Cholesterol Embolism Causing Bleeding Gastric Ulcers*

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ABSTRACT

Two cases of atheromatous embolism of the small arteries of the stomach are reported. Insofar as has been ascertained, they are the first reported cases in the literature which presented symptoms of severe gastric bleeding and were found to have bleeding gastric ulcers on endoscopy. Both patients were successfully treated surgically, and their ulcers were found to be secondary to small arteriolar occlusions owing the atherosclerotic embolization. Awareness of clinicians as well as pathologists of this phenomenon in elderly males with symptoms of abdominal pain and other upper gastrointestinal symptoms unrelated to the ingestion of food is stressed. Pathophysiology of atherosclerotic emboli is also discussed.

Introduction

Protruding ulcerated atheromatous plaques of the large arteries are common autopsy findings; however, embolization of the fragments of atheroma occurring either spontaneously or following surgical manipulation is uncommon.

Involvement of the gastrointestinal tract has been mentioned infrequently, and demonstration of atheromatous emboli in gastric ulcers is even less common. There are two cases reported by Taylor in which the association of gastric ulcers with atheromatous emboli is mentioned. The first patient had a three year history of periumbilical non-radiating pain associated with nausea, which was unrelated to the ingestion of meals. Eventually, protracted bleeding developed and the patient died owing to shock. At autopsy, cholesterol emboli accompanied superficial hemorrhagic erosions in the gastrointestinal wall. The second patient was clinically asymptomatic and died owing to cerebral infarction. Upon autopsy, stomach ulcers were an incidental finding. Following microscopic examination, cholesterol emboli were found in the stomach, appendix, kidney, pancreas, and spleen. Bourdages et al reported another case of atheromatous embolization in a patient with upper gastrointestinal bleeding; however, there was no gross evidence of ulcers present in the stomach. Finally, in patients with...
Clinical peptic gastric ulcer, atheromatous embolization has never been documented.

Thus, this is the first report, as far as the present authors can ascertain, of clinical endoscopic and pathologic correlation in two patients with symptoms of gastric ulcer who were found to have extensive atheromatous embolization in surgical specimens and biopsies. The atheromatous emboli were determined to be the cause of the ulcers and the bleeding. Both cases were successfully treated by surgical intervention.

Case Reports

Case 1

A 77-year-old white male was admitted for vomiting a "large amount" of bloody-black material. He was well until six months prior to admission when he was hospitalized with an acute inferior wall myocardial infarction. He did well in the post infarction period and remained well until four days prior to admission, when he first noted mild nausea. Nausea remained intermittent over the next several days until the hematemesis started. Prior to this admission, he had no gastrointestinal symptoms.

Physical examination on admission was remarkable for a soft, non-tender abdomen with active bowel sounds, heme-positive stool, and good peripheral pulses. Laboratory data obtained upon admission were significant for a hemoglobin of 9.8; hematocrit, 29.7; white blood cells, 14,000 per cubic mm; and normal platelets.

An endoscopy was performed on admission which revealed a large clot on the greater curvature of the stomach and a serpiginous ulcer on the posterior wall in the midbody measuring two cm in greatest diameter. Red irregular folds were seen around the ulcer which was bleeding slowly. Duodenum and esophagus were normal.

A similar second ulcer was discovered in endoscopy several days later. Multiple biopsies were taken.

Several days after the biopsy, the patient had another episode of hematemesis and melena. He was taken to the operating room where two-thirds of his stomach was resected with a Billroth I anastomosis. The patient did well postoperatively.

Case 2

A 75-year-old white female was admitted to the hospital with a one to two day history of fever, rigors, and general malaise. The present illness began with a sore throat and flu-like symptoms. Three days prior to admission, she developed watery diarrhea without any blood. She complained of a non-productive cough, myalgia, and arthralgias especially involving the knees and small joints of the hands. The patient was diabetic and had a past medical history of hypertension which was treated. Peripheral vascular disease with intermittent claudication was diagnosed five years earlier; however, no operative intervention was considered necessary at that time. Three years later, an x-ray of the abdomen revealed extensive atherosclerotic disease of the aorta without aneurysm. Compression fracture of D-11 vertebra was also noted.

Initial laboratory data revealed a hemoglobin of 12.4 g; hematocrit, 32; white blood cells, 24,000 per cubic mm; erythrocyte sedimentation rate, 96; blood-urea nitrogen (BUN) 58; blood sugar, 266; creatinine, 3.5; calcium, 9.0; and magnesium, 2.1. At the time of admission, the patient was febrile with a temperature of 101°F. Blood pressure was normal, and physical examination showed no significant abnormalities. With a history of sore throat and fever, the patient was treated with antibiotics.

On the second day of admission, the patient suddenly became hypotensive, and her fever rose to 104°F. The results of the blood culture revealed beta hemolytic streptococcus Group A, which was treated with penicillin. She remained hypotensive and had to be maintained on Levophed®. Her renal function remained poor with high BUN and creatinine and low urinary output. Five days after admission, she started to have blood in her stools. At that point, an endoscopy revealed stress-type ulcers in the proximal half of the stomach and fresh blood in the stomach. In spite of Levophed® lavages and blood replacement, the patient continued to bleed heavily from the N-G tube and had to be taken to surgery. A total gastrectomy was performed and a Hunt-Lawrence jejunal pouch was created.

Pathologic Findings:

Both cases showed identical findings. There were multiple superficial ulcers in the anterior and posterior walls of stomach. The largest ulcer was three cm in greater dimension and belonged to the case 2. Microscopically, the ulcers penetrated the submucosa and resembled peptic ulcer disease with the exception of marked regenerative activity of the adjacent mucosa and presence of numerous atheromatous emboli in the arteries and arterioles in and around the ulcer bed in the submucosa (figure 1). The atheromatous emboli were characterized by cholesterol clefts and secondary fibrin thrombosis (figure 2). Of interest
Figure 1. Low power view of an ulcer bed showing clusters of atheromatous emboli in small arteries and arterioles.

Figure 2. High power view of an atheromatous embolus characterized by the presence of cholesterol crystals and intervening secondary fibrin.

Figure 3. The mucosal biopsy specimen from edge of an ulcer shows atheromatous embolus in an arteriole within the mucosa. Notice regenerative activity and dilatation of the crypts of the surrounding glands.
was the presence of occasional mucosal atheromatous emboli which were discovered both in the biopsy specimens and the remaining mucosa in the gastrectomy specimen (figure 3). The mucosa of the stomach showed foci of coagulative necrosis which were interpreted to be the early infarcts preceding ulceration. Adjacent uninfarcted mucosa often showed florid regenerative activity, dilation of some of the glands and crypt abscess.

Since clusters of atheromatous emboli were present involving almost exclusively small arteries and arterioles (figure 1), it was postulated that they were caused by a shower of microscopic fragments of atheromatous plaques arising from one of the proximal main arteries such as the aorta.

Discussion

Historically, Panum in 1862 and Flory in 1945 are the original investigators who pointed out the significance of the atheromatous embolization as a cause of ischemic damage in various organs. Subsequently, cholesterol embolization was reported in almost every organ. Flory observed nine instances of vascular occlusion owing to atheromatous emboli among 267 autopsies who had advanced atherosclerosis of the aorta. Thurlbeck and Castleman found a higher incidence of 15 percent of spontaneous embolization in 38 cases of severe atherosclerosis. Subsequently, the literature contained only isolated reports of similar occurrences. In these reports the kidney, pancreas, and spleen were the structures most frequently involved. Rarely had “spontaneous embolization” been reported involving the gastrointestinal tract and, in particular, the stomach. The first report appeared in Thulbeck and Castleman’s article in 1957. In this report, the clinical significance of such involvement is not mentioned. Winter, for the first time, observed an ulcerated lesion in the duodenum and suggested that atheromatous emboli should be considered as a possible cause of peptic ulcers. Goul and cohorts noticed “an area of sclerosis and atrophy in the wall of the pylorus, where the muscular coats had disappeared and had been replaced by fibrosis.” This area corresponded to the area described as an ulcer by the radiologist years previously. The small arterial branches supplying that part of the stomach wall were considered to be the site of an old atheromatous embolus. Finally, Taylor, Gueff, and Lebowich reported two postmortem cases of atheromatous embolization to the gastrointestinal tract—one of which showed gastric ulcer.

Careful review of the literature shows no cases of the atheromatous emboli causing bleeding gastric ulcer which were endoscopically diagnosed and successfully treated. Such a report is significant both for the clinicians and pathologists. Clinically, intermittent atheromatous embolization should be considered as a cause of intermittent epigastric pain in the elderly, regardless of the presence or the absence of a demonstrable ulcer. The pain is usually unrelated to food consumption. If ulcers are demonstrated, they tend to be multiple and in unusual sites. Some of these episodes may not accompany formation of documented anatomic lesions. A pathologist awareness of this phenomenon will encourage the careful observance necessary to identify cholesterol emboli in surgical specimens as well as in postmortem examination of the stomach in patients with the described history and/or in those patients prone to atherosclerosis. The concerted efforts of both clinicians and pathologists in the correct identification of atheromatous embolization of the
stomach and the intestinal tract will undoubtedly verify a greater frequency than is generally recognized.

**Pathophysiology**

It is believed that arterial occlusion containing cholesterol crystal spaces is the result of the organization of emboli from eroded aortic atheromata. The mass of cholesterol crystals mixed with lipid and thrombus material is torn loose by the flow of blood and is carried into the medium size or small arteries, where it lodges. Additionally, a thrombus is formed above the embolus which is partially resolved and organized. However, the cholesterol crystals remain and are encased by intimal tissue and foreign body giant cells. Recanalization of the fibrin thrombus takes place among the crystals with the crystals forming slit-like spaces.

There is ample evidence, both experimentally and clinically, that points to the embolization theory of atheromatous occlusion of vessels versus *in situ* formation of them:

A. Experimental injection of material scraped from atheromatous plaques and suspended in physiologic saline in ear veins of rabbits and into the thoracic aorta of rabbits by Flory resulted in widespread atheromatous embolization of arteries and arterioles of the abdominal organs and the lower extremities.

B. Acute lesions were seen after aortic surgery, and their evolution and organization could be followed and dated from the related infarcts.

C. The emboli have been morphologically identical to the fragments of atheromatous material and came to lie chiefly at the bifurcation of the arteries.

D. In a large number of autopsy studies by Flory, no arterial occlusion containing cholesterol crystals was found in a group of 63 patients with atheromatosis of the aorta without erosion. In the second group of 147 cases with slight erosion of atheromatous plaque, only two instances of these arterial occlusions were found. In the third group of 57 cases in which erosion of the plaque in the aorta was marked, seven cases or 12.3 percent had arterial occlusion containing cholesterol crystals. This observation is in strong support for the theory of embolization rather than *in situ* formation of cholesterol crystals in the small arteries.

E. Another argument against the theory of *in situ* formation of these crystals is the location of these crystals in the arteries. If the lipid in the thick intimal tissue of atherosclerotic arteries were to crystallize, vessels in which the lumina were filled with crystals would be expected. Crystals have not been found in the intima of medium sized unoccluded arteries.

**Type of Emboli**

Three types of emboli have been described: (1) jagged fragments of almost acellular hyalin material containing cholesterol crystals are the most common in one report; (2) jagged fragments of hyalin material only without cholesterol crystals; and (3) a rare type consisting of an aggregate of lipid-filled histocytes.

Reported atheromatous emboli have occurred with overwhelming preponderance in elderly males mostly older than 60 years. The aorta is the most common site of origin of these emboli.
The histologic picture of these emboli may go through different stages. Stage one represents the lodging of cholesterol crystals and atheromatous material. Stage two is characterized by pronounced fibroblastic reaction of the intima. In the third stage, fibroblasts are a few in number and collagen increases. In the fourth stage, cholesterol crystals are completely encased in dense collagenous tissue.9,11

References