

may surround the ulcer(s), or they may occur in the absence of discrete ulceration.¹¹ A biopsy can help exclude infection and neoplasia. We did not perform a biopsy during endoscopy for the present cases because of typical symptoms and endoscopic presentations.

A variety of other conditions can be associated with the development of esophageal injury. Herpetic esophagitis can be indistinguishable from a drug-induced esophageal ulcer. However, viral-induced ulcers tend to have a more widespread distribution than drug induced ulcers. Patients with herpetic esophagitis are likely to be immunocompromised due to an underlying malignancy or treatment with radiation or chemotherapy. Occasionally, herpetic esophagitis can occur as an acute self-limited disease in otherwise healthy patients. These patients usually present with a characteristic flu-like prodrome, such as fever, headaches, myalgias, and upper respiratory infection prior to the sudden onset of severe odynophagia. Reflux esophagitis is a more common cause of esophageal ulcers. Ulcers of reflux esophagitis are always located in the distal part, and are often combined with a hiatal hernia. Candida esophagitis can cause ulceration, but the ulcers typically occur on a background of diffuse plaque formation. Crohn's disease can present small aphthous ulcers in the esophagus, but these patients almost always have evidence of small bowel or colon disease. Giant esophageal ulcers can also be caused by nasogastric intubation, endoscopic sclerotherapy, ulcerated carcinoma, and infection with HIV or cytomegalovirus (CMV).⁹ In our 2 cases, these diagnoses could be excluded simply by clinical manifestations and endoscopic pictures.

Pills are more likely to stick if swallowed without water or while supine, and these predisposing factors are commonly documented in published case reports, as in our cases. Aging, esophageal dysmotility, and extrinsic esophageal compression also favor pill retention,¹⁰⁻¹³ but it may occur in normal patients at 2 physiologically narrowed sites, i.e., the aortic indentation and the lower esophageal sphincter. We did not perform an esophageal motility study for the present cases; however, the 2 patients had no previous esophageal symptoms, such as dysphagia, chest pain, heartburn, or acid regurgitation, and thus esophageal

dysmotility was not likely. The chest radiograph of the 2 patients showed no tortuous aorta or enlarged left atrium, so extrinsic esophageal compression was not present. The characteristics of the pills are related to esophageal injury. Large pills and pills with sticky surfaces are more commonly retained. The mechanism of injury for many pills remains obscure. Tetracycline, ascorbic acid, and ferrous sulfate produce acidic solutions (pH < 3.0) when dissolved in 10 ml of water, suggesting that they may produce acid burns. Phenytoin sodium produces an alkaline solution and may induce alkaline burns.¹² The pKa is 6.9 for glucosamine sulfate, so acidic or alkaline injury is not likely. Postulated mechanisms of injury for other pills include induction of gastroesophageal reflux by theophylline and anticholinergics, local hyperosmolarity by KCl, and intracellular poisoning by doxycycline or NSAIDs. Several reports suggest that sustained-release formulations may be more injurious to the esophagus than standard preparations of the same medication.¹¹⁻¹³

Most uncomplicated cases of drug-induced esophageal injury heal spontaneously in a few days to weeks. The best treatment is removal of the offending drug, followed by supportive care, such as oral sucralfate or antisecretory drugs, parenteral or liquid oral analgesics, and parenteral hydration. Esophageal hemorrhage is treated by therapeutic endoscopy. Inflammatory stricture may resolve spontaneously, but chronic stricture may require endoscopic dilatation.^{9,11-13}

Prevention includes education of patients in the proper methods for taking pills. Patients should drink at least 100 ml of fluid with any pill, take pills while in an upright posture, remain upright for 10 min after taking pills and for at least 30 min after taking pills that are especially like to cause serious esophageal injury. Pills implicated as causing frequent or severe esophageal injury should be avoided in bedridden patients or patients with esophageal compression, stricture, or dysmotility.^{9,11-13}

In conclusion, we report on 2 cases of glucosamine sulfate-induced esophageal injury. We suggest that it is necessary for clinicians to instruct patients on the proper method of taking pills to prevent the development of esophageal injury.