Complete Recovery from Iron-Induced Esophageal Ulcer While Continuing Pill Ingestion

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ABSTRACT

Iron is one of the common causes of pill-induced esophagitis with a proposed mechanism involving direct esophageal injury. Diagnostic endoscopic finding includes finding an intact pill or its residue on endoscopy, but they are rarely found. Pathology typically reveals luminal brown-black crystalline materials adjacent to the injured surface epithelium or in combination with luminal fibroinflammatory exudate. Brown crystalline material on Perl's staining is the typical finding of iron-induced esophagitis. Crucial treatment is cessation of medication. We report an elderly woman diagnosed with iron-induced esophageal ulcer whose ulcers improved while iron medication was maintained.

Keywords: Iron; esophageal ulcer

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INTRODUCTION

Pill-induced esophageal injury (PIE) is usually considered as an uncommon condition. It can occur at any age from commonly used medications including ferrous compounds. We report an elderly woman with an iron-induced esophageal injury who recovered completely while maintaining ingestion of iron medication.

CASE REPORT

An 89-year-old woman presented with melena for 2 days. She denied hematemesis or abdominal pain. Her past medical history include type 2 diabetes mellitus, hypertension, adrenal insufficiency, stage 3 chronic kidney disease, and a benign thyroid nodule. She had a history of right half colectomy due to a large hamartomatous polyp at the cecum. Her medications were atorvastatin 20 mg/day and amlodipine 10 mg/day. One month before she had melena, she was admitted due to a compression fracture of L1 vertebrae. During admission, she developed atelectasis, and pulmonary rehabilitation was performed. Her appetite decreased and iron deficiency anemia developed. Ferrous fumarate was prescribed. She had a history of recumbent position while taking the pills. Physical examination revealed mildly pale conjunctiva. Vital signs were stable. Stigmata of chronic liver disease and hepatosplenomegaly were absent. Complete blood count showed hemoglobin 7 g/dl, WBC 16,000/mm^3 with neutrophil 84%, and platelet 738,000/mm^3. Prothrombin time was 16 second (normal 12-14.6) and partial thromboplastin time was 39.6 second (normal 25-35). Endoscopy examination showed a circumferential ulcer with necrotic tissue at lower esophagus

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(5 cm. above the esophagogastric junction) (Fig 1-2). Black discoloration of the esophageal mucosa was seen distal to the ulcer. Pathological

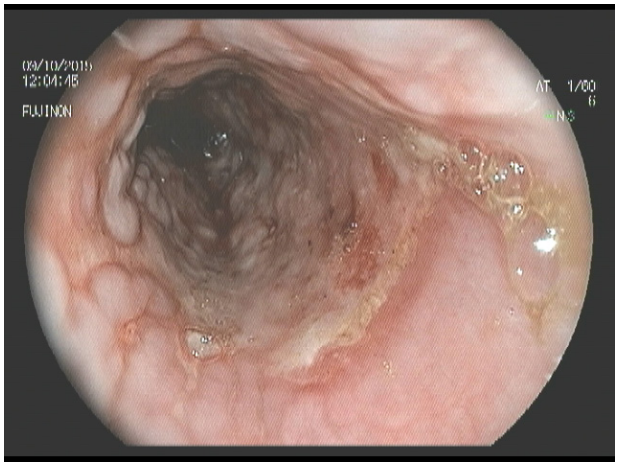

Fig 1. Endoscopic finding of the lower esophagus reveals circumferential ulcer.

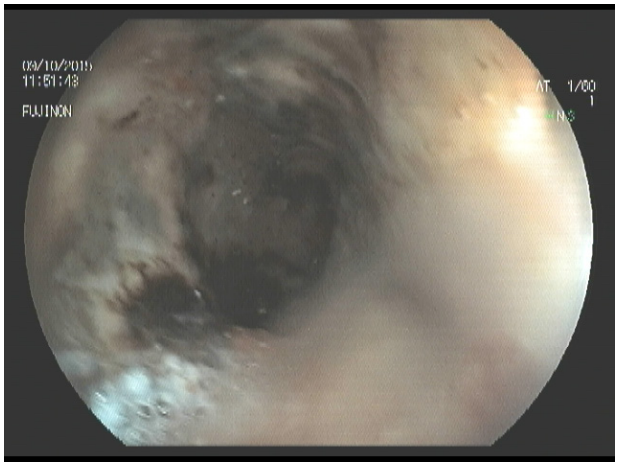

Fig 2. Endoscopic finding of the lower esophagus shows circumferential ulcer with necrotic tissue.

examination revealed ulcer base covered with fibrinous exudate and containing many reactive newly-formed vessels, numerous neutrophils, and reactive fibroblasts (Fig 3-4). Pearl staining was positive (Fig 5). Cytomegalovirus staining and Gomori Methenamine Silver stain were negative. Proton pump inhibitor (PPI) was prescribed for 8 weeks. Hydration and blood transfusion were also given. She was able to take the pills in upright position. Her symptoms improved while waiting for the pathological results and ferrous fumarate was continued. Re-endoscopy was done after 8 weeks which showed complete healing with scar formation (Fig 6).

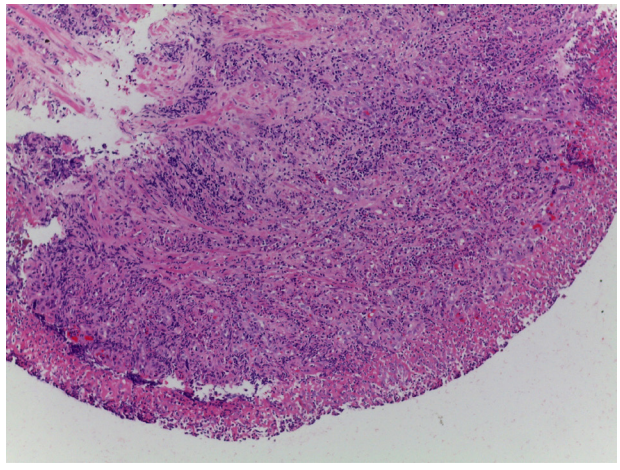

Fig 3. Histopathologic finding (low power) shows active ulcer with granulation tissue and necrotic debris.

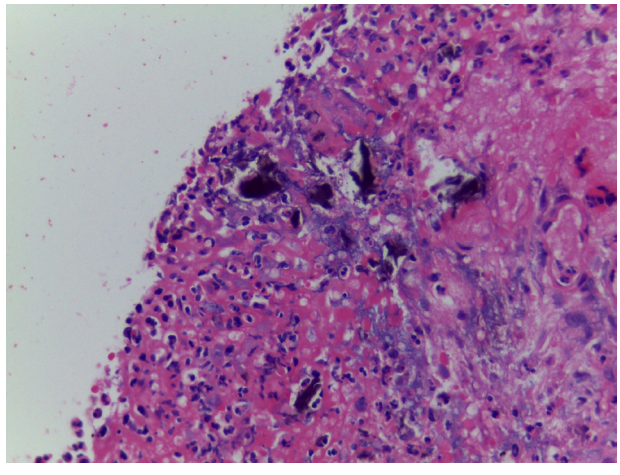

Fig 4. Histopathologic finding (high power) reveals irregular brown and dark brown foreign body material, morphologically compatible with pills fragments.

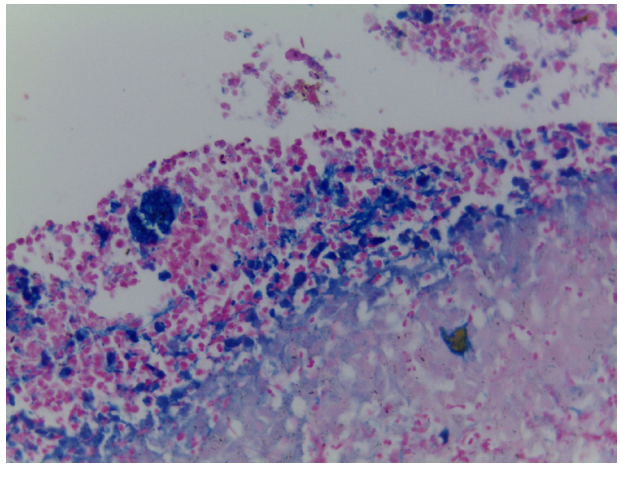

Fig 5. Histopathologic finding (Iron stain, Perls' Prussian blue) highlights numerous iron material (bright blue stain) in the necrotic debris.

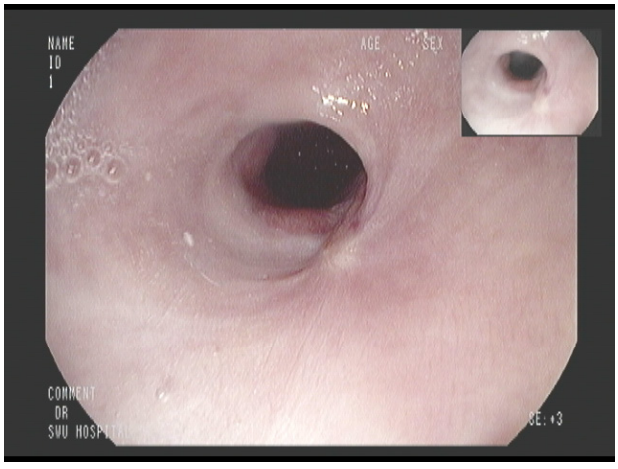

Fig 6. Endoscopic finding of the lower esophagus 8 weeks later demonstrates healing of the esophageal ulcer.

DISCUSSION

Pill-induced esophageal injury (PIE) can be caused by many medications. The mechanism of PIE involves direct esophageal injury. Clinical manifestation of PIE includes chest pain, odynophagia, dysphagia, and heartburn. Patients with PIE commonly have a history of recumbent position or sleeping immediately after pill ingestion and ingestion of a pill without enough water. Endoscopy with biopsy is usually done to confirm the diagnosis. Intact pills or their residue seen on endoscopy provides a diagnosis. Even histology is nonspecific to provide an unequivocal diagnosis, as other conditions such as infectious esophagitis need to be excluded. Crucial treatment for PIE is discontinuing the medication. PPI, and sucralfate, lidocaine solutions and narcotics may be used.

Typically, iron induced mucosal injury occurs only in the upper gastrointestinal tract. Iron-induced esophageal injury (IIE) is commonly found in two patterns. The first pattern consists of a dramatic injury which is usually seen in the esophagus. The second pattern consists of iron deposits in the epithelium, lamina propia, and glands which are found in the stomach and duodenum.[1] Iron is the common cause of pill-induced esophageal injury. Pathogenesis of IIE has not been completely defined. A proposed mechanism of IIE involves direct esophageal injury. In the areas with high iron concentration, iron is absor-bed rapidly and passively through a complex energy-dependent, carrier-mediated system, or via paracellular movement across tight junctions. It is a concentration-dependent absorption mechanism. After iron has been absorbed, it is metabolized to reactive oxygen metabolites which lead to mucosal injury.[2] IIE occurs when ingesting tablet formulations. It is usually found in elderly.[2,3] Endoscopic finding of IIE is often nonspecific. Diagnostic endoscopic finding includes finding an intact pill or its residue on endoscopy. However, these are rarely found. Pathology typically reveals luminal brown-black crystalline material adjacent to the injured surface epithelium or admixed with luminal fibroinflammatory exudate.[1,4] Iron stain is the confirmation test. Brown crystalline material on Perl's staining is the typical finding of IIE. Exuberent proliferation of reactive fibroblasts and regenerative epithelial changes near esophageal ulcers may also be found.[4] Treatment of IIE is similar to that of PIE from other medications, namely discontinuing the medication is the important treatment.

Acute esophageal necrosis (AEN) or black esophagus or acute necrotizing esophagitis is defined by diffuse circumferential black discoloration of distal esophagus. It was first described by Goldenberg et al in 1990.[6] Combination of an ischemic event of esophagus, impaired local defense barriers and injury from gastric contents is proposed to be the pathogenesis of AEN.[6] Ischemic events of esophagus may be caused by sepsis, arrthymias, heart failure, third space loss, systemic inflammatory response, lactic acidosis, ketoacidosis, acute blood loss, hypothermia, trauma and shock. Most common clinical manifestation is upper gastrointestinal bleeding. On endoscopy, AEN is characterized by circumferential black discoloration at distal esophagus and sharp transition to normal mucosa at esophagogastric junction. Histopathology is used to differentiate AEN from other conditions. Severe necrosis of esophageal mucosa with necrotic debris is usually found. Crucial treatment of AEN is correction of coexisting medical conditions. Other treatments are intravenous hydration, blood transfusion and PPI. Nasogastric tube placement should be avoided.

In our patient, she had a history of history of swallowing the pill in a recumbent position which predisposes to PIE. Hypomotility of esophagus from diabetes mellitus and aging might have contributed to PIE. She had atherosclerotic risk that was prone to AEN. However, she did not have the ischemic event before AEN was developed. Endoscopy revealed esophageal ulcer with AEN. From the histopathology, it showed numerous iron staining in the ulcer which supports the diagnosis of IIE. No previous case report of iron induced AEN was found, IIE and AEN might be coexisting in our case. The ulcer was completely healed after 8 weeks of PPI without iron discontinuation. There is no previous case report of complete healing of IIE while the pill is continued. We report an elderly woman who was diagnosed IIE with AEN and the ulcers improved while oral iron medication was continued. It might be due to the predisposing factor (swallowing the pill in recumbent position) was corrected and the effect of PPI.

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