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CASE REPORTS

Intramural Hematoma of the Esophagus Presenting as Chest Pain

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Intramural hematoma of the esophagus (IHE) is a rare clinical entity. The majority of cases occur following esophageal instrumentation; however, other causes have been described.[1–4] Rarely, IHE may develop spontaneously. We report a case of apparent spontaneous IHE (SIHE) in a patient presenting with acute-onset chest pain and dysphagia who was taking low-dose aspirin, bisphosphonate, and iron supplementation therapy. We highlight the evaluation of chest pain in these patients and the importance of considering the association between esophageal pathology and less commonly implicated medications which may increase the risk of esophageal injury.

Case Report

An 80-year-old Hispanic female with a history of osteoporosis, hypertension, and anemia presumed secondary to long-standing noninsulin-dependent diabetes mellitus presented with severe, abrupt-onset, epigastric and retrosternal chest pain following ingestion of a banana. Home medications included aspirin (81 mg daily), alendronate (70 mg weekly), and ferrous sulfate (300 mg 3 times daily). She experienced nausea and minimal vomiting without hematemesis following the onset of pain. She admitted to several weeks of progressive dysphagia leading up to this event, but denied persistent vomiting, straining, foreign body ingestion, or trauma. At admission, the patient was afebrile with heart rate (HR) = 88, blood pressure (BP) = 172/88, pulse oximetry = 99% on room air, hemoglobin = 9.0 g/dL, hematocrit = 26.5%, platelets = 191,000, and international normalized ratio (INR) = 1.04. Electrocardiogram and cardiac enzymes were negative for myocardial infarction. Chest radiograph did not show a widened mediastinum. A computed tomography (CT) scan of the chest demonstrated diffuse thickening of the esophageal wall. Upper endoscopy demonstrated a large, purple, nonpulsatile submucosal mass protruding into and nearly occluding the esophageal lumen (Figure 1A). This mass extended 22 cm along the esophagus and terminated at the esophagogastric junction. There was suggestion of a potential distal mucosal tear and visible clot (Figure 1B, C). An endoscopy performed 6 years prior was unremarkable for esophagitis, stricture, mass, or hemorrhage.

The patient remained nil-per-os and was managed conservatively with intravenous fluids, antiemetics, and acid-suppression therapy. Due to persistent odynophagia, the patient did not tolerate per-os nutrition, and a percutaneous gastrostomy tube was placed nonendoscopically for temporary nutritional support. The patient's hospital stay was complicated by deep vein thrombosis of the right peroneal vein, for which she underwent inferior vena cava filter placement. She was discharged 18 days following admission. Alendronate and aspirin were discontinued and not reinitiated, and a follow-up CT scan 6 weeks posthospitalization demonstrated complete resolution of the hematoma.

Discussion

Esophageal injuries include lacerations (Mallory-Weiss syndrome), perforations (Boerhaave's syndrome), and hematomas (ie, IHE). IHE is by far the least common of these 3 pathologies and, despite increasing reports, it remains a rare clinical entity. Criblez et al.,[4] in a review of 91 cases, found that only 35% of patients present with the classic triad of retrosternal chest pain, dysphagia/odynophagia, and hematemesis, while 99% present with at least 1 of these.[5] Presentations mimic other cardiothoracic emergencies including myocardial infarction,[6] pulmonary embolism,[2] aortic dissection,[6] and aortoesophageal fistula. Misdiagnosis of IHE and treatment with anticoagulant or thrombolytic therapy can have disastrous consequences, including death.[5] Electrocardiograms, chest radiographs, and cardiac enzymes are often normal, as in this case. Endoscopy, performed cautiously, typically reveals a nonpulsatile, purple, submucosal mass. CT, which is rapid, noninvasive, and capable of differentiating between esophageal and life-threatening thoracomediastinal pathology, frequently demonstrates thickening of the posterior wall of the esophagus with a long, smooth filling-defect and luminal narrowing.[7] Conservative management is the mainstay of treatment with most patients receiving acid suppression and antiemetic therapy. Surgical treatment and antibiotics (in cases of suspected infection) are required infrequently and should be used conservatively when necessary. The vast majority of patients recover spontaneously. Long-term complications are rare.

IHE most frequently results from esophageal instrumentation, but other antecedent causes have been described. In contrast, SIHE occurs without warning, frequently developing in the absence of vomiting or hematemesis. Since SIHE was first reported in 1970,[8] many authors have postulated potential mechanisms of hematoma formation. Controversy

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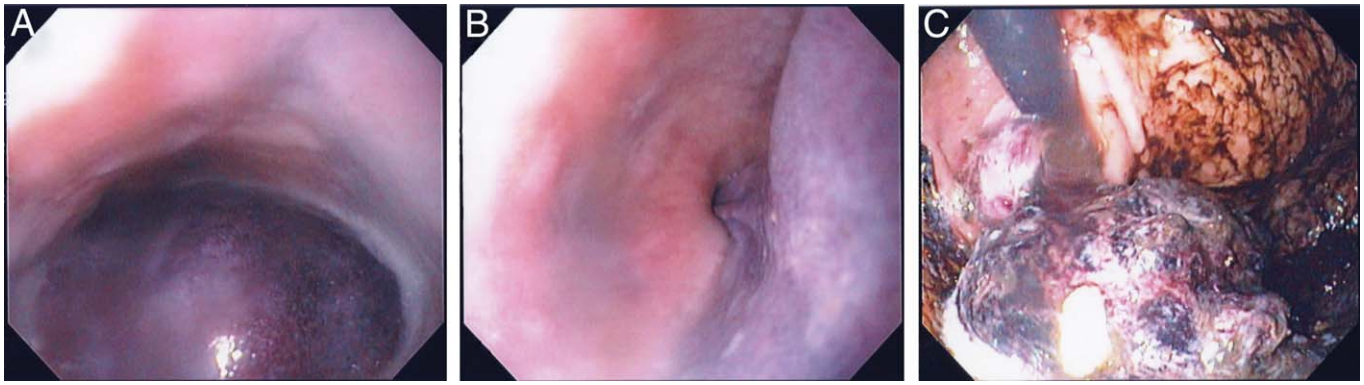

FIGURE 1. Endoscopy results. Endoscopy performed on day 2 showing: (A) a large, deep purple, nonpulsatile mass almost completely occluding the esophageal lumen; (B) the extension of this mass 22 cm inferiorly toward the esophagogastric junction; and (C) a large distal clot within the cardia of the stomach that was associated with a potential small distal esophageal mucosal tear.

remains as to the precise etiology, but recent reports emphasize the association between SIHE and antiplatelet therapy, including low-dose aspirin,[9,10] aspirin plus dipyridamole,[11] and clopidogrel.[12] Few studies have identified mechanisms for why the hemorrhage remains in the esophagus and why other parts of the gastrointestinal tract or other organ systems are not involved.

We report a case of apparent SIHE in a patient taking low-dose aspirin, alendronate, and ferrous sulfate. While a subclinical traumatic event cannot be completely excluded, this patient lacked any apparent antecedent symptoms or other etiologic explanation. Alendronate and ferrous sulfate have been implicated in upper gastrointestinal irritation, but have not previously been associated with SIHE. Park et al.[13] estimated a 3.0% incidence of esophageal or gastric events in alendronate users. Recently, esophagitis dissecans superficialis,[3] esophageal dissection,[14] and even fatal esophageal perforation[16] have been reported in patients taking alendronate. Iron supplementation is also a recognized cause of esophageal injury. High local iron saturation may lead to concentration-dependent absorption and thereby the formation of reactive oxygen metabolites and mucosal injury.[16]

We hypothesize that alendronate in combination with ferrous sulfate therapy resulted in subclinical esophageal injury predisposing our patient to SIHE. The patient reported 2 weeks of dysphagia prior to admission, suggesting a period of esophageal irritation. On endoscopy, a potential distal esophageal mucosal tear and clot were observed, which may represent a focus of injury. The interaction between this alendronate-induced injury and chronic antiplatelet therapy may have resulted in hematoma expansion 22 cm along the esophagus. We are aware of one other report of IHE in a patient taking aspirin and alendronate published as an abstract in the Iranian *Govaresh Journal*.[17]

A spectrum of less-commonly-implicated medications may exert local toxicity on the esophagus and lead to de novo esophageal damage, predisposing patients to a broad spectrum of esophageal pathology, ranging from focal esophageal damage to large hematoma or perforation. Numerous medications are known to be associated with esophageal pathology through a variety of mechanisms (Table 1). Anatomic and motility disorders, as well as pill-specific factors including contact time, coating materials, and sustained release formulations, may influence toxicity and predispose to injury.[18] Elderly patients may be especially susceptible to the combined interactions between antiplatelet therapy and these commonly prescribed or over-the-counter medications.

TABLE 1. Medications Commonly Associated with Esophageal Injury

Nonsteroidal antiinflammatory drugs	Aspirin, naproxen, ibuprofen
Bisphosphonates	Alendronate, etidronate, pamidronate
Antibiotics	Tetracycline, doxycycline, clindamycin, penicillin
Antiviral agents	Zalcitibine, zidovudine, nelfanavir
Chemotherapeutic agents	Dactinomycin, bleomycin, cytarabine, daunorubicin, 5-fluorouracil, methotrexate, vincristine
Others	Ferrous sulfate, potassium chloride, ascorbic acid, multivitamins, quinidine, theophylline

NOTE: Medications commonly associated with esophageal injury through a variety of mechanisms, including production of caustic acidic or alkaline solution (ie, ascorbic acid, ferrous sulfate, alendronate), creation of a hyperosmolar solution in contact with the esophageal mucosa (ie, potassium chloride), or direct toxicity to the esophageal mucosa (ie, tetracycline).

Conclusions

We report a case of apparent SIHE in an elderly woman taking low-dose aspirin, iron, and alendronate therapy who presented with acute-onset retrosternal chest pain and dysphagia. We emphasize the importance of including esophageal pathology in the evaluation of chest pain in these patients, particularly elderly women. We encourage a thorough examination of symptoms, including dysphagia/odynophagia, and an exhaustive medication history to identify medications

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less-commonly implicated with esophageal pathology. In patients with chest pain taking these medications, clinicians must remain vigilant in their diagnostic approach to prevent misdiagnosis and inappropriate treatment.

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