Drug induced oesophageal injury have been reported. The causation of oesophageal disease and more than 1000 cases of drug induced oesophageal disease. We report a doxycycline induced acute erosive oesophagitis in a young healthy college student without prior history of oesophageal disease. We report a doxycycline induced acute erosive oesophagitis and Presenting as Acute Dysphagia

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Abstract

Introduction: Drug induced oesophageal disease is common. Doxycycline is one of the commonest cause of drug induced oesophageal ulcers. The medical community often under recognizes the importance of drug induced oesophageal lesions and fails to deliver proper advice and instructions related to drug ingestion. The diagnosis is usually clinical although endoscopy is the gold standard diagnostic tool. Treatment is symptomatic with discontinuation of the drug often being sufficient. Long-term sequelae are infrequent and acute complications uncommon.

Clinical picture: A 22-year-old college student was prescribed doxycycline capsules for acne and developed dysphagia. Upper gastrointestinal endoscopy revealed acute erosive oesophagitis.

Treatment and outcome: She was managed symptomatically with proton pump inhibitors and her dysphagia improved over a period of three days. She was discharged with proper advice regarding medication ingestion and proton pump inhibitor for four weeks.

Conclusion: Drug induced oesophageal disease is a preventable self-limiting condition. Proper advice regarding medication ingestion is essential for prevention.

Introduction

Drug induced oesophageal disease (DIOD) was first reported in 1970. More than 100 drugs have been implicated in the causation of oesophageal disease and more than 1000 cases of drug induced oesophageal injury have been reported. Common medicines include tetracycline, doxycycline, minocycline, acetylsalicylic acid, potassium chloride, ferrous sulphate, quinidine, alpenolol, alendronic acid, vitamin C, penicillins, clindamycin and non-steroidal anti-inflammatory drugs. Chemical content, drug formulation and patient factors are specific for the drug induced oesophageal lesions. The possibility of drug induced oesophageal damage should be suspected in a patient who complains of dysphagia, odynophagia and retrosternal chest pain. The oesophageal injury ranges from mild inflammation to acute ulceration, haemorrhage, perforation or oesophageal stricture.

Gastrointestinal endoscopy will confirm the diagnosis in appropriate cases and also helps to rule out sinister oesophageal disease. It is not necessary in the acute setting if the history is specific and discontinuation of the offending drug has already started to relieve the symptoms. Acid reduction is commonly advised, but its role is not evidence based. Giving appropriate instructions to the patient can many times prevent such oesophageal injuries. We report a doxycycline induced acute ulcerative oesophagitis in a young healthy college student without prior history of oesophageal disease.

Case Report

A 22-year-old female college student went to a local polyclinic to seek advice for acne. The acne distribution was facial and had not responded to topical over the counter preparations. She was prescribed doxycycline capsules for six weeks. She did not have any past history of oesophageal disease. There was also no history of smoking or alcohol intake. She did not have any known drug allergies and was fit and healthy. After two days of doxycycline ingestion, she developed retrosternal chest pain and odynophagia. She stopped consuming the drug after three days. The odynophagia continued and on the fourth day she presented to the emergency department.

She had no history of fever, headache, myalgia and symptoms of upper respiratory tract infection. She had no other skin lesions, history of caustic ingestion or irradiation. She did not have a history of diabetes. She was afebrile and hemodynamically stable. Her general and systemic examination was unremarkable apart from mild dehydration. She was admitted for her complains of odynophagia.

She received intravenous fluids and underwent an upper gastrointestinal endoscopy the next morning. The gastrointestinal endoscopy revealed a kissing oesophageal ulcer at the level of the aortic arch (Fig. 1). The rest of the oesophagus and stomach was unremarkable. She was prescribed a course of proton pump inhibitors. The symptoms improved over the next day and she was started on clear feeds. This was progressed to a normal diet the following day. Her symptoms gradually improved and she was discharged home on the third day. The histology of the ulcer revealed acute erosive oesophagitis (Fig. 2). The histology was negative for cytomegalovirus and there was no evidence of malignancy. Naranjo score of seven confirmed this case to be a probable adverse drug reaction rather than due to other factors.

Discussion

Drug induced oesophageal disease is a common condition
that is under reported and largely preventable. The incidence of 3.9 to 4 cases per 1,00,000 populations appear to be very low. Doxycycline is commonly prescribed for pelvic inflammatory disease and acne. Doxycycline induced oesophageal injury is hence more common in females. 

Patient factors have been implicated in the causation of oesophageal injury. For instance, an elderly patient who takes multiple medications is at high risk for oesophageal injury. Such patients may not remember the advice given by pharmacists. Patient with pre-existing oesophageal diseases such as reflux oesophagitis, scleroderma or oesophageal motility disorders also fall into this high-risk group. Our case though, demonstrates that even young and healthy individuals are not immune to drug induced injury and there are other factors that are equally important.

Medication factors play an important role in DIOD. The manner in which the prescribed drug is ingested is often overlooked. Medicine taken with less or no water or taken at bed time may remain in contact with the oesophageal mucosa for a long duration and can cause direct mucosal injury. There is decreased salivation and swallowing during sleep and this may increase the transit time through the oesophagus.

Liquid formulations are less likely to cause oesophageal injury compared to tablets. Sustained release formulations may cause oesophageal injury as they tend to be large in size and hence difficult to swallow. Gelatin based capsules may stick in the oesophageal lumen at the sites of anatomical narrowing (eg. aortic arch) or pathological narrowing (eg. enlarged left atrium) and can cause local mucosal injury. The chemical nature of the formulation is also important in the causation of damage. Most of the oesophagus damaging medicines are acidic and cause direct toxic effects when they remain in contact with the mucosa for a long duration. Anticholinergics cause reduced salivation and has been associated with drug induced oesophageal disease. Table 1 summarises the common medicines that can cause oesophageal injury and their relevant important clinical details.

Doxycycline can produce a pH of less than three when dissolved in ten millilitres of water or saliva. It is also shown that doxycycline capsules remain in oesophagus for three times long as doxycycline tablets. Our patient was taking doxycycline capsules at bed time with minimal water. In a reported series of eight patients with tetracycline induced oesophagitis, seven patients were taking the drug in capsule form. It is recommended that such medicines be taken in the sitting or standing position and with at least 100 millilitres of water. Applegate GR et al have reported a shorter oesophageal transit time when medication is swallowed with more liquids. Also, it is advisable to remain upright for at least 15 minutes after the ingestion of medicine.

### Table 1: Common medicines causing oesophageal injury with relevant clinical features

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Antibacterials</td>
<td>Accounts for 60% of cases of DIOD. Commonest antibiotic is doxycycline. A typical patient is a young female without any past history of oesophageal disorder complaining of odynophagia and chest pain. The capsule form of tetracycline has also been commonly implicated.</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>Can affect any level of the gastrointestinal tract from the oesophagus to the large intestine. Accounts for 8% of cases of DIOD. More than a third of cases have stricture or haemorrhage.</td>
</tr>
<tr>
<td>Alendronate</td>
<td>Increasingly recognised as a cause of DIOD. Causes local chemical mucosal damage. Should be taken early in the morning with at least 200ml of water.</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>Has been associated with massive bleeding due to erosion through the oesophagus into the aorta, left atrium or bronchial artery. Most patients have progressive dysphagia and little pain, hence presentation is delayed and strictures are common. Any oesophageal symptom in a heart disease patient who is on potassium chloride should be investigated immediately.</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Less than twenty cases have been reported. Gross oedema that develops at the site of injury can be radiologically confused as a filling defect similar to malignancy.</td>
</tr>
<tr>
<td>Iron formulations</td>
<td>The patients are commonly elderly, bedridden and on polypharmacy. Oesophageal perforation has also been reported.</td>
</tr>
<tr>
<td>Emepronium bromide</td>
<td>This is an anticholinergic used in urinary conditions. Its local irritant effect can be compounded by gastroesophageal reflux.</td>
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Fig. 1: Kissing oesophageal ulcers at the level of aortic arch

Fig. 2: Photomicrograph showing acute erosive oesophagitis
been reported to cause oesophageal injury.

The common symptoms of DIOD are dysphagia, odynophagia and retrosternal chest pain. Patients may also complain of a foreign body sensation lodged in the throat. The symptoms start variably after ingestion of medicine and typically get better within a few days of discontinuing the drug. Diagnostic endoscopy is unnecessary if the history is typical. It is reserved for cases where the history is atypical; where symptoms persist for a long duration of time, presence of a pre-existing oesophageal disorder, when there is haematemesis or when other causes of dysphagia are considered as differentials. Endoscopy is the gold standard and radiological investigations are not informative in acute drug induced oesophagitis. The common endoscopic finding is one to several discrete shallow, small ulcers. Particles of medicine can also be found at the site or ulcer formation. Our patient had kissing ulcers at the level of aortic arch and the surrounding mucosa was normal.

DIOD is self-limiting and symptoms usually improve on discontinuation of the medicine. Our patient already stopped taking doxycycline after the third day. Proton pump inhibitors or H2 receptor antagonists have no proven role in the absence of reflux oesophagitis. Topical protective agents and local anaesthetics such as liquid sucralfate or lignocaine may be of benefit for ulcer healing and pain relief. Delayed oesophageal stricture formation may require endoscopic dilatation.6

DIOD is a common and largely preventable condition. A detailed history and high index of suspicion is the key to an accurate diagnosis. If left undiagnosed it can have serious consequences. The simple advice of swallowing medication with plenty of water in an upright position can prevent the consequence of erosive oesophagitis.

References

8. Applegate GR, Malmud LS, Rock E. It’s a hard pill to swallow: or don’t take it lying down (letter). Gastroenterology 1980;78:1132.