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Esophageal ulcer associated with inappropriately taken doxycycline: A benign mimicker of esophageal cancer

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A 16-year-old girl visited our clinic because of chest pain that was exacerbated with swallowing. Ten days previously, the patient had spilled boiling water on herself and burned her legs. She saw a dermatologist, who prescribed doxycycline (100 mg per day in tablet form) to prevent skin infection. Five days previously, the patient took a doxycycline tablet with a small amount of water just before going to bed. She fell asleep in the supine position soon after taking the tablet. The following morning, she noticed chest pain and a dry cough. She visited our clinic complaining of difficulty swallowing because it exacerbated the associated chest pain. Physical examination, chest X-ray, and electrocardiograph results were unremarkable. Endoscopy of the upper gastrointestinal tract revealed a geographic ulcer that encompassed the entire circumference of the esophagus around the bronchoaortic constriction (Figure 1), which is often interpreted as suggesting esophageal cancer. However, because she had taken doxycycline the day before onset, the patient was diagnosed with doxycycline-induced esophageal ulcer and treated with intravenous fluid alimentation, a proton pump inhibitor, and analgesics. Her symptoms subsided within 1 week. All examinations to exclude other disorders revealed no remarkable findings, as follows: biopsy specimen of the ulcer indicated pathologically inflammatory granulation without malignancy; serum antinuclear antibodies, antidesmoglein antibodies, antiherpes simplex virus antibodies, and anticytomegalovirus antibody were all negative. Follow-up endoscopies performed 2 weeks and 6 months thereafter confirmed improvement.

Approximately 100 types of medication are reported to cause esophageal injuries.[1] Drug-induced esophageal injuries are classified by their etiology as follows: (i) injury resulting from acidic antibiotics, (ii) chemical esophagitis caused by bisphosphonates such as alendronate, (iii) hyperosmotic injury caused by potassium chloride or quinidine, and (iv) distal esophagitis associated with nonsteroidal anti-inflammatory drugs in patients with gastroesophageal reflux disease.[2] Older people are prone to develop drug-induced esophageal injury because of decreased esophageal motility and saliva production, cardiac enlargement, and polypharmacy.[1,2] Antibiotic-related esophageal injury, however, frequently occurs in young women without underlying disorders. Doxycycline most commonly causes antibiotic-related esophageal injury, and this causative medication and its indication can explain the occurrence of antibiotic-related esophageal injury in young women. When administered orally, doxycycline causes chemical injury to adjacent tissues because of acidic conditions generated by the dissolution

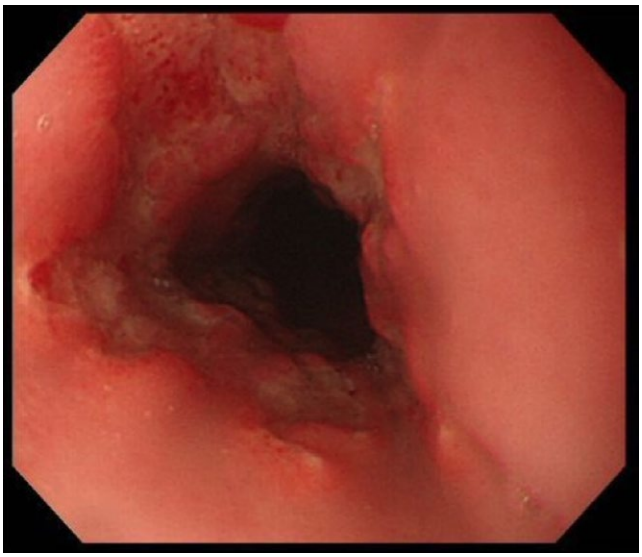

FIGURE 1 Endoscopy of the upper gastrointestinal tract revealed a geographic ulcer that encompassed the entire circumference of the esophagus around the bronchoaortic constriction, which can be misdiagnosed as the finding of esophageal cancer

of the tablet. Dissolved doxycycline also accumulates and injures the esophageal epithelial cells by inhibiting protein synthesis. In some cases, this injury leads to an esophageal ulcer.[1-3] Doxycycline is frequently prescribed to sexually active young women to treat urogenital infections or acne vulgaris.[3] Several previous reports stated that most patients took doxycycline with insufficient water just before going to bed or in the supine position.[3-5]

In Japan, doxycycline is less well known as a potential cause of esophageal ulcer than bisphosphonate or potassium chloride because it is infrequently prescribed. However, the latest nondisclosure domestic reports from the brand-name drug manufacturer of doxycycline to the Ministry of Health, Labor and Welfare of Japan revealed that 13 cases of doxycycline-induced esophageal ulcer have been reported as doxycycline became commercially available; three of these cases occurred within the past 11 years.[6] In the domestic report, the patients' characteristics are comparable with previous reports from abroad; the median age of onset was 22 years (female, 7 [53.8%]) and 61.5% of the patients took doxycycline without water or with only a small amount before going to bed. Doxycycline was prescribed to treat skin infections such as acne vulgaris for six patients.

Given that doxycycline can be effectively used for various conditions including rickettsiosis, acne vulgaris, or *Stenotrophomonas maltophilia* infections without dose adjustment in patients with renal or hepatic impairments, clinicians should be familiar with its adverse effects. Given that doxycycline-induced esophageal ulcer mimics esophageal cancer, particular attention to doxycycline use is important for correct diagnosis.[7] All patients taking doxycycline must be given detailed instructions about the appropriate administration methods of doxycycline including the amount of water with which to swallow the tablet (at least 100 mL), the optimal body position (upright for at least 90 seconds after swallowing), and timing of taking the medication (at least 30 minutes before going to bed) to prevent esophageal injury.[4,8]

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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