

Pill-Induced Esophagitis From Intake of Dietary Supplements

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ABSTRACT

Cases of pill-induced esophagitis can be associated with significant acute symptoms leading to hospitalization and have resulted in mediastinal penetration and hemorrhage. Clinicians often consider the diagnosis in patients taking classically associated medications. However, because many patients take dietary supplements, it is important to consider these as a potential etiology in a patient presenting with esophageal symptoms. We present a case of pill-induced esophagitis in a 40-year-old woman after the ingestion of L-arginine, selenium, and vitamin E supplements. Literature review revealed 6 cases of L-arginine-induced esophagitis reported, and no previous cases associated with vitamin E or selenium.

INTRODUCTION

Pill-induced esophagitis is a diagnosis commonly entertained by the gastroenterologist facing a hospitalized patient with acute retrosternal chest pain whose prescription list includes medications classically linked to the condition, including antibiotics such as tetracyclines, anti-inflammatory medications, and bisphosphonates. It is important to remember, however, that more than 50% of the American population use dietary supplements (DSs) in conjunction with or as alternatives to prescription medications and that these have the potential to cause harm.¹ Because DSs are regulated as foods by the U.S. Food and Drug Administration, they are not subject to the same evaluations of safety and efficacy as other drugs. Reporting rare adverse events associated with DSs is therefore important.

To our knowledge, there are only 6 previously reported cases of L-arginine-induced esophagitis, and no reported cases of esophagitis associated with vitamin E or selenium.²⁻⁴ These supplements are often taken in combination as an “alternative” fertility treatment, despite little supportive evidence—in fact, high-dose vitamin E intake is associated with increased all-cause mortality risk.^{5,6}

CASE REPORT

A 40-year-old woman with a medical history of Kallmann syndrome and scoliosis presented to the emergency department with a 4-day history of progressive retrosternal chest pain and odynophagia. Her current home medications included injectable menopins as part of ongoing fertility treatment. She denied any nicotine intake, alcohol, and recreational drug use.

On history, she was in her usual state of health until ingesting 2 large 500 mg tablets of L-arginine (Now Supplements, Guelph, Ontario) followed directly by a softgel E-400 tablet: vitamin E unesterified d-alpha tocopherol 400 IU; natural mixed tocopherols d-beta, d-gamma, d-delta 48 mg; selenium 100 µg (Now Supplements). Immediately thereafter, she reported a sensation of retrosternal pain, but this was not severe, and she went to sleep. The following morning, she experienced progressive retrosternal pain and odynophagia worse for solids than liquids. Over the next several days, her symptoms progressed, and she presented herself to the local emergency department. On review of systems, she otherwise denied any nausea, vomiting, cough, hemoptysis, or shortness of

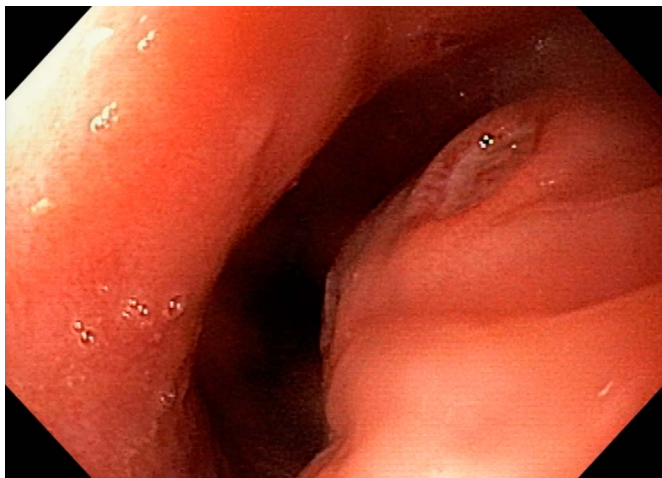


Figure 1. Esophagogastroduodenoscopy demonstrating 3 ulcers at the 30-cm mark from the incisors.

breath. There was no change in her bowel habits, abdominal pain, or constitutional symptoms. She had no history of atopic disease, allergies, recent anti-inflammatory or aspirin use, or previous history of gastroesophageal reflux symptoms.

On examination, the patient was comfortable and alert. Her vital signs were within normal limits. Her head and neck examination revealed a normal oropharynx, absence of goiter, and absence of lymphadenopathy. Her abdomen was soft, nontender, and nondistended.

Laboratory investigations demonstrated the following: hemoglobin 13.3 g/dL (12.1–15.1 g/dL) and white blood cell count 8,400/mm³ (27% neutrophils and 0% eosinophils). Her chest radiograph showed thoracic scoliosis with no evidence of perforation or air in the mediastinum. Her electrocardiography showed normal sinus rhythm with no ischemic changes.

Because of her worsening symptoms and to provide definitive diagnosis, urgent esophagogastroduodenoscopy was performed. This demonstrated 3 clean-based ulcers with surrounding erythema on opposite sides of the esophagus at the 30-cm mark from the incisors

(Figure 1). The remainder of the assessment was unremarkable. Biopsy of the ulcer and surrounding esophageal mucosa revealed squamous mucosa and fibrinopurulent exudate with inflamed granulation tissue (Figure 2). Immunohistochemical stains for cytomegalovirus, herpes simplex virus, and periodic acid–Schiff for fungal elements were negative.

Given the constellation of symptoms and signs, pill-induced esophagitis was diagnosed secondary to her DSs. She was prescribed pantoprazole 40 mg twice daily by mouth and sucralfate 4 times daily. Her diet was resumed as tolerated. Her symptoms improved in 7 days, and complete resolution occurred 10 days of symptom onset.

DISCUSSION

A case of pill-induced esophagitis after the ingestion of DSs including L-arginine, vitamin E, and selenium is presented. We have identified 6 previous cases of L-arginine-induced esophagitis and no cases of vitamin E or selenium-associated esophagitis.^{2–4} Previous cases involved 5 adolescents taking L-arginine to supplement growth and one 22-year-old cyclist using it to increase his strength and exercise performance. Outcomes were favorable for all subjects after cessation of L-arginine intake. Similar cases have been seen with other DSs including ascorbic acid.⁷

Pill-induced esophagitis often presents with retrosternal chest pain and heartburn symptoms (60%) and odynophagia (50%).⁸ Although most of these esophageal injuries are self-limited, they have been associated with mediastinal penetration, hemorrhage, and death.⁹

It has been suggested that mechanisms for the development of pill-induced esophagitis include direct irritant effects caused by contact of the medication with the esophageal mucosa leading to local acid burn or hyperosmolality or by disruption of the cytoprotective barrier.¹⁰ Prolonged contact time between the offending compound and esophageal mucosa seems to increase the likelihood of injury. Ulcers are commonly located in the middle third of the esophagus, where the aortic arch may provide extrinsic compression of the esophagus and narrow its lumen.⁹ Mucosal

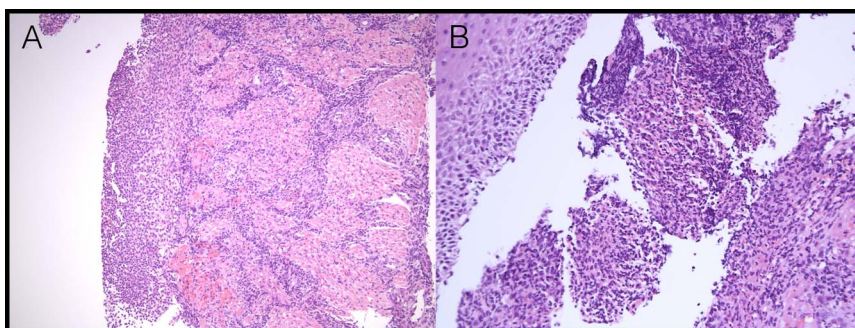


Figure 2. Biopsy of ulcer at (A) a lower magnification showing squamous mucosa with granulation tissue and at (B) a higher magnification tissue highlighting fibrinopurulent exudate with inflamed granulation tissue.

contact time is further influenced by patient position, medication form (capsule or tablet), and inadequate amounts of fluid swallowed with the medication. Common themes in all previously reported cases of L-arginine-induced esophagitis and our case are that the DS was taken with very little or no water, shortly before sleeping or with the patient in the decubitus position.

Our case demonstrates a rare side effect of commonly used DSs. However, we are limited by the inability to attribute the esophagitis because of the specific DS entity (L-arginine vs vitamin E vs selenium). Nevertheless, it highlights the need to caution and educate patients with regard to taking DSs, especially in populations where there is no evidence of benefit.^{5,11} Patients consuming DSs, in particular L-arginine as suggested by a growing number of reports, should be instructed on proper administration techniques. Patients should be advised to drink sufficient fluid to flush the capsules or tablets down to the stomach.¹² A preliminary bolus of fluid can also help to lubricate the mouth and esophageal mucosa to improve successful passage into the stomach.¹³ Finally, the supplements should be ingested in an upright position, well before retiring to bed. These simple steps may help reduce the incidence of pill-induced esophagitis and associated morbidity.

DISCLOSURES

Author contributions: C. O'Donnell drafted the manuscript and is the article guarantor. P. Tandon, V. Govardhanam, and F. Habal edited the manuscript.

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Informed consent was obtained for this case report.

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