest dimension, with a smooth serosal surface, prominent vasculature, and a 2.5 × 1.5 cm central ulcer (Figure 4). Microscopic examination revealed spindle-cell neoplasm with no cytologic atypia or mitosis; however, there were atherosclerotic changes of large submucosal blood vessels with multiple intraluminal clefts and spaces consistent with atheroemboli (Figure 5). Immunostaining was consistent with leiomyoma. This was officially signed out as leiomyoma, atherosclerotic changes of large submucosal blood vessels with cholesterol emboli. The patient's postoperative course was uncomplicated, and upon discharge his hemoglobin was 9.7 g/dL and hematocrit 29.7%. Unfortunately, his renal

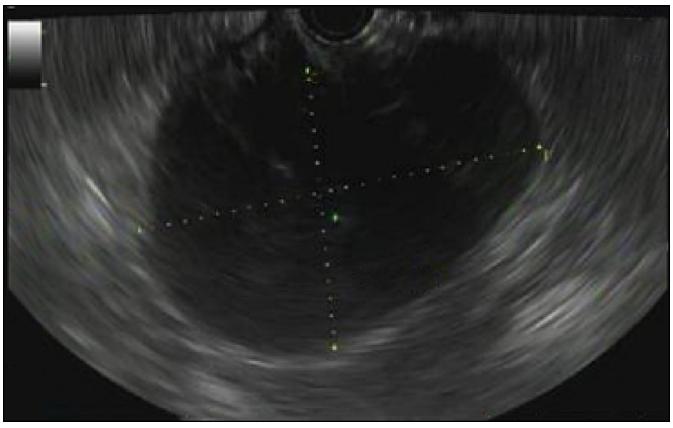

Figure 2. An exophytic solid mass measuring 8 × 5 cm arising from the muscularis propia of the duodenum.

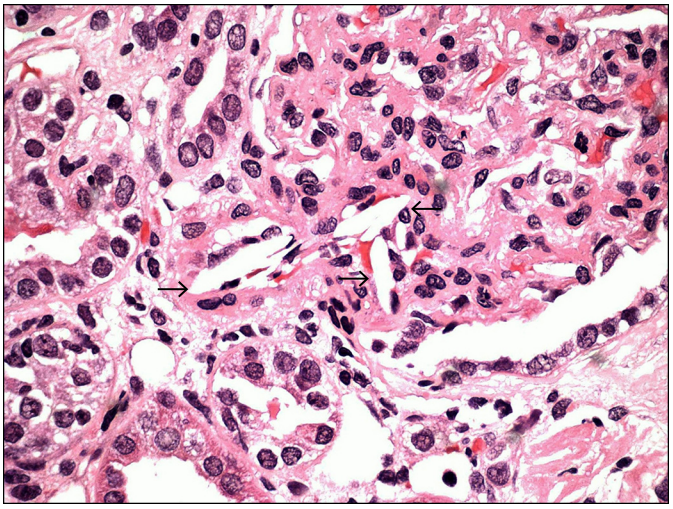

Figure 3. Renal biopsy showing multiple intraluminal clefts and spaces within the glomerulus (arrows) consistent with an atheroemboli and indicative of renal atheroembolic disease.

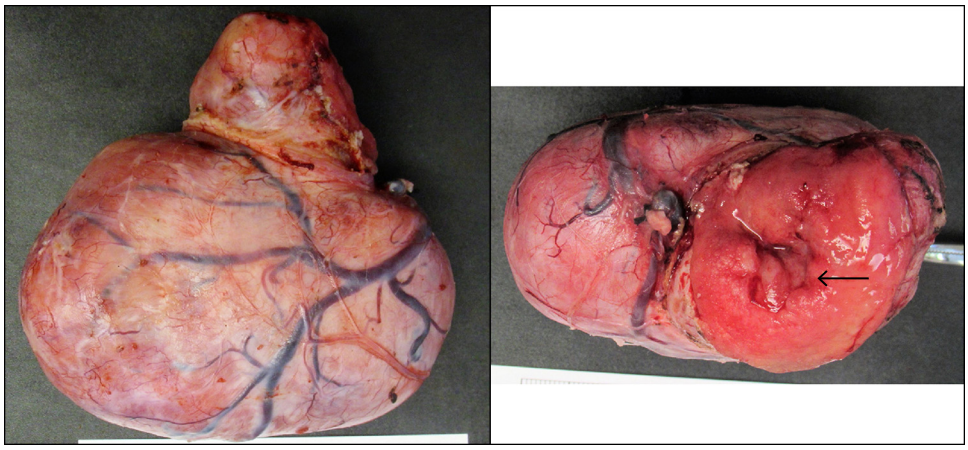

Figure 4. Gross pathology showing an irregular ovoid mass measuring 9 cm in its greatest dimension, with a smooth serosal surface, prominent vasculature, and a 2.5 × 1.5 cm central ulcer (arrow).

function did not return to baseline, and upon discharge his serum BUN and creatinine were 79 mg/dL and 3.4 mg/dL, respectively.

DISCUSSION

The terms atheroembolism and CCE are frequently used synonymously. It was first recognized in 1862 by Dr. Peter Ludwig Panum, a Danish pathologist, who observed needle-shaped lacunae in the lumen of arterioles in histological sections.[1] Curtis M Flory in 1945 was able to reproduce this phenomenon experimentally and concluded that eroded atheroma was the source of emboli.[2] Microscopically, the cholesterol crystals are dissolved during the histotechnical procedure, leaving the pathognomonic needle-shaped lacunae in the lumen of arterioles in the histological sections. CCE has been estimated to have an incidence of 1.4% after coronary catheterization, and the frequency of embolization to the GI system in an autopsy study done by Moolennar and Lamers was estimated to be 0.046%.[3,4] The true incidence may be higher, however, because it may be underreported due to its protean manifestations mimicking other diseases, which can obscure the diagnosis.[5]

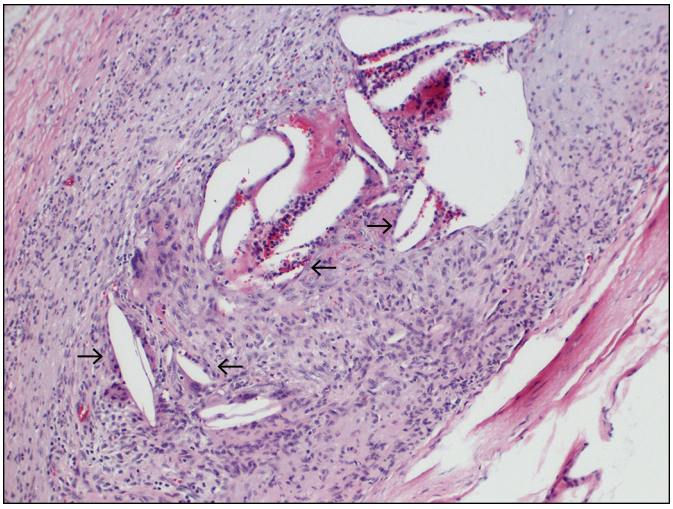

Figure 5. Microscopic examination showing atherosclerotic changes of large submucosal blood vessels with multiple intraluminal clefts and spaces (arrows) consistent with atheroemboli (40× magnification).

CCE can be spontaneous or iatrogenic, precipitated by vascular manipulation during arteriography or surgery. The risk of cholesterol crystal formation is directly related to the severity of risk factors for atherosclerosis, such as smoking, hypercholesterolemia, hypertension, obesity, and diabetes. Risk factors for embolization include presence of abdominal aortic aneurysm, vascular instrumentation, anticoagulation, and thrombolytic therapy. Embolization can occur in any organ. The skin and kidneys are the most common organs involved, presenting as livedo reticularis and worsening azotemia. These abnormalities can appear weeks to months after the initial embolic event.[6,7] In the GI system, the colon and small bowel are the organs most commonly affected, likely due to the rich blood supply directly from the aorta. Embolization can present as ileus, abdominal pain, diarrhea, GI bleeding, obstruction, and perforation.[4] These GI presentations can manifest as acute catastrophic multi-organ failure like infarction, obstruction, and perforation, or as more indolent or chronic complaints such as abdominal pain, diarrhea, and bleeding. It is believed that these different clinical presentations are related to the variability in the size and number of emboli, the degree of occlusion of the blood vessels, and the extent of the inflammatory response and subsequent obliteration of the arterial blood supply.[8] CCE is also known to mimic other diseases such as pancreatic mass, acute cholecystitis, and pseudomembranous colitis.[9-11] CCE to a primary neoplasm in the small bowel has not been described previously, probably due to the unusual and low incidence of primary neoplasms of the small bowel. Leiomyoma is the most common benign tumor of the small bowel, typically found in

the jejunum, followed by the ileum; its occurrence in the duodenum is rare.[12] Most of these lesions are small and asymptomatic, and they are often discovered incidentally during endoscopy or autopsy. Occasionally, these benign tumors will present with abdominal pain, spontaneous GI bleed, obstruction, or perforation. It is difficult to differentiate spontaneous bleeding due to leiomyoma from bleeding due to CCE.

The diagnosis of CCE requires a high index of suspicion of the condition. Laboratory findings are not specific, and noninvasive testing with available imaging may be inadequate for diagnosis. Histological findings of needle-shaped lacunae in the lumen of arterioles are necessary for a definitive diagnosis.

Treatment for CCE involves supportive therapy by managing cardiovascular risk factors, management of end-organ ischemia, and prevention of recurrent embolization. Anticoagulation therapy for the treatment of CCE remains controversial, and steroid therapy is not routinely advocated. The prognosis in medically treated patients with CCE is poor, in part because of severe underlying atherosclerosis. In-hospital mortality ranges between 5% and 16%, but overall mortality rates may be as high as 80% when cases diagnosed postmortem are included.[13] Thus, CCE should be part of the differential diagnosis in patients with vascular intervention within weeks or months prior to presenting with GI bleeding and worsening renal failure, because the symptoms of CCE can often be delayed.

DISCLOSURES

Author contributions: All authors contributed equally to the manuscript. AM Sy is the article guarantor.

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