

Case Report

## Esophagitis Caused by Ciprofloxacin; A Case Report and Review of the Literature

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### ABSTRACT

Ingestion of ciprofloxacin can be associated with esophagitis and esophageal ulcer. We report a 46-year-old man with odynophagia and dysphagia following ciprofloxacin ingestion, with a glance on diagnosis and treatment. Also, we propose recommendations for prevention of drug-induced esophagitis, according to shape, size, formulation and their etiologic role on esophagitis.

**Keywords:** Ciprofloxacin, Drug-induced esophagitis, Endoscopy

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### INTRODUCTION

Esophagitis of varying degrees and significance is caused by reflux, infections, radiation, and ingestion of chemical agents. Pemberton reported the first case of medication-induced esophageal injury in 1970.(1), Since that time many case reports regarding esophageal injuries caused by drugs have been published;(2-10), however, many physicians and even more patients are not aware of this problem.(11, 12)

Ingestion of ciprofloxacin can be associated with esophagitis and esophageal ulcer(13) and we report a rare case of ciprofloxacin-induced pill-esophagitis. We also discuss about the role of posture, amount of fluid which was drunk in pursuit of medication and risk factors, as well as the diagnosis, prevention and management in the cases of pill-esophagitis.

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### CASE REPORT

A case of esophagitis associated with the use of ciprofloxacin is described. A 46-year-old male university professor with no past history of heartburn or dyspepsia, suffered from odynophagia, dysphagia, globus sensation and retrosternal chest pain since 2 weeks before admission to gastrointestinal clinic. The patient started taking ciprofloxacin (500 mg orally, every 12 hours) for chronic prostatitis from 4 weeks ago by taking the drug with a glass of tap water at 7 am and 7 pm both in upright position.

Our accessible Ciprofloxacin is either round, film-coated with diameter of 13 mm or oval, film-coated 20×7 mm pills.

He took oval capsules during the first week but changed them to the round ones for the second week. The complications began gradually 2-3 days after this change and took a week to reach the peak severity (6 out of 10), but remained at this level thereafter. It was not fluctuating. He described his complaint as a bulging foreign body which he could localize as an apparent

compressing point at the middle of the neck just below thyroid cartilage. It was not radiating. He then felt discomfort while taking the medication or swallowing saliva. Although his discomfort was present between swallows, it was not considerable. He also experienced retrosternal-burning pains. Swallowing solid foods was more laborious than swallowing liquids. So, he preferred foods in liquid form but didn't limit the amount of food. The patient did not mention any weight loss during these weeks. His wife, who is a doctor, prescribed Aluminium Mg, Ranitidine and Digestive pills for his heartburn but he didn't feel any relief.

There were no history of immunosuppressives intake, HIV infection, homosexuality, diabetes, malignancy or other systemic diseases. Laboratory studies revealed normal CBC, ESR, FBS, U/A, BUN, Cr, cholesterol, triglycerides and stool exam. HIV test was negative. After admission to our institution, endoscopy was performed with a PENTAX EPM-3300 using EG 2940 endoscope.

Endoscopic findings indicated a kissing ulcer of the upper third of the esophagus with surrounding inflammation compatible with chemical esophagitis. Ulcers were 8×3 mm and 10×5 mm, superficial and white base with no visible vessel or bleeding. No thickening of the esophageal wall or narrowing of the lumen was identified (Figures 1-3). Stomach and duodenum were normal. No biopsy specimens were obtained.

Following the procedure, the patient was advised to discontinue Ciprofloxacin and to take Omeprazole (20 mg, bid). After 2 months all symptoms were disappeared except heartburn. He was advised to continue Omeprazole. One month later he had no more complaint despite self-discontinuation of Omeprazole.

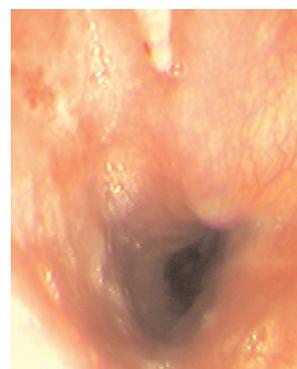
The patient did not permit re-endoscopy and biopsy but one year follow up showed no more esophageal or systemic symptoms.

## DISCUSSION

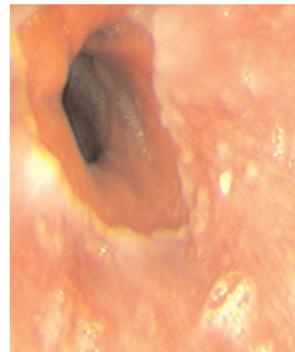
Pill esophagitis is primarily the result of a chemical reaction between the released contents of a pill and the lining of the esophagus. History and



**Figure 1:** Esophagus, 1/3 Upper; Drug induced esophagitis (Kissing ulcer).



**Figure 2:** Esophagus, 1/3 Upper; Drug induced esophagitis (Kissing ulcer).



**Figure 3:** Esophagus, 1/3 Lower, LES, Z-line; Normal.

clinical characteristics of these cases suggest that the medications failed to transit the esophagus and acted locally to produce esophagitis. Pressure necrosis may also play a role in the causation of this disorder.<sup>(14)</sup>

Despite high prevalence of drug-induced esophagitis, Ciprofloxacin-associated esophageal ulceration has not been described in detail. As far as we searched there is only one report of Ciprofloxacin induced esophagitis<sup>(1)</sup>, and this is

the second one.

Our report emphasizes that even medications not known to cause esophagitis may produce considerable esophageal damage. It is important for the physicians as well as patients to be aware of drug-induced esophagitis, especially when someone is suspected to have reflux, stricture, tumor or esophageal motility disorder.

### ***Differential diagnosis and complications***

The presenting symptom of this disorder is odynophagia (pain on swallowing), with or without dysphagia. The odynophagia is sudden in onset. Although a history of difficulty swallowing a pill followed by pain on swallowing is most suggestive of the disorder, this history may not be present.<sup>(14)</sup> The differential diagnosis of pill esophagitis includes viral, fungal, and rarely, bacterial esophagitis. Candida and herpes simplex virus are the most common infectious agents causing esophagitis.<sup>(15)</sup> Gastroesophageal reflux may cause similar symptoms. Both infectious esophagitis and gastroesophageal reflux typically have a more gradual onset of symptoms and are characterized by burning esophageal pain unrelated to swallowing. Complications of pill esophagitis include hemorrhage, particularly when caused by nonsteroidal anti-inflammatory drugs, esophageal perforation, mediastinitis, and stricture formation.<sup>(14)</sup>

While most of these esophageal injuries are self-limited and produce no morbidity beyond transient retrosternal pain, odynophagia, and dysphagia; major complications, such as mediastinal penetration, hemorrhage, and death may occur.<sup>(8, 15, 16)</sup>

### ***Diagnosis***

History alone suggests the diagnosis, although endoscopy findings are definitive. Endoscopy is indicated in the evaluation of odynophagia in immunocompromised patients, in individuals with progressive and prolonged symptoms, in those with excessive dysphagia or hemorrhage, and when the diagnosis is in doubt.<sup>(8, 16)</sup> The

endoscopic finding of ulcerations located at one level circumferentially in the mid esophagus is most suggestive of this disorder.<sup>(14)</sup>

### ***Prevention and treatment***

Characteristics of medications may greatly affect their potency for caustic effects. It is shown that the tendency of products to adhere to the esophageal mucosa can be modified to a great extent by shape and formulation. Products with low adherence can be obtained by film coating with aqueous dispersions or by sugarcoating. In contrast, gelatin capsules and some cellulose films appear to have a high tendency to adhere to the esophagus.<sup>(17)</sup>

Channer KS *et al.* showed oval tablets pass the esophagus more easily than round ones. Overall, the transient time of larger sizes are longer and retention of tablets are more frequent when they been swallowed in supine position than standing position.<sup>(18)</sup>

Medications with a prolonged dissolution time can more likely lead to acute inflammation.<sup>(19)</sup> New and novel oral drug formulations, such as tablets that dissolve in seconds on the tongue without water, may alleviate the problem. They offer substantial advantages over ordinary tablets, are more convenient to administer, and enhance the potential for improved compliance in patients who experience difficulty in taking tablets.<sup>(20)</sup>

Esophageal damage occurs when the caustic contents of a drug remain in the esophagus long enough to produce mucosal lesions.<sup>(12)</sup> The incidence of this iatrogenic injury can be reduced by emphasizing the importance of taking pills while upright and with plenty of fluids.<sup>(8,12-15,21)</sup> Additional caution should be given to bedridden patients with strictures or esophageal dysmotility who are at a greater risk for developing this complication.<sup>(15)</sup>

Clinical and laboratory data propose no underlying disease or predisposing status in our patient. As shown in images, the kissing ulcers caused by the pill, declare the pathogenesis: round tablets - with considerable diameter - interrupt

within esophagus, where oval ones tend to pass easily. This interruption prepare enough time for caustic reaction, although no difference is mentionable in formulation of these pills.

In our case, it seems that the shape of medication played the most important role in this side effect; since it appeared just after switching from oval tablets to round ones while he did not change the dose or manner of taking the medication.

In order to minimize the risk of serious side effects, it is important to give detailed instructions regarding medication and to ensure that the instructions are properly understood. The risk of serious complications can be reduced by early recognition of esophageal symptoms and appropriate intervention.(23)

Although the benefit of treatment of pill esophagitis is unproven, sucralfate and other agents that result in acid suppression may promote faster healing. Resolution in symptoms generally occurs in a few days to weeks.(12,16, 22,24)

Since it is seriously harmful and easily preventable, healthcare providers should be alert to the possibility of pill-induced esophagitis in susceptible patients; especially handicaps and elders. Patients with predisposing factors for the development of pill-induced esophagitis should also be educated about proper swallowing of oral medications.

Balzer *et al.*(26) offered a few keypoints for prevention of pill-induced esophagitis; we modified these strategies as the following “TEN COMMANDMENTS”:

1- Take the medication sitting up at a 45- to 90-degree angle.

2- Take the medication with at least 100 mL of water or other appropriate carrier. Consider more water for high-risk drugs and patients.

3- Take a small sip of water or other appropriate carrier before and after taking the medication.

4- Take medications that must be taken “at bedtime” at least 30 minutes before sleeping or 10 minutes before reclining.

5- Take one medication at a time.

6- Consult a pharmacist before crushing tablets

or opening capsules.

7- Request the liquid form of the medication; consult with a pharmacist regarding equivalent doses.

8- Consult your physician if it is possible to take a couple of medium-sized tablets instead of each large one.

9- Take oval form of tablets, if present.

10- Call in a doctor if you experience pain or discomfort on ingestion.

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