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Doxycycline-induced esophagitis: A case report on a preventable adverse event and review of strategies

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Abstract
Doxycycline, a widely prescribed antibiotic, is a leading cause of drug-induced esophagitis resulting from direct chemical injury to the esophageal mucosa. We present the case of a 24-year-old male on doxycycline for acne who developed acute retrosternal chest pain and severe odynophagia. His symptoms began shortly after ingesting the medication with minimal fluid before lying down. After excluding cardiopulmonary etiologies, an urgent upper endoscopy revealed a distinct ulcer in the mid-esophagus, confirming the diagnosis. The offending drug was discontinued, and supportive care with a proton pump inhibitor was initiated, leading to a rapid and complete resolution of symptoms. This case underscores that doxycycline-induced esophagitis is an entirely preventable iatrogenic condition. It highlights the critical importance of patient counseling by clinicians on proper medication administration specifically, taking pills with a full glass of water and remaining upright to prevent this painful adverse event and its associated healthcare burden.

Keywords: Doxycycline, healthcare burden, etiologies, strategies, preventable adverse

Introduction
Doxycycline, a semisynthetic second-generation tetracycline antibiotic, is widely utilized in clinical practice for its broad-spectrum activity and favorable pharmacokinetic profile [1]. It is effective against a variety of pathogens, making it a first-line treatment for respiratory tract infections, acne vulgaris, urinary tract infections, and certain sexually transmitted diseases [2]. Unlike older tetracyclines, its absorption is minimally affected by food, and it has a longer half-life, which allows for once or twice-daily dosing, thereby enhancing patient adherence [3]. While generally considered safe and well-tolerated, doxycycline is not without potential adverse effects. The most common side effects are gastrointestinal, including nausea and diarrhea; however, a more direct and injurious effect on the esophageal mucosa, known as pill-induced esophagitis, is a significant but often overlooked complication [4].
Pill-induced or drug-induced esophagitis refers to direct injury to the esophagus from a medication [3]. This occurs when a pill remains in contact with the esophageal mucosa for an extended period, leading to localized inflammation, erosion, and ulceration [5]. Several factors contribute to this phenomenon, including the chemical properties of the drug itself, the volume of fluid taken with the medication, and the patient's posture after ingestion [6]. Doxycycline is consistently cited as one of the most common culprits of pill esophagitis due to its acidic nature and ability to cause caustic injury upon prolonged contact with the esophageal lining [7]. Despite its prevalence, this condition is frequently underdiagnosed, as its symptoms of chest pain and painful swallowing can mimic more common conditions like Gastroesophageal Reflux Disease (GERD) or even acute coronary syndrome [8]. This case report describes a young male who developed severe esophagitis after taking doxycycline with insufficient fluid, highlighting the classic presentation, diagnostic process, and the critical role of patient education in preventing this iatrogenic injury.

Case Presentation
A 24-year-old male with no significant past medical history presented to the emergency department with a 12-hour history of severe retrosternal chest pain, odynophagia (painful swallowing), and dysphagia to both solids and liquids.

The patient reported that he had been prescribed doxycycline 100 mg twice daily for the treatment of acne vulgaris by his dermatologist and was on his sixth day of treatment. He recalled taking his dose on the fifth day with a very small amount of water before lying down. Symptoms of odynophagia began to develop gradually thereafter, culminating in the intense, non-radiating chest pain that prompted his visit. The patient denied any history of melena, hematemesis, fever, chills, or previous gastrointestinal issues.

Upon presentation, the patient was afebrile with a temperature of 37.0°C. His vital signs were stable, with a heart rate of 80 beats per minute, a respiratory rate of 22 breaths per minute, and blood pressure of 104/62 mmHg. Physical examination was largely unremarkable, except for notable epigastric tenderness on deep palpation. Initial laboratory investigations revealed a mild leukocytosis with a white blood cell (WBC) count of 13,700/µL and a hemoglobin level of 11.2 mg/dL. A 12-lead electrocardiogram (ECG) was performed to rule out a cardiac etiology for the chest pain and showed a normal sinus rhythm without any ischemic changes. A chest X-ray was also unremarkable, showing no acute cardiopulmonary abnormalities.

Given the high suspicion of an esophageal pathology, the patient was admitted for further evaluation and management. He was made nil per os and initiated on intravenous pantoprazole 40 mg twice daily to suppress gastric acid, along with supportive care including intravenous fluids and analgesics (Paracetamol) as needed. An urgent upper gastrointestinal endoscopy was performed, which revealed a discrete, healing ulcer in the mid-esophagus, spanning approximately 3 cm in length (from 26 to 29 cm from the incisors). There was surrounding mucosal erythema and edema, but no signs of active bleeding or perforation. These findings were pathognomonic for drug-induced esophagitis.

Following the definitive diagnosis, doxycycline was immediately discontinued. The patient's diet was gradually advanced, starting with clear liquids, which he tolerated well. His symptoms of odynophagia and chest pain resolved rapidly over the next 48 hours. He was able to tolerate a normal diet without difficulty by the third day of admission. The patient was discharged on the fourth day in a stable and asymptomatic condition. He was prescribed a course of oral pantoprazole 40 mg once daily for two weeks and was given strict instructions regarding proper medication administration in the future. He was also scheduled for a follow-up appointment with his dermatologist to discuss alternative treatments for his acne.

Discussion

This case illustrates a classic, yet frequently missed, presentation of doxycycline-induced esophagitis in a young, otherwise healthy individual. Pill esophagitis, first described by Pemberton in 1970 in a patient taking potassium chloride, is a direct chemical injury to the esophageal mucosa [9]. While more than 100 different medications have been implicated, antibiotics, particularly tetracyclines, non-steroidal anti-inflammatory drugs (NSAIDs), potassium chloride, and bisphosphonates are the most common offenders [10]. Among antibiotics, doxycycline is consistently reported as the leading cause, accounting for a significant percentage of all cases [11, 12]. The mechanism of injury is multifactorial but is primarily due to a direct caustic effect. Doxycycline hyclate is highly acidic; when the capsule dissolves and the contents are released, the low pH creates a localized chemical burn if transit through the esophagus is delayed [13]. This acidic environment can lead to mucosal necrosis, inflammation, and ulceration. Gelatin capsules, the common formulation for doxycycline, can become sticky when moistened, increasing their adherence to the esophageal mucosa and prolonging contact time, thereby exacerbating the injury [14].

The clinical presentation of pill esophagitis is typically characterized by the sudden onset of retrosternal chest pain, odynophagia, and/or dysphagia, usually occurring several hours after taking the medication [15]. As seen in our patient, the symptoms can be severe enough to mimic a myocardial infarction, often leading to extensive cardiac workups that are ultimately negative [16]. A thorough medication history is the most crucial element in reaching the correct diagnosis. Key historical details include not only which medications are being taken but also how they are being administered.

Our patient's admission of taking the capsule with very little fluid just before bed is a textbook risk factor [17]. Ingestion of medication with an inadequate volume of fluid (<100 mL), in a supine or recumbent position, and just before sleep are the three most significant risk factors for delayed esophageal transit and subsequent esophagitis [18]. The supine position impairs the normal gravitational and peristaltic clearance of the esophagus, allowing a pill to lodge, particularly at sites of natural physiological narrowing such as the aortic arch or the gastroesophageal junction [19]. The diagnosis of pill-induced esophagitis is primarily clinical, based on the characteristic history. However, upper gastrointestinal endoscopy is the gold standard for confirming the diagnosis, assessing the severity of the injury, and ruling out other pathologies [20]. Endoscopic findings typically include one or more discrete, "kissing" ulcers in the mid-esophagus, often with surrounding normal mucosa [21]. This location corresponds to the physiological narrowing caused by the compression from the aortic arch and left mainstem bronchus, a common site for pill retention [22]. In our case, the endoscopic finding of a healing ulcer spanning 26 to 29 cm from the oral cavity was definitive. While biopsy is not always necessary, it can be useful in atypical cases to exclude other causes of esophagitis, such as eosinophilic, infectious (e.g., Candida, CMV, HSV), or malignant etiologies [23].

The management of doxycycline-induced esophagitis is straightforward and highly effective. The cornerstone of treatment is the immediate withdrawal of the offending agent [24]. This single intervention leads to the resolution of symptoms in the vast majority of patients within a few days, as demonstrated in our case. Supportive care is aimed at symptom relief and promoting mucosal healing. This includes the use of acid-suppressive therapy, typically with proton pump inhibitors (PPIs) or H2-receptor antagonists, to reduce reflux of gastric acid that could further irritate the injured mucosa [25]. While evidence for their efficacy in accelerating healing from direct pill injury is limited, they are widely used and considered beneficial [26]. A liquid or soft diet may be necessary initially until the odynophagia subsides. More potent local anesthetic agents like viscous lidocaine can be used for severe pain, but caution is advised due to the risk of aspiration. Complications such as severe hemorrhage, perforation, or stricture formation are rare but

can occur, especially in cases of delayed diagnosis or with particularly caustic agents like bisphosphonates [20]. Fortunately, the esophageal mucosa has a remarkable capacity for healing, and with the removal of the offending agent, most injuries resolve completely without long-term sequelae within one to two weeks [27].

The most critical aspect of pill-induced esophagitis is its preventability. This iatrogenic condition can be almost entirely avoided through proper patient education by both prescribing physicians and dispensing pharmacists [28]. Patients should be explicitly counseled to take potentially caustic medications, like doxycycline, with a full glass of water (at least 150-200 mL) and to remain in an upright position for at least 30 minutes after ingestion [29]. Taking medication well before bedtime is also a crucial recommendation, as this allows sufficient time for the pill to pass into the stomach before the patient assumes a recumbent position. This simple counseling can significantly reduce the incidence of a painful and distressing condition that can lead to unnecessary emergency department visits, invasive procedures, and hospitalizations. The case of our patient underscores a failure in this educational step, which is a common theme in reported cases of pill esophagitis [20]. It serves as a powerful reminder for all healthcare professionals to prioritize medication counseling as an integral part of the prescribing process.

Conclusion

Doxycycline-induced esophagitis is a common but preventable adverse drug event characterized by acute retrosternal chest pain and odynophagia. The diagnosis relies on a high index of clinical suspicion and a detailed medication history, focusing on the method of administration. As this case demonstrates, taking doxycycline capsules with insufficient fluid and in a recumbent position are primary risk factors for esophageal injury. Endoscopy remains the definitive diagnostic tool, typically revealing localized ulcers in the mid-esophagus. Management is centered on withdrawing the offending drug and providing supportive care with acid-suppressive therapy, which generally leads to rapid symptom resolution and complete mucosal healing.

The true importance of this case lies not in its clinical rarity but in its educational value. It highlights a significant gap in patient communication and emphasizes that the responsibility of a healthcare provider extends beyond simply writing a prescription. Proactive counseling on the proper administration of medications specifically, to take capsules or tablets with ample water while remaining upright is a simple, no-cost intervention that can effectively prevent this painful iatrogenic condition. Increased awareness among clinicians and pharmacists is essential to reduce the incidence of pill esophagitis, thereby preventing patient distress, reducing unnecessary diagnostic investigations for more serious conditions, and minimizing healthcare costs associated with emergency visits and hospital admissions. Ultimately, this case reaffirms that patient education is a cornerstone of safe and effective pharmacotherapy.

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Authors' contributions

Both authors have contributed equally to data collection, interpretation, and manuscript preparation

Conflict of interest

The authors declare no conflict of interest

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