

Doxycycline-Induced Esophageal Ulceration: Report of two cases

DOKSISIKLINE BAĞLI ÖZOFAGUS ÜLSERASYONU. İKİ OLGU SUNUMU

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Summary

In this study, two female patients with doxycycline-induced esophageal ulcer were presented. The first patient, 25-year-old, was referred to us with dysphagia, severe odynophagia and retrosternal chest pain. Second, 29-year-old, had permanent pain in the midsternal region, exacerbating on swallowing. In these patients, endoscopy revealed ulcers 28, and 30 cm from the teeth. Using liquid sucralphate the patients recovered in a few days.

Key Words: Drug-induced esophageal injury, Doxycycline, Sucralphate

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Özet

Doksisikline bağlı olarak özofagus ülseri gelişen iki olgu sunulmuştur. Yirmibeş yaşındaki ilk olgu, disfaji, şiddetli odinofaji ve retrosternal göğüs ağrısı ile; 29 yaşındaki ikinci olgu ise midsternal bölgesinde duyduğu, yutma ile artan sürekli ağrı nedeniyle gönderilmişti. Bu hastalarda endoskopide özofagus- ta 28 ve 30. cm'lerde ülser saptandı. Tedavilerinde sukralfat kullanılarak semptomları birkaç gün içinde kayboldu.

Anahtar Kelimeler: İlaça bağlı özofagus lezyonu, Doksisiklin, Sukralfat

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Doxycycline is a tetracycline antibiotic that has been reported to be responsible of great majority of patients with drug-induced esophageal injury. Kikendall (1) realized an extensive literature review on drug-induced esophageal injury cases, and reported nearly 100 different medications associated with 979 cases of esophageal damage. Antibiotics and antivirals have been implicated in 479 of 979 reported cases of pill esophagitis, nearly half of all reported cases. Coates et al (2) reported that drug-induced esophagitis is related to doxycycline in 43% cases. The true prevalence of drug-induced esophageal injury is not well known due to unreported cases. In a prospective study, Alvares et

al (3) found that 40% of patients receiving doxycycline or indomethacin developed esophageal injury.

In this study we describe two patients in whom esophageal ulcers developed after they ingested doxycycline preparations.

Case 1

A 25-year-old woman had had acne vulgaris for which she started taking doxycycline, 100 mg once daily, one-month before the onset of her symptoms. She was referred to us with dysphagia, severe odynophagia and retrosternal chest pain, radiating to her back during four days, despite discontinuation of the doxycycline and institution of H2 blocker, and antacids. Her pain was exacerbated with either solid or liquid ingestion, but was constantly present. She noticed no improvement with changes in position. She usually took medications just before bedtime, and with a small amount of water. She had no history of esophageal disease.

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Findings on physical examination, ECG, and chest X ray were normal. Endoscopy showed a discrete ulcer 28 cm from incisors with normal mucosa at the rest of the esophagus. Previous medications was stopped and intra-venous fluids and liquid sucral-fate, 1 g qid was started. After three days, she was able to take oral fluids and a soft diet. Her symptoms completely disappeared on 5th day of hospitalization. Repeat endoscopy one week later revealed disappearing the ulcer.

Case 2

A 29 yr old woman was under treatment of doxycycline for several days, 100 mg twice a day, for pelvic inflammatory disease. She applied for complaints of a permanent pain in midsternal region, exacerbating on swallowing, for five days. She had taken last dose of doxycycline six days ago, with minimal water before going to bed. After the last dose, in the early morning she awoke with midsternal pain. Although, she was already using omeprazole and cisapride, started four days ago, symptoms insistently continued. No history of esophageal disease was elicited. Her chest X ray, ECG and cardiac enzymes were normal. Endoscopy revealed a discrete ulcer 30 cm from the teeth with normal mucosa both above and below the area of the ulcer. She did not accept hospitalization. The patient was recommended liquid diet and sucralfate, 1 g qid. Her symptoms completely resolved four days after onset the treatment. The patient did not allow a control endoscopy.

Discussion

In the literature, the clinical presentations of doxycycline-induced esophageal injury have usually been described as dysphagia, pain on swallowing, a sudden onset and continuous retrosternal/midsternal pain (1-4). As a difference, Tzianetas et al (5) have reported a patient who had suffered from hiccups, after a single dose of doxycycline, due to endoscopically revealed esophageal ulcer that penetrated the mucosa. Our cases are young women. It is interesting that females are more frequent than males in reported cases of doxycycline-induced esophageal injury and lesions occur more frequently in young or middle aged individuals (1, 2, 4). Endoscopically, the ulcers are either single or multiple and are sometimes circumferential (1-7).

The mechanism of the ulceration may be multifactorial. It is reported that doxycycline- and other medication-induced esophageal injury patients generally gave a history of having taken their pills with little or no fluid or just before going to bed, likely in our patients (1-8). It has been shown that the transit of medications from mouth to the stomach may be delayed significantly if they are ingested with minimal or no water, while the patient is in the supine position (6). Decreased swallowing and salivation, as well as a slowing in esophageal peristalsis, have been noted during sleep (7). On the other hand, the esophageal injuries were 22 times more frequent with capsules than with tablets, because of their easier adhesion to the esophageal surface (7). Pill lodgement in the esophagus with subsequent local cytochemical effects of doxycycline has an important role in esophagel ulceration. Doxycycline produces an acid environment when mixed with water. In addition, tissue damage can occur as a result of doxycycline accumulation in the epithelial cells of the esophagus and its inhibition of protein synthesis (8).

In the most cases, doxycycline-induced esophageal injury resolves without sequela and symptoms disappear several days after discontinuation of the drug; on rare occasions, they persist as long as six weeks (1-9). Orr et al (10) have described a 35-year-old woman, as a single case in the literature, with esophageal perforation secondary to the use of doxycycline. Sucralfate is bound selectively to diseased mucosa and to necrotic tissue in an ulcer base and stimulates mucosal generation and release of prostaglandins. In cases presented here, it was used, and the patients recovered markedly in a few days.

Physicians should be aware of this possible effect of doxycycline and it must be recommended to administer this medication with adequate liquid and a considerable period before bedtime.

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