

Oesophageal ulcers secondary to doxycycline and herpes simplex infection in an immunocompetent patient

Thangavelu Saravanan¹, MBBS, Pemasari Upali Telisinghe², MBBS, FRCPath, Vui Heng Chong¹, FAMS, FRCP

ABSTRACT Oesophageal ulcerations are generally rare occurrences that are most commonly associated with gastro-oesophageal reflux disorder. Other causes include medications and infections in immunocompromised patients. Among the medications used in daily practice, doxycycline is most commonly implicated. Multiple aetiologies are generally uncommon. We report a case of mid-oesophageal ulcerations secondary to doxycycline and herpes simplex virus infection in an immunocompetent patient.

Keywords: doxycycline, herpes simplex infection, immunocompetent, oesophageal ulcer, oesophagitis
Singapore Med J 2012; 53(4): e69–e70

INTRODUCTION

Oesophageal ulcers are uncommon in clinical practice and are associated with significant comorbidity. The most common cause of oesophageal ulcers is gastro-oesophageal reflux disorder, followed by medications and infections, especially in immunocompromised individuals.⁽¹⁻³⁾ Multiple aetiologies are generally uncommon. We report a case of mid-oesophageal ulcerations secondary to doxycycline and herpes simplex virus in an immunocompetent patient.

CASE REPORT

A 45-year-old Malay woman was referred to our hospital with a two-day history of mid-chest discomfort associated with odynophagia. Her past medical history was relevant for chronic granulomatous mastitis with recurrent spontaneous discharge, which was treated with incision drainage. Prior to the latest presentation, purulent discharge had recurred, for which she was treated with a ten-day course of doxycycline (100 mg daily). She began to experience chest discomfort four days following completion of the antibiotic treatment. The initial suspicion was that of doxycycline-induced oesophagitis or ulcerations.

Endoscopy revealed near circumferential mid-oesophageal ulcerations, circumferential scar (Fig. 1) and a cervical inlet patch. The rest of the examination was normal. Biopsies were taken from the ulcers' edge and base. The patient was started on acid suppression medications (omeprazole 20 mg bid), domperidone (10 mg tid) and Gaviscon 10 ml as required. Her symptoms improved over the next few days. Surprisingly, the biopsies showed herpes simplex inclusion bodies in addition to ischaemic changes, which were consistent with drug injury (Fig. 2). There were no features of ectopic gastric mucosa. On further

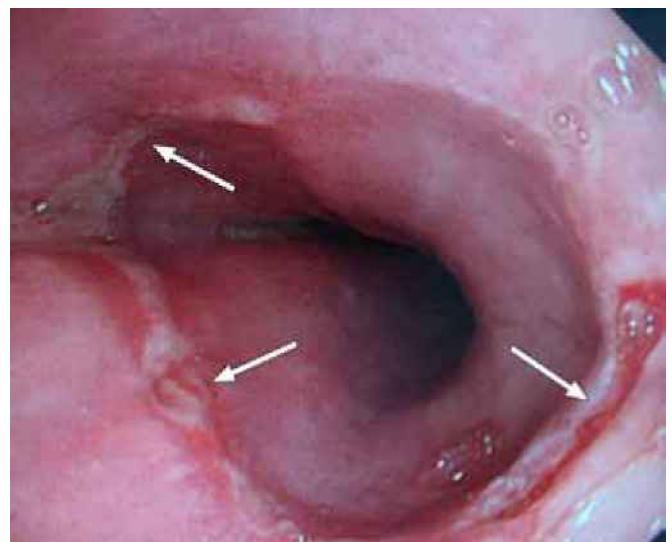


Fig. 1 Endoscopic image shows mid-oesophageal ulcerations (arrows).

questioning, the patient mentioned that she had just recovered from cold sores a few days before the endoscopy. Blood investigations, which included a complete blood count, were normal. She denied taking any other medications, such as steroids, which could have led to her immunocompromised state. The patient remained well without any further recurrence of symptoms.

DISCUSSION

Four decades after the first report, approximately 1,000 cases of drug-induced oesophageal injury caused by almost 100 different drugs have been reported. Antibiotics accounted for almost half of these cases, and doxycycline alone accounted for 27% of them.⁽³⁾ Medication-associated oesophageal injuries commonly occur at the aortic arch level or above the lower oesophageal sphincter.⁽⁴⁾ These two areas are the sites of physiological

¹Department of Medicine, ²Department of Pathology, Raja Isteri Pengiran Anak Saleha Hospital, Bandar Seri Begawan, Brunei Darussalam

Correspondence: Dr Chong Vui Heng, Consultant Gastroenterologist, Department of Medicine, Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Bandar Seri Begawan BA 1710, Brunei Darussalam. chongvuih@yahoo.co.uk

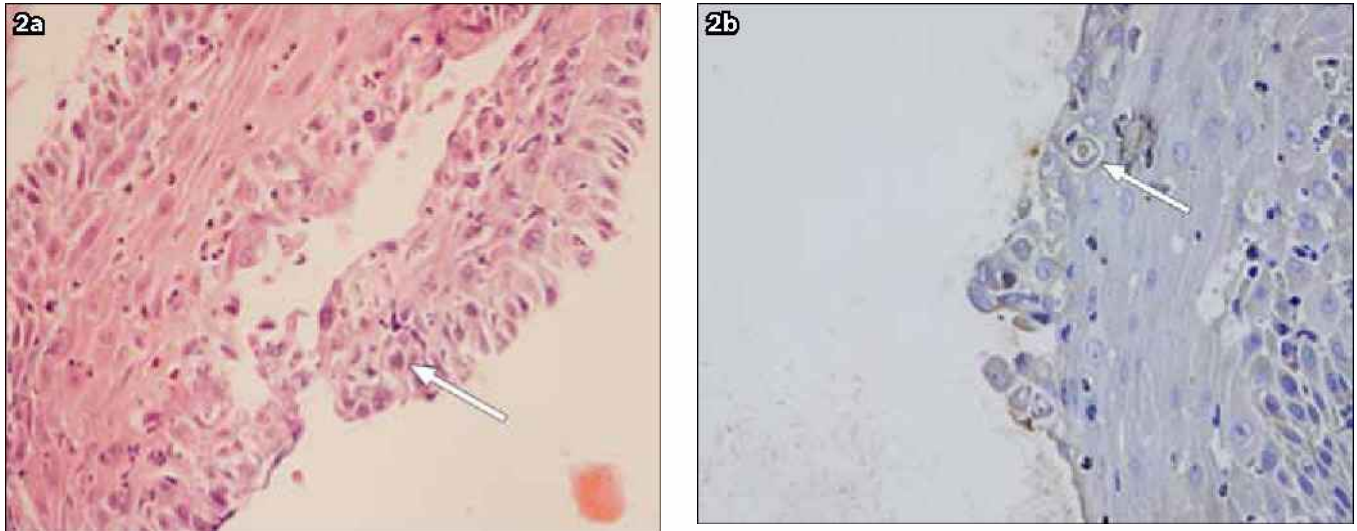


Fig. 2 (a) Photomicrograph shows herpes simplex inclusion body or Cowdry's body (arrow) (Haematoxylin & eosin, $\times 20$), which is better highlighted using (b) immunostaining (arrow, $\times 40$).

narrowing, where medications can get stuck. In contrast, reflux disorder-related ulcerations are typically found in the distal oesophagus, proximal to the gastro-oesophageal junction. In severe cases, this can extend proximally, but often with the distal being involved. The formulations of medications have also been reported to be important, with bigger size and capsule formulation associated with higher risk.⁽⁵⁾ Other medications that have been reported to cause oesophageal ulcerations include non-steroidal anti-inflammatory drugs, bisphosphonates, potassium chloride, ferrous sulfate, nifedipine and antibiotics such as tetracyclines, erythromycin, amoxicillin-clavulanate and alendronate.⁽⁶⁾

Herpes simplex is an important cause of oesophagitis or ulcerations and is typically associated with an immunocompromised state. Herpes simplex oesophagitis has a predilection for the distal or mid-oesophagus. It histologically appears as multinucleated giant cells with eosinophilic intra-nuclear inclusions (Cowdry type A intra-nuclear inclusions) and nuclear chromatin with a ground glass appearance.⁽⁷⁾ Other infective causes include cytomegalovirus, human immunodeficiency virus and tuberculosis. All these infections also occur in patients who are immunocompromised. Occurrence of oesophageal ulcers secondary to infections is very uncommon in otherwise healthy and immunocompetent patients. Oesophageal tissue injuries from any aetiology have been reported to predispose immunocompromised patients to secondary herpes simplex oesophagitis.⁽⁸⁾ Our patient was already on doxycycline and had almost completed the treatment when she developed herpes labialis. It is highly possible that the oesophageal ulcerations were already present when she developed herpes labialis.

Interestingly, ulceration and bleeding from a heterotopic gastric mucosal patch of the oesophagus has previously been reported.⁽⁹⁾ Although commonly found in the proximal oesophagus, ectopic gastric mucosal patch found in the mid-oesophagus has also been reported.⁽¹⁰⁾ Oesophageal ulcerations typically present with chest discomfort, odynophagia and dysphagia. Clinical history in

the presence of an associated aetiology may be sufficient for a clinical diagnosis. However, endoscopy with biopsies remains an important procedure, especially in cases where there are multiple aetiologies, as in our patient. The main treatment for medication-related oesophageal ulceration is symptomatic treatment and withdrawal of the culprit medications. The use of acid suppression can relieve symptoms and hasten recovery. In immunocompromised patients, treatment is often required for herpes simplex oesophagitis or ulcerations, whereas specific anti-viral therapy may not be required in immunocompetent individuals.

In conclusion, our report highlights a rare case of oesophageal ulcerations with multiple aetiologies. Such occurrence may be underestimated or underdiagnosed.

REFERENCES

- Higuchi D, Sugawa C, Shah SH, Tokioka S, Lucas CE. Etiology, treatment, and outcome of esophageal ulcers: a 10-year experience in an urban emergency hospital. *J Gastrointest Surg* 2003; 7:836-42.
- Kikendall JW, Johnson LF. Pill-induced esophageal injury. In: Castell DO, ed. *The Esophagus*, 2nd ed. Boston: Little Brown, 1995: 619-34.
- Kikendall JW. Pill esophagitis. *J Clin Gastroenterol* 1999; 28:298-305.
- Akbayir N, Alkim C, Erdem L, Sakiz D, Sökmen HM. A case report of doxycycline induced esophageal and gastric ulcer. *Turk J Gastroenterol* 2002; 13:232-5.
- Channer KS, Virjee JP. The effect of formulation on oesophageal transit. *J Pharm Pharmacol* 1985; 37:126-9.
- Corleto VD, D'Alonzo L, Zykaj E, et al. A case of oesophageal ulcer developed after taking homeopathic pill in a young woman. *World J Gastroenterol* 2007; 13:2132-4.
- Geraci G, Pisello F, Modica G, et al. Herpes simplex esophagitis in immunocompetent host: a case report. *Diagn Ther Endosc* 2009; 2009:717183.
- Ramanathan J, Rammouni M, Baran J Jr, Khatib R. Herpes simplex virus esophagitis in the immunocompetent host: an overview. *Am J Gastroenterol* 2000; 95:2171-6.
- Bataller R, Bordas JM, Ordi J, et al. Upper gastrointestinal bleeding: a complication of "inlet patch mucosa" in the upper esophagus. *Endoscopy* 1995; 27:282.
- Katsanos KH, Christodoulou DK, Kamina S, et al. Diagnosis and endoscopic treatment of esophago-bronchial fistula due to gastric heterotopy. *World J Gastrointest Endosc* 2010; 2:138-42.