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Single Case

Esophageal Perforation Due to a Calcium Supplement Tablet

Michael K. Zijlstra[a] Robert I. Silvers[b] Claus J. Fimmel[c] Seth Krantz[d]

[a]Department of Medicine, University of Chicago (NorthShore) Program, Chicago, IL, USA; [b]Department of Radiology, NorthShore University Health System, Chicago, IL, USA; [c]Division of Gastroenterology, NorthShore University Health System, Chicago, IL, USA; [d]Department of Surgery, NorthShore University Health System, Chicago, IL, USA

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Esophageal perforation · Pill ulcer · Calcium supplement

Abstract
Pill-induced esophagitis due to calcium supplements is extremely uncommon. We present a 60-year-old female patient with pill-induced esophageal perforation complicated by mediastinal abscess and esophago-pleural fistula following ingestion of a single over-the-counter "bone supplement" tablet containing mainly calcium.

Introduction

Medication-induced esophagitis – also known as pill-induced esophagitis – has an annual incidence of 3.9 per 100,000 people. It typically occurs in the fourth decade of life and is more frequent in females [1]. The medications most commonly associated with this condition include alendronate, quinidine, tetracycline, doxycycline, potassium chloride, and ferrous sulfate. In contrast, calcium supplements have rarely been implicated – with only 1 case reported in the literature [2].

Here, we describe a patient who presented with esophageal perforation after ingestion of a single, over-the-counter supplement tablet containing primarily calcium. At the time of preparing the present report, we did not find any documented cases of calcium tablet-induced esophageal perforation in the medical literature. We believe this case to be relevant from a public health perspective, given the widespread emphasis on increased calcium intake by both the medical community and the lay public.

Correspondence to:
Michael K. Zijlstra, mzijlstra@northshore.org

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Table 1. Composition of "Osteo Guardian" dietary supplement

Ingredient	Amount per serving	% Daily Value
Vitamin C (as calcium ascorbate & ascorbic acid)	250 mg	417%
Vitamin D3 (as cholecalciferol)	400 IU	100%
Vitamin K (as phytonadione)	80 μg	100%
Calcium (as carbonate, citrate, Aquamin™, & ascorbate)	1,000 mg	100%
Magnesium (as oxide, glycinate, & Aquamin™)	500 mg	125%
Zinc (as citrate & glycinate)	15 mg	100%
Copper (as gluconate & glycinate)	2 mg	100%
Manganese (as glycinate & chloride)	1 mg	50%
Isoflavones (as kudzo)	40 mg	n.a
Boron	2.8 mg	n.a

Serving size, 4 tablets.

Case Presentation

A 60-year-old Caucasian female presented to the emergency department with a 2-week history of progressive epigastric pain, odynophagia with solid foods and liquids, belching, anorexia, and a 6.4-kg unintentional weight loss. The pain was steady for 5 days, then suddenly increased to become "excruciating", with radiation to the right rib cage and associated difficulty breathing. The patient denied vomiting, dysphagia, melena, or changes in bowel habits. She gave a history of intermittent heartburn and occasional H_2 blocker usage. However, she had not been taking any acid blockers in the weeks prior to the onset of symptoms. She had a history of osteopenia for which she had been taking an over-the-counter supplement ("Osteo Guardian"), ingredients shown in Table 1, for several years. She noted that the pill dimensions had recently changed, resulting in a longer, more oblong shape.

On initial evaluation, the patient appeared nontoxic. Her vital signs were within normal limits, except for a slightly elevated blood pressure. The mucus membranes were dry. The lungs were clear to auscultation, and the heart examination was regular without murmurs, rubs, or gallops. The abdomen was soft and non-distended. Mild epigastric tenderness was noted. Murphy's sign was absent. No masses were appreciated. Normal bowel sounds were present. Routine laboratory studies were within normal limits. The electrocardiogram was normal. A chest radiogram showed no acute cardiopulmonary processes. A COVID-19 test – performed for cough and low-grade fevers – was negative. A bedside right-upper-quadrant ultrasound was unremarkable. The patient was given antacids and simethicone solution, viscous lidocaine, and intravenous pantoprazole. Her symptoms improved, and she was discharged to go home with a prescription for oral famotidine. She was advised to follow up with her primary care physician and to schedule an outpatient esophagogastroduodenoscopy (EGD).

A few days later, the patient presented to her PCP with complaints of continued epigastric pain, anorexia, belching, and continued low-grade fevers. An abdominal contrast CT scan demonstrated a radiopaque object, measuring approximately 2 cm, in a cavity adjacent to the distal esophagus, initially thought to represent a hiatal hernia. A small right pleural effusion was present (shown in Fig. 1). No new recommendations were made.

The patient underwent an EGD 3 weeks later. This showed an asymmetric narrowing of the distal esophagus, with a raised mucosal surface and superficial erosions (shown in Fig. 2a, b). No hiatal hernia was present, and no other abnormalities were found. Biopsies taken from

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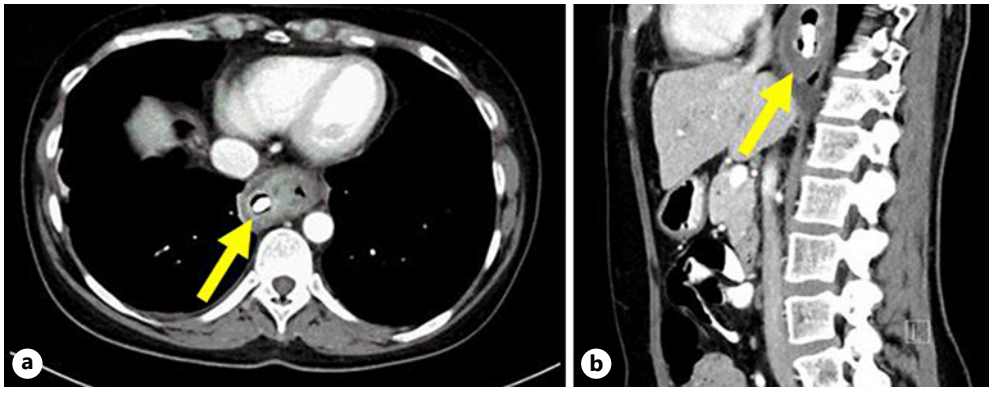

Fig. 1. Computed tomography chest with contrast (A, transversal view B, sagittal view). A radio-opaque object (arrow) is seen in the posterior right mediastinum, with a small amount of adjacent fluid and marked surrounding inflammatory changes. No gas is present within the collection. A small right-sided pleural effusion is noted.

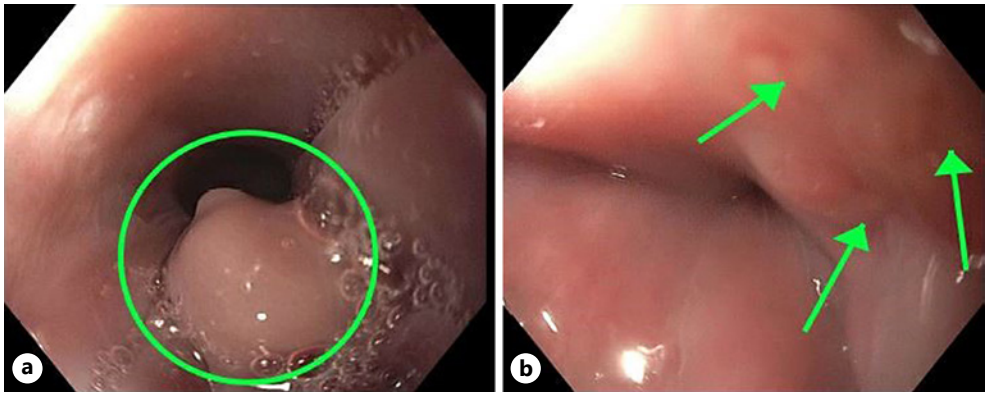

Fig. 2. a EGD showing heaped up mucosa (circle) in the distal esophagus, 37 cm from the incisors. **b** Abnormal esophageal mucosa 38 cm from the incisors (arrows). Biopsies showed nonspecific inflammatory changes.

the abnormal esophageal mucosa subsequently demonstrated non-specific ulcerations. Review of the patient's original CT scan in light of the endoscopic abnormalities resulted in a presumptive diagnosis of esophageal perforation and prompted an urgent referral to the thoracic surgery service. The patient was admitted to the hospital the next day. She underwent video-assisted thoracoscopic surgery with debridement of a mediastinal abscess, partial right pleural decortication, and removal of a foreign body from a contained perforation of the distal esophagus. Inspection of the foreign body revealed an intact calcium supplement pill (shown in Fig. 3). Intraoperative endoscopy and saline instillation followed by air insufflation showed no esophageal leak. The patient recovered uneventfully and was discharged on postoperative day 3.

Over the ensuing days, the patient noticed intermittent fevers and sour-smelling, cloudy drainage from her chest incision. A repeat chest CT obtained 1 week after the initial surgery revealed an esophago-pleural fistula and a persistent mediastinal abscess. The patient was readmitted to the hospital and started on broad spectrum antibiotics and antifungal medications. Ten days after the initial surgery, she underwent repeat video-assisted thoracoscopic surgery. A mediastinal abscess was re-demonstrated. The abscess cavity communicated with

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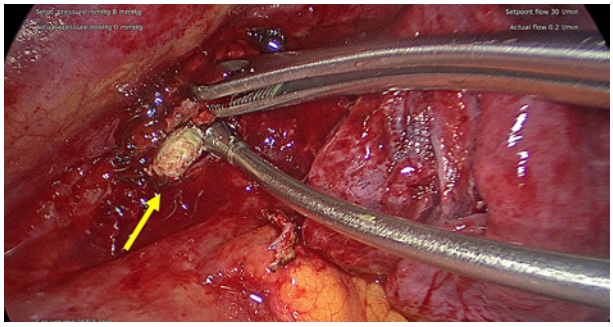

Fig. 3. Intraoperative photograph demonstrating an intact calcium supplement pill in the mediastinal abscess cavity.

the pleural space, resulting in an esophago-pleuro-cutaneous fistula. The surgical procedure included abscess drainage, pleural decortication and mobilization of the right lung off the mediastinum, wash-out of the pleural cavity, and chest tube placement. In addition, a percutaneous endoscopic gastrostomy was placed. A repeat chest CT on postoperative day 4 demonstrated a persistent esophageal fistula but no large fluid collection in the pleural space. The patient's PEG tube was converted to a PEJ tube, and her tube feedings were optimized while she remained NPO. She was discharged on postoperative day 13. An outpatient barium esophagram showed a 6 mm peri-esophageal fluid collection with no leak or other abnormalities. The chest tubes were removed and the antibiotics were stopped 1 month after surgery. The tube feedings were stopped, and the patient's condition advanced. One year postoperatively, she is tolerating a regular diet with minimal residual dysphagia.

Discussion/Conclusion

Our case highlights the potential risks associated with pill supplements containing primarily calcium. Our observation is pertinent since esophageal injury with calcium supplements appears to be an extremely rare occurrence. We found only a single published case report of a patient who developed a high-grade, mid-esophageal stricture after ingestion of a calcium multimeric complex pill [2].

Our observation appears timely since patients, especially women, are widely encouraged to increase their daily calcium intake. A growing number of over-the-counter and prescription calcium supplements are available, often containing large quantities of calcium necessitating large tablet sizes.

The patient routinely took the supplement with a drink of water and had not changed this routine prior to her presentation. Interestingly, she had noticed a change in pill dimensions immediately prior to the onset of her symptoms. This resulted in a narrowly oblong shape as opposed to a widely oblong shape. It is tempting to speculate that this change in formulation played a role in its esophageal entrapment, especially since the composition of the pills had remained unchanged.

In general, pill-induced esophageal mucosal injury and esophagitis are due to the disruption of the esophageal mucosal barrier [1]. Endoscopic studies demonstrating small, circumscribed ulcers support the concept of localized mucosal irritation by the dissolving pill [3–6]. In some cases, localized alkalotic or acidotic pH initiates the injury process [1, 7]. Alternatively, localized hyperosmolarity – as in the case of potassium chloride supplements – may play a role. In the case of NSAIDs, local inhibition of cyclooxygenase 1 is thought to contribute to mucosal injury by disrupting prostaglandin-dependent cytoprotection [8]. The physical properties of the pills may play an important role. For example, gelatin capsules can evade

esophageal emptying by adhering to the esophageal wall, resulting in their dissolution in the esophagus instead of the stomach [1, 7]. Interestingly, sustained-release formulations may cause mucosal injury more frequently than immediate-release formulation [1, 7]. Finally, patient-related factors influence the occurrence and severity of this complication. For example, the amount of water swallowed with the pill appears to play a critical role. In their 1982 landmark study, Hey and Jorgensen recommended ingestion of at least 100 mL of water in a standing position to ensure esophageal clearance [9]. Increasing patient age is important as the disease occurs more commonly in the elderly. Age-related decreases in salivary gland activity, changes in esophageal motility, anatomical changes, or simply an increase in the number of daily tablets in elderly patients have all been implicated [1, 7, 10].

With regard to the clinical presentation, patients with pill-induced esophagitis typically complain of heartburn, chest pain (71.8%), dysphagia (38.5%), or odynophagia (29.5%) [6]. The diagnosis is typically suspected on the basis of the history; however, an EGD is recommended in patients with severe symptoms such as hematemesis, abdominal pain, weight loss, or symptoms that persist despite discontinuation of the offending agent [7]. Endoscopic findings may include esophageal mucosal erythema and erosion, ulcers with and without active bleed, pill fragments, and strictures [1, 7]. Cases of pill-related esophageal perforation are rare, with an estimated incidence of 3/100,000 people in the USA [11]. Our literature search for pill-induced esophageal perforation and mediastinitis identified several culprit medications, including valproate, aspirin-caffeine, and iron supplements [12–14]. Based on our report, calcium supplements should be added to the list. A high index of clinical suspicion is required as a delay in the diagnosis may result in significant morbidity and in mortality rates of up to 40% [11]. In our patient, the initial CT interpretation of a hiatal hernia contributed to a delayed diagnosis. Once the diagnosis was established, aggressive surgical management resulted in favorable resolution of this life-threatening problem.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this report and its accompanying images. Ethical approval was not required for this study in accordance with local and national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose in association with this study.

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Author Contributions

Michael K. Zijlstra was involved in summarizing case presentation as well as drafting the manuscript and submitting final manuscript. Robert I. Silvers was involved in reading the patients computed tomography scan and edited manuscript. Claus Fimmel was provided history of case and edited manuscript. Seth Krantz was provided history of case and edited manuscript.

Data Availability Statement

The authors used no data for this case report. All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Kikendall JW, Friedman AC, Oyewole MA, Fleischer D, Johnson LF. Pill-induced esophageal injury. Case reports and review of the medical literature. Dig Dis Sci. 1983;28(2):174–82.
2 Wardlaw R, Victor D, Feagans J, Smith J. Calcium multimineral complex induced esophageal stricture. Ochsner J. 2007;7(3):125–8.
3 Antunes C, Sharma A. Esophagitis. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
4 Hey H, Jorgensen F, Sorensen K, Hasselback H, Wanberg T. [Esophageal transit of 6 common types of tablets and capsules]. Riv Inferm. 1985;4(2):82–5.
5 Dag MS, Ozturk ZA, Akin I, Tutar E, Cikman O, Gulsen MT. Drug-induced esophageal ulcers: case series and the review of the literature. Turk J Gastroenterol. 2014;25(2):180–4.
6 Kim SH, Jeong JB, Kim JW, Kim BG, Lee KL, Chang MS, et al. Clinical and endoscopic characteristics of drug-induced esophagitis. World J Gastroenterol. 2014;20(31):10994–9.
7 Saleem F, Sharma A. Drug induced esophagitis. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
8 Sostres C, Gargallo CJ, Arroyo MT, Lanas A. Adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs, aspirin and coxibs) on upper gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2010;24(2):121–32.
9 Hey H, Sørensen K, Jørgensen FB, Hasselbalch H, Wamberg T. [The passage time for capsules and tablets through the esophagus]. Ugeskr Laeger. 1983;145(32):2432–5.
10 Hollis JB, Castell DO. Esophageal function in elderly man. A new look at "presbyesophagus". Ann Intern Med. 1974;80(3):371–4.
11 Nirula R. Esophageal perforation. Surg Clin North Am. 2014;94(1):35–41.
12 Yamaoka K, Takenawa H, Tajiri K, Yamane M, Kadowaki K, Marumo F, et al. A case of esophageal perforation due to a pill-induced ulcer successfully treated with conservative measures. Am J Gastroenterol. 1996;91(5):1044–5.
13 Corsi PR, de Aguiar JR, de S Kronfly F, Saad R Jr, Rasslan S. [Esophageal injury due to pill ingestion]. Rev Assoc Med Bras. 1995;41(5):360–4.
14 Serck-Hanssen A, Stray N. [Esophageal lesions induced by iron tablets]. Tidsskr Nor Laegeforen. 1994;114(18):2129–31.