

Pill esophagitis masquerading as esophageal cancer on endoscopy and endoscopic ultrasound.

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Introduction:

“Pill-induced” esophagitis is a well known complication related to use of certain medications. To date, more than 100 different medications are reported to cause pill esophagitis. While majority of the cases of pill esophagitis are self limited, complications like esophageal hemorrhage, strictures, perforations and fatal injuries have been reported all around the world. We describe a case of quinidine related esophagitis and stricture that masqueraded as esophageal cancer and remained undiagnosed after several endoscopic procedures.

Methods of Image Capture: Endoscopic images were captured using standard 9.8mm diameter Olympus upper endoscope (Olympus, U.S.A.). Endoscopic ultrasound images were captured using 13.8mm diameter Olympus electronic radial echoendoscope (Olympus, U.S.A.).

Case Report:

A 79 year old man was referred at M.D. Anderson Cancer Center for evaluation of distal esophageal stricture that was thought to be malignant. The patient presented with a 2 month history of progressive solid dysphagia and weight loss. At another medical center, upper endoscopy revealed distal esophageal stricture and esophageal biopsies revealed inflammatory change without malignancy. He underwent trial of proton pump inhibitor (PPI) without clinical resolution of symptoms. Repeat endoscopy and biopsies after trial of PPI did not show any improvement in the endoscopic appearance but the biopsies did not show any evidence of malignancy.

At our institution PET-CT scan demonstrated a focal area of increased metabolic activity with a maximum SUV (standardized uptake value) of 5.5 and corresponding focal esophageal wall thickening concerning for primary esophageal carcinoma. No enlarged or metabolically active regional lymph nodes or other evidence of metastatic disease were identified. (*Figure 1*)

Repeat endoscopy demonstrated a persistent circumferential stricture in the distal esophagus (35-38cm). The mucosa within the stricture was edematous, friable and inflamed with diffuse erythema, granular nodularity, focal ulceration and soft thick whitish exudate (*Figures 2, 3*). A circumferential thickening of the esophageal wall was seen. With esophageal stenosis and the 9.8mm diameter endoscope was advanced past the stenosis

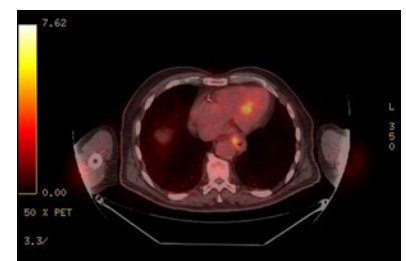


Figure 1

into the stomach which was unremarkable including retroflexed view of the cardia. The 13.8mm diameter Olympus electronic radial echoendoscope GF-UE160-AL5 was introduced to the level of the stenosis but could not be advanced past the stricture as resistance and clumping of sloughed exudate was encountered. Sonographic imaging of the proximal edge of the stricture (at 7.5 and 10MHz) showed uniform circumferential hypoechoic thickening of the esophagus (*Figures 4, 5*). The EUS images were consistent with either a circumferential malignant process or a severe inflammatory process depending on endoscopic biopsy results. Biopsies showed benign esophageal squamous epithelium with ulceration, granulation and necroinflammatory debris with both acute and chronic changes. No evidence of infection (viral or fungal), dysplasia or malignancy was found.



Figure 2

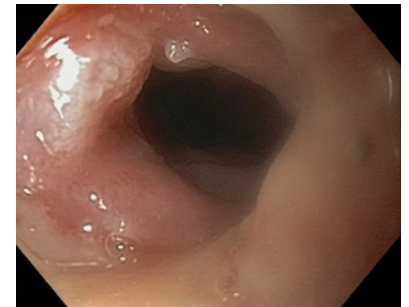


Figure 3

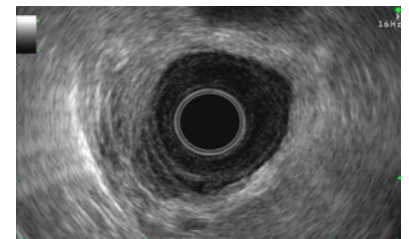


Figure 4

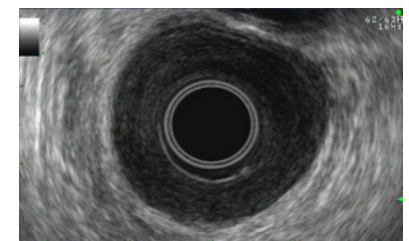


Figure 5

Patient's past medical history was significant for hypertension, diabetes, dyslipidemia, mitral valve prolapse, and atrial fibrillation. His medications included lisinopril, glyburide, pravastatin, lansoprazole, aspirin, clopidogrel, digoxin and quinidine gluconate. On closer questioning, he was taking 648 milligrams of quinidine twice daily. His evening dose of quinidine was just prior to bedtime with one to two mouthfuls of water. Diagnosis of quinidine induced esophagitis was made based on patient's history, endoscopic and biopsy findings and after exclusion of infection, dysplasia, and malignancy. Patient was advised to stop quinidine and if possible take other pills in liquid or elixir form. He was instructed to drink half a glass of water before taking pills and then to take pills with full glass of water. He was also instructed not to lie down for at least two hours after taking the pills. With above conservative approach his symptoms improved and follow up endoscopy at three months showed resolution of necroinflammation and ulceration with residual stricture which was treated with dilatation. Patient continues to do well without any dysphagia or weight loss at one year follow up.

Discussion:

Pill-induced esophageal injury due to many different medications including quinidine has been well described¹⁻⁶. Although risk of pill induced injury may be enhanced if there is underlying esophageal disease, most patients have normal esophageal function, motility and anatomy, and are subjectively unaware of retention⁴. Injury typically occurs as a direct result of prolonged mucosal contact with caustic tablets or capsules⁴. Factors such as swallowing position, adequate fluid ingestion, pill size and advanced age may increase risk.

The clinical presentation and precise mechanism of injury has been shown to vary with pill type. While drugs may cause injury via production of acidic (i.e. ferrous sulfate, doxycycline and tetracycline) or alkaline solutions (i.e. phenytoin), some drugs like quinidine (i.e. NSAIDs, aspirin, potassium chloride) produce neutral solutions which are directly cytotoxic to esophageal mucosa. Still others may act by indirect means such as induction of gastroesophageal reflux (i.e. theophylline, anticholinergics) or systemic action.³⁻⁶

The most common presenting symptoms in patients with pill esophagitis are acute odynophagia, chest pain and/or vomiting which is usually self-limited although serious complications such as stricture, massive hemorrhage and perforation have been reported⁷. Patients with pill induced esophageal injury from quinidine are much

more likely to develop stricture than most other medications. Gradual progression of dysphagia with the development of strictures and relatively little pain may occur and has been observed repeatedly (up to 50% 7/13 in some series) with quinidine and a few other select medications such as potassium chloride, ferrous sulfate, and alprenolol². Because these patients may experience gradually progressive dysphagia rather than acute pain they often fail to associate symptoms with the medication⁴. Another unusual feature of quinidine induced esophageal injury is the occasional presentation with extensive exudates (necrotic debris sometimes mixed with retained pill fragments) that may be so thick and tenacious as to mimic neoplasia at either endoscopy or endosonography^{2,4,7-10}. This was the case in our case where despite negative endoscopic biopsies the patient was strongly suspected to have esophageal cancer and was referred from a great distance in another state to our tertiary cancer center in Texas for further care and management.

In the vast majority of cases and in those uncomplicated by stricture, spontaneous resolution of symptoms will occur with discontinuation of the offending medication and symptomatic care. Most cases of pill induced esophageal injury probably remain unrecognized since most patients fully recover. However patients who develop fibrotic stricture from repetitive injury may require dilation or even surgery.

Awareness among health care professionals of the caustic nature of certain medications is necessary. Medication history should be obtained in any patient with esophagitis, benign inflammatory esophageal stricture or in the presence of an esophageal mass that looks malignant but repeated endoscopic biopsies fail to confirm malignancy.

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