Case Reports

Not the Yeast of Our Worries: A Case of Amphetamine-Induced Esophagitis

Simon Wu, MD[1,2], Punya Chittajallu, MD[3], Kelley Chuang, MD[1,2]

[1] Medicine, University of California, Los Angeles,
[2] Department of Medicine, Division of Hospital Medicine, VA Greater Los Angeles Healthcare System,
[3] Department of Medicine, Digestive Diseases Fellowship Program, University of California, Los Angeles

Journal of Brown Hospital Medicine
Vol. 3, Issue 3, 2024

Article Information

Keywords: Esophageal rupture, Candidal esophagitis, amphetamine-induced esophagitis

https://doi.org/10.56305/001c.119029

Submitted: May 16, 2024 EDT

Accepted: June 11, 2024 EDT

Abstract

A 68-year-old male with active amphetamine use presented to the hospital with acute emesis, odynophagia, and mid-sternal chest pain. Imaging was initially concerning for esophageal perforation. After full evaluation including barium esophagram and serial computed tomography (CT) of the chest, no esophageal perforation was confirmed. He underwent endoscopy, which identified white, circumferential plaques along the length of the esophagus. Gross appearance on endoscopy was consistent with Candidal esophagitis. Ultimately, pathology was negative for fungal elements, and esophagitis was attributed to amphetamine use. We report a rare case of amphetamine-induced esophagitis and discuss the initial management of esophageal perforation, risk factors for, and diagnostic mimickers of Candidal esophagitis.

BACKGROUND

Acute odynophagia in the context of emesis and chest pain should prompt consideration for esophageal perforation. Esophageal perforation is a medical emergency associated with high mortality rates.[1-3] It is often difficult to diagnose due to its non-specific symptoms, and often presents late in the course with mediastinitis progressed to sepsis.[1,3] Clinicians should have a low threshold to obtain imaging with contrast-enhanced computed tomography (CT). When odynophagia presents in the context of immunosuppression, clinicians should also consider Candidal esophagitis in the differential diagnosis, among other causes of infectious esophagitis. *Candida albicans* is a common colonizer of the gastrointestinal (GI) tract.[4] Candidal esophagitis often presents with dysphagia, odynophagia, and oral thrush.[4] Stimulant-induced esophagitis can mimic the appearance of Candidal esophagitis.[5,6] Although this diagnosis is exceedingly rare, clinicians should understand that there are diagnostic mimickers of common conditions like Candidal esophagitis.

CASE PRESENTATION

A 68-year-old male experiencing homelessness with a past medical history of hypertension, post-traumatic stress disorder, substance use disorder (SUD) with active methamphetamine use, and severe, longstanding gastroesophageal reflux disease (GERD) presented to the hospital with acute emesis, odynophagia, and mid-sternal chest pain. Three days prior to admission, he experienced a sudden onset of sharp, mid-sternal chest pain following an episode of coffee-ground-appearing emesis. The chest pain was episodic and exacerbated by swallowing. He also described acute dysphagia and odynophagia with a sensation of food impaction after eating solids. A review of systems was notable for sore throat, subjective fever, and chills over the same period. Otherwise, he denied worsening chest pain with exertion, night sweats, unintentional weight loss, abdominal pain, or dysuria.

Of note, he had a longstanding history of severe GERD complicated by episodes of food impaction necessitating hospital admission, most recently three months prior. Esophagogastroduodenoscopy (EGD) during that admission revealed poor esophageal motility with retained food and liquid in the esophagus. Appearance of the esophagus was consistent with Los Angeles grade B esophagitis.[7] Features of eosinophilic esophagitis were not seen on EGD. He was discharged with a prescription of pantoprazole 40 milligrams twice daily and famotidine 10 milligrams twice daily with a plan to follow up in the gastroenterology clinic. In the interim, he was lost to follow-up and had intermittent medication adherence in the context of ongoing illicit drug use.

On initial presentation, vital signs were within normal limits except for blood pressure of 168/96 mmHg. The physical exam was benign other than mild distress while swallowing; heart sounds were normal, and chest wall crepitus was absent during palpation. Laboratory studies, including a chemistry panel, complete blood count, and urinalysis, were notable for leukocytosis with 15,830 white blood cells/μL (reference range: 4,500 – 11,000/μL), hemoglobin 18.1 g/dL (reference range: 13.3 – 17.7 g/dL), and serum bicarbonate 32 mmol/L (24 – 31

mmol/L). A urine drug screen was qualitatively positive for amphetamines, with positivity for methamphetamine on confirmatory quantitative testing. An electrocardiogram and a high-sensitivity troponin did not show evidence of cardiac ischemia. A portable chest X-ray was unremarkable. A computed tomography (CT) scan with intravenous contrast of his thorax then revealed severe wall thickening and fluid opacification of the esophagus. Amorphous fluid was seen extending circumferentially around his distal esophagus and descending aorta, which raised concern for esophageal perforation. There was no evidence of pneumomediastinum or pleural fluid.

Due to concern for esophageal perforation, thoracic surgery was consulted, which recommended keeping the patient strictly nil per os (NPO), intravenous fluids, and empiric broad-spectrum antimicrobial coverage with piperacillin-tazobactam and fluconazole. Gastroenterology recommended an urgent Gastrografin esophagram, with plans to perform an EGD afterward. Esophagram did not show extravasation of oral contrast. On hospital day 2, the patient elected to self-discharge prematurely to manage urgent financial affairs. He returned for readmission on the same day after drinking one liter of a sports drink without recurrence of odynophagia or emesis. He subsequently had an interval CT scan with oral contrast of the chest, which again showed persistent but decreased concentric esophageal wall thickening without extravasation of oral contrast. Antibiotics and antifungal therapy were stopped, and he was allowed a liquid diet while awaiting EGD.

On hospital day 4, the patient underwent EGD under monitored anesthesia care (initially delayed by anesthesiology's request to allow a washout period for amphetamines). Diffuse circumferential white thick plaques were visualized along the entire esophagus (**Figure 1**). There was no evidence of a mass, reflux esophagitis, or Barrett's esophagus. Biopsies were sent, but the patient was preliminarily diagnosed with severe Candidal esophagitis. He was started on fluconazole, and serology testing for human immunodeficiency virus (HIV) was sent. He had not taken any corticosteroids recently. His hemoglobin A1c was within normal limits. When HIV serologies returned nonreactive, the patient was discharged to transitional housing with a referral to an infectious disease clinic to discuss further testing for an immunodeficiency state.

One week later, pathology from his gastric and esophageal biopsies returned with no fungal elements seen on Grocott Methenamine Silver (GMS-F) and Periodic Acid and Schiff (PAS-F) special stains and no evidence of malignancy. The pathologic appearance of denuded mucosa of the esophagus with ulcer and marked inflammation, in the context of the patient's methamphetamine use, suggested a diagnosis of methamphetamine-induced acute esophagitis. This appeared to be a new finding compared to EGD three months prior. Two

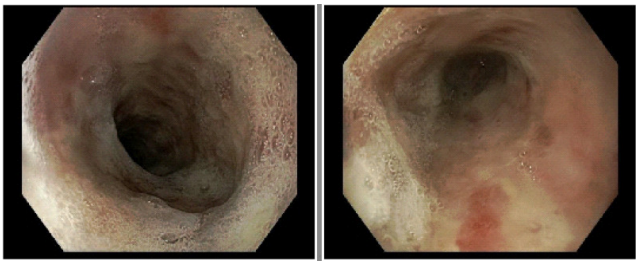

Figure 1A. Endoscopic view of the esophagus showing diffuse circumferential white thick plaques along the extent of the esophagus.

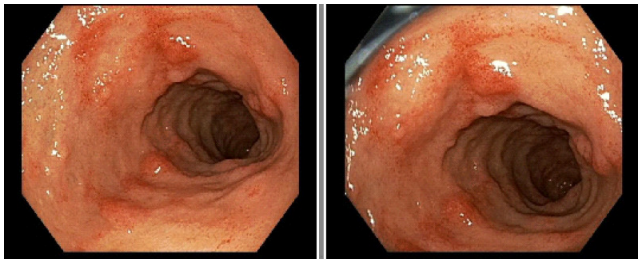

Figure 1B. Endoscopic view of the duodenum showing a few areas of erythema and nodularity.

weeks later, he was readmitted with recurrent coffee-ground emesis and melena, resulting in iron deficiency anemia. Repeat EGD was deferred as his bleeding stopped prior to admission. He denied methamphetamine use in the interim. After a period of observation during which his bleeding self-resolved, he was discharged back to transitional housing with a prescription for maximal proton pump inhibitor (PPI) therapy and referral to a substance use disorder (SUD) clinic.

DISCUSSION

Our patient initially presented with concern for esophageal rupture, which requires prompt medical attention given its high mortality risk (10-60%).[1-3] Spillage of digestive contents into the peri-esophageal spaces, such as the mediastinum or pleural space, can quickly progress to sepsis if left untreated.[1] Diagnostic delay for esophageal rupture is unfortunately common due to often non-specific symptoms, including chest/neck pain, dysphagia, and odynophagia, though the clinical presentation may be more severe if mediastinitis has progressed to sepsis.[1,3] Risk factors for rupture include hyperemesis, recent endoscopic procedures, malignancy, foreign body impaction, caustic ingestion, seizure, and trauma.[1,2]

When a patient presents with possible esophageal rupture, clinicians must have a low threshold to obtain further imaging with contrast-enhanced computed tomography (CT).[1,3] Compatible findings include extraluminal contrast, mediastinal air, periesophageal fluid collections, and esophageal thickening.[3] An esophagram with con-

trast can provide further information about the exact location of perforation.[1]

Keeping the patient NPO and starting empiric broad-spectrum antibiotics are also necessary steps in the initial management.[1] Empiric coverage should target common gut flora (e.g., gram-negative and anaerobic organisms). Some controversy surrounds which patients also require empiric anti-fungal coverage (e.g., fluconazole). In a report by Elsayed et al., the majority of 27 patients with confirmed esophageal rupture developed invasive Candidal infections, leading to their recommendation to start empiric anti-fungal therapy in all cases of rupture.[8] However, this recommendation was based on a relatively small retrospective cohort, so its generalizability is unclear.[8] In addition to the above, clinicians should consult with surgical and gastrointestinal (GI) specialists to determine the patient's candidacy for either primary surgical repair or endoscopic treatments, such as stenting.[1] Fortunately, after extensive workup, our patient was confirmed not to have esophageal rupture; we attributed his initial CT findings to severe localized inflammation of his esophagitis.

As part of this workup, he did undergo EGD, which revealed several whitish plaques on his esophageal mucosal lining, raising suspicion for candida esophagitis. Candidal esophagitis is a condition most often caused by Candida albicans, a common colonizer of the GI tract. This often presents with dysphagia, odynophagia, and simultaneous oral thrush. Though the preliminary diagnosis is often made based on its classic appearance on endoscopy, biopsies are still recommended in order to confirm the presence of invasive yeasts and pseudohyphae.[4]

Our patient's preliminary diagnosis of Candidal esophagitis was unexpected, as it is typically associated with states of significant immunosuppression, such as in human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), hematologic malignancies, and chronic corticosteroid use. It is rarely diagnosed in immunocompetent patients.[4] In the absence of known immunosuppression, a workup for HIV should be pursued. A detailed review of the patient's medication list is also recommended. In particular, PPI and histamine (H2)-blockers have been implicated as risk factors for Candidal esophagitis in the immunocompetent host.[4, 9,10] Proposed mechanisms for this association center around decreased gastric acid secretion's effects on C. albicans' pathogenicity or disrupting GI tract flora.[4] While whitish mucosal plaques can be highly suggestive of esophageal candidiasis, there are other diagnoses that may share the same appearance on endoscopy.

These diagnostic mimickers include other infections (e.g., actinomycosis), malignancy, eosinophilic esophagitis, and parakerotosis.[11-13] Our case presents another diagnosis to consider in the differential when Candidal esophagitis is suspected in the proper clinical context: amphetamine-induced esophagitis. Amphetamine use has well-known effects on the oral cavity, including dental caries and oral candidiasis, likely due to drug-induced xerostomia.[14] Complications elsewhere in the GI tract include peptic ulcer disease and ischemic colitis.[15-19] The pathophysiology behind these presentations is likely due to the sympathomimetic effects of amphetamines causing vasoconstriction and subsequent mucosal ischemia. Similar presentations have been attributed to cocaine use, another substance with sympathomimetic properties.

Amphetamine-induced esophagitis is much less frequently described in the literature. Lyles et al. published a case report of a young girl who developed acute esophagitis, with EGD showing erythematous and friable patches; there was no identifiable cause besides her urine drug screen being positive for methamphetamines.[5] This patient likely ingested an edible containing the drug, so it is unclear if her mechanism of injury was via direct drug-to-mucosa contact or triggered by catecholamine release after drug digestion and metabolism. Chewing Khat leaves, a naturally found simulant with a chemical structure similar to amphetamine, has also been associated with esophagitis.[6]

Our patient reported smoking methamphetamine as his primary route of use. His histopathologic finding of an ulcerated esophageal mucosa along with recent methamphetamine use, supports the diagnosis of amphetamine-induced esophagitis, likely due to vasoconstriction and localized tissue ischemia as discussed above. His history of GERD was considered as another contributing cause, though the diffuse location of our patient's patches throughout the entirety of his esophagus argued against GERD, which usually involves primarily distal esophagitis.

Although not much is known about this clinical entity, the management of amphetamine-induced esophagitis consists of supportive care with intravenous fluids and analgesia. Vasodilators can be used to manage associated severe hypertension. PPIs should be started to protect the esophageal mucosa from further insult, though the optimal duration of therapy is unclear. Patients should be counseled to abstain from further amphetamine use and referred for substance use treatment when available.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Dennis Jensen (gastroenterology) for supervising the acquiring of endoscopic images, and Dr. Ying Zhao (pathology) for providing diagnostic input on the biopsy specimens.

DISCLOSURES/CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

Corresponding Author

Kelley Chuang, M.D.
VA Greater Los Angeles Healthcare System
11301 Wilshire Blvd. Building 500 Mail Code 111
Los Angeles, CA 90073
Phone: 310-478-3711, ext. 44003
Email: kelleychuang@mednet.ucla.edu

REFERENCES

1. Chirica M, Kelly MD, Siboni S, Aiolfi A, Riva CG, Asti E, et al. Esophageal emergencies: WSES guidelines. *World J Emerg Surg*. 2019;14(1):26. doi:10.1186/s13017-019-0245-2

2. Shahriarirad R, Karoobi M, Shekouhi R, Ebrahimi K, Ranjbar K, Amirian A, et al. Esophageal perforation etiology, outcome, and the role of surgical management – an 18-year experience of surgical cases in a referral center. *BMC Surg*. 2023;23(1):177. doi:10.1186/s12893-023-02080-w

3. Lampridis S, Mitsos S, Hayward M, Lawrence D, Panagiotopoulos N. The insidious presentation and challenging management of esophageal perforation following diagnostic and therapeutic interventions. *J Thorac Dis*. 2020;12(5):2724-2734. doi:10.21037/jtd-19-4096

4. Nassar Y, Eljabbour T, Lee H, Batool A. Possible Risk Factors for Candida Esophagitis in Immunocompetent Individuals. *Gastroenterol Res*. 2018;11(3):195-199. doi:10.14740/gr1019w

5. Lyles JL, Wadhwani SI, Bolton SM, Mouzaki M. Methamphetamine-induced Acute Esophagitis in a 16-Year-old Girl. *J Pediatr Gastroenterol Nutr*. Published online April 2020. doi:10.1097/MPG.0000000000002644

6. Al-Habori M. The potential adverse effects of habitual use of Catha edulis (khat). *Expert Opin Drug Saf*. 2005;4(6):1145-1154. doi:10.1517/14740338.4.6.1145

7. Genta RM, Spechler SJ, Kielhorn AF. The Los Angeles and Savary-Miller systems for grading esophagitis: utilization and correlation with histology. *Dis Esophagus Off J Int Soc Dis Esophagus*. 2011;24(1):10-17. doi:10.1111/j.1442-2050.2010.01092.x

8. Elsayed H, Shaker H, Whittle I, Hussein S. The impact of systemic fungal infection in patients with perforated oesophagus. *Ann R Coll Surg Engl*. 2012;94(8):579-584. doi:10.1308/003588412X13373405388095

9. Kochhar R, Singh S, Talwar P, Mehta SK. Candidiasis after cimetidine therapy. *Gastrointest Endosc*. 1988;34(3):283-284. doi:10.1016/S0016-5107(88)71336-X

10. Kimchy AV, Ahmad AI, Tully L, Lester C, Sanghavi K, Jennings JJ. Prevalence and clinical risk factors for esophageal candidiasis in non-human immunodeficiency virus patients: A multicenter retrospective case-control study. *World J Gastrointest Endosc*. 2023;15(6):480-490.

11. Palmitessa V, Cuppone R, Monno R, Fumarola L, Lippolis A. A case report of esophageal actinomycosis in an immunocompetent patient and review of the literature. *New Microbiol*. 2019;42(1):55-60.

12. Yamazaki K, Kojima K, Iwata H, Kushima R. Eosinophilic Esophagitis Mimicking Candida Esophagitis. *Intern Med*. 2019;58(6):887-887. doi:10.2169/internalmedicine.1933-18

13. Romana B, Hundal J, Yousef M, Kuwajima-Smith V, Bechtold M, Tahan V. Esophageal Parakeratosis: Not All White Plaques Are Candida. *Am J Gastroenterol*. 2018;113(Oct):S993-994. doi:10.14309/00000434-201810001-01740

14. Balali-Mood M, Sinclair RD, Darchini-Maragheh E, Etemad L. Mucocutaneous alterations and complications in amphetamine abusers: a narrative review. *Cutan Ocul Toxicol*. 2023;42(4):219-231. doi:10.1080/15569527.2023.2235425

15. Turan B, Eroğlu H, Sultanoğlu B, Demirbakan K. Methamphetamine-related peptic ulcer perforation: a growing medical concern. *Ulus Travma Ve Acil Cerrahi Derg Turk J Trauma Emerg Surg TJTES*. 2023;29(12):1357-1363. doi:10.14744/tjtes.2023.53146

16. Anderson JE, Brown IE, Olson KA, Iverson K, Cocanour CS, Galante JM. Nonocclusive mesenteric ischemia in patients with methamphetamine use. *J Trauma Acute Care Surg*. 2018;84(6):885-892. doi:10.1097/TA.0000000000001855

17. Green P, Battersby C, Heath R, McCrossan L. A fatal case of amphetamine induced ischaemic colitis. *Ann R Coll Surg Engl*. 2017;99(7):e200-1. doi:10.1308/rcsann.2016.0350

18. Panikkath R, Panikkath D. Amphetamine-related ischemic colitis causing gastrointestinal bleeding. *Proc Bayl Univ Med Cent*. 2016;29(3):325-326. doi:10.1080/08998280.2016.11929455

19. Choi K, Imrie A, Lourie R, Cross T. Intestinal ischemia due to methamphetamine use: A case report. *Int J Surg Case Rep*. 2019;58:11-13. doi:10.1016/j.ijscr.2019.03.061