

# PILL-INDUCED ESOPHAGEAL ULCER

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## ABSTRACT

We describe nine cases of esophageal injury associated with the ingestion of prescribed medications. Antibiotics were the most commonly implicated drugs. Odynophagia, retrosternal chest pain and dysphagia were the usual presenting symptoms. The typical endoscopic finding was that of discrete ulcers in the mid-esophagus. All patients recovered uneventfully with discontinuation of the offending drug and symptomatic treatment. Drug induced esophageal injury should be considered in patients presenting acutely with the above mentioned symptoms and having discrete esophageal ulcers on endoscopy.

*Keywords: pills, medication, esophageal ulcers, endoscopy, antibiotics*

SINGAPORE MED J 1993; Vol 34: 257-258

## INTRODUCTION

Esophageal injury caused by ingestion of oral medications was first reported in 1970<sup>(1)</sup>. Antibiotics accounted for half of the reported cases with tetracyclines being the most common antibiotic implicated. Many cases of pill-induced esophageal injury probably remain unrecognised and unreported since most patients recover fully. Increased awareness with proper history taking will lead to greater accuracy in diagnosis.

## MATERIAL AND METHODS

From October 1988 to February 1992, nine cases of esophageal ulcers induced by oral medications were seen at the Division of Gastroenterology, National University Hospital. Clinical details of these patients are presented in Table I. None of the patients had previous esophageal symptoms or clinical evidence of systemic diseases which may be associated with esophageal ulceration. All of them developed symptoms shortly after taking the offending drugs. Diagnoses were made at endoscopy and malignancy and infection were excluded by histology.

## RESULTS

There were 7 women and 2 men and their mean age was 30 years (range 21-55). All were healthy prior to the occurrence of esophageal ulceration. The main presenting symptoms were odynophagia which was noted in 6 patients (67%), retrosternal chest pain noted in 5 patients (56%) and dysphagia noted in 3 patients (33%). The mean duration of symptoms was 5 days (range 2-14). In eight of the nine patients (89%), the lesions were in the mid esophagus while the remaining patient had ulceration of the lower esophagus (11%). Seven patients had discrete ulcers (78%), 2 patients had shallow confluent ulcers (22%) and one patient had generalised erythematous esophagitis

surrounding superficial ulcers.

Tetracycline was implicated in 5 patients (56%), an ampicillin/cloxacillin preparation in 2 patients (22%). Paracetamol was taken by one patient before symptoms started and another person took a 'fat burner' (dieting tablet which contained choline, inositol, Betaine L-carnitine, L-Lysine Lecithin, Fe, Linoleic acid, oleic acid). All patients recovered symptomatically with discontinuation of the causative agent and symptomatic treatment. Repeat endoscopy after 2 - 4 weeks revealed complete healing of the ulcers with no complications.

## DISCUSSION

Medication induced esophageal injury is often missed. Kikendall et al reviewed 221 cases of esophageal ulcers caused by 26 different types of pills in 1983<sup>(2)</sup>. Bott et al found 127 reported cases from 1970 to 1987 in the English language literature<sup>(3)</sup>. The true prevalence is unknown as many cases are not reported or not diagnosed. A survey from Sweden in 1978 estimated that the incidence was 3.9 per 100,000 population per year<sup>(4)</sup>.

Almost twice as many female patients suffered medication induced esophageal injury as males<sup>(2)</sup>. This predominance was thought to reflect the higher frequency of drug taking among females eg emepronium bromide and antibiotics for urinary tract infections, and diuretics which require potassium chloride supplements. The fact that females live longer than males may contribute to this. A female preponderance was also noted in our patients. The youngest patient with medication induced esophageal ulcer reported was a 9-year-old girl and the oldest was an 89-year-old woman<sup>(5,6)</sup>. Quinidine and potassium induced injury tended to occur in older patients and antibiotic induced injury occurred more frequently in younger individuals. The mean age of patients with antibiotic induced esophageal ulcers was younger (30 years) than that of patients with esophageal ulcers caused by potassium chloride (56 years) or quinidine (64 years)<sup>(3)</sup>. The mean age of our patients was 30 years and three-quarters of our cases were due to antibiotics.

Retrosternal chest pain, odynophagia and dysphagia were the most commonly reported symptoms<sup>(2,3)</sup>. Odynophagia is more often caused by injury due to antibiotics and non-steroidal anti-inflammatory drugs whereas dysphagia is more common in injuries related to potassium chloride or quinidine. Complications like hematemesis, perforation, stricture and low grade fever were not seen in our patients. Symptoms occurred from a few hours to a few days after pill ingestion and resolved in a few days with symptomatic treatment and discontinuation of the offending medication.

Flexible fiberoptic endoscopy is more sensitive than barium swallow in the diagnosis of drug-induced esophageal injury. The usual findings are discrete erosions or ulcerations from pinpoint size to circumferential lesions up to several centimetres in length. The most common site of this condition is the mid esophagus at the level of aortic arch or the area adjacent to the left atrium. The distal third of the esophagus is involved in only 19% of reported cases<sup>(2)</sup>. Eighty-nine percent of our pa-

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**Table I - Clinical details of patients with medication induced esophageal ulcer**

| Patient | Sex | Age | Duration of Symptoms (Day) | Symptoms                      | Drug Ingested | Endoscopy findings                                     | Outcome   |
|---------|-----|-----|----------------------------|-------------------------------|---------------|--|---|
| 1. HHL  | F   | 21  | 3                          | odynophagia                   | ampiclox      | discrete circumferential ulcers at 25 cm               | symptomatic treatment rescoped at 2 wks ulcer healed  |
| 2. FCM  | M   | 23  | 6                          | odynophagia retrosternal pain | tetracycline  | discrete circumferential ulcer at 28 cm                | antacid treatment rescoped at 2 wks ulcer healed      |
| 3. HHJ  | F   | 24  | 4                          | odynophagia dysphagia         | ampiclox      | superficial ulcers with esophagitis at lower esophagus | motilium & gaviscon rescoped 2 wks later ulcer healed |
| 4. TBS  | M   | 21  | 14                         | retrosternal pain             | doxycycline   | discrete esophageal ulcer scar at 30 cm                | symptomatic well 2 wks later when reviewed            |
| 5. CSF  | F   | 25  | 7                          | dysphagia                     | tetracycline  | discrete ulcers at mid esophagus                       | symptomatic rescoped 3 wks ulcer healed               |
| 6. CCN  | F   | 21  | 2                          | odynophagia                   | doxycycline   | shallow ulcers at 27 - 30 cm                           | mucaine symptom improved                              |
| 7. CLM  | F   | 55  | 2                          | odynophagia retrosternal pain | paracetamol   | discrete ulcers at 30 - 35 cm                          | mucaine rescoped 4 wks later ulcer healed             |
| 8. LCM  | F   | 34  | 2                          | dysphagia retrosternal pain   | fat burner    | discrete ulcer at 30 cm                                | mylanta well at 2 wks when rescoped                   |
| 9. MAH  | F   | 45  | 5                          | odynophagia retrosternal pain | doxycycline   | discrete ulcer of 35 cm                                | mylanta rescoped 2 wks later ulcer healed             |

tients had lesion in the mid esophagus and only one patient (11%) had an ulcer at the lower esophagus. Discrete ulcers are most commonly seen in antibiotic associated injury and indeed discrete ulcers were seen in 78% of our patients. Most patients with medication induced esophageal injury have no apparent abnormality of esophageal transit or prior esophageal disease. However, pathological narrowing due to external compression or enlarged left atrium or tumours and motility disorders might also be expected to predispose the area to injury.

The mechanism of medication-induced injury is probably prolonged contact of high local concentrations of a drug. Tablets may be held up by anatomical narrowing. The patient may lie down immediately after swallowing the capsule before it has entered the stomach. The capsule or tablet may be refluxed into the esophagus from a hiatus hernia in patients with abnormal peristalsis. The chemical formula of the drug, its concentration and method of delivery are important factors. Agents which aid dispersement may slow drug transit and increase the duration of contact with the mucosa. A recent study by Hey et al<sup>(7)</sup> showed that large (oval and round) tablets were delayed more frequently than smaller tablets irrespective of the amount of water taken with the tablets. When the subject was in the supine position, delay was more likely to occur if only a small amount of water was taken. For subjects swallowing medications while in the upright position, the quantity of water was not a significant factor with smaller preparations but delay occurred when larger tablets were swallowed with small quantities of water. It is recommended that patients should remain

standing for at least 90 sec after taking medications, that tablets should be swallowed with at least 100 ml of fluid and that small oval tablets are preferable to other shapes. Alteration in the mucosa barrier which occurs with aspirin and other non-steroidal anti-inflammatory drugs may be the mechanism for damage rather than direct caustic effect.

Most cases of drug-induced esophageal injury are self-limited and resolve without sequelae. The offending medication should be discontinued and liquid preparations may be substituted if it is not possible to discontinue the medication. Symptomatic treatment is all that is needed. Prevention is the best approach to the problem. Patients should be advised to take their medications with sufficient quantities of water and avoid taking medications immediately before bedtime. Elderly or bed-ridden patients who have difficulty in swallowing should be given liquid medication.

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