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Oral gel choline salicylate induced refractory gastric ulceration

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Lesson
Common over the counter oral ulcer soothing gel can be an unexpected source of salicylate and cause refractory gastrointestinal ulcers if not identified.

Introduction

Refractory gastric ulcers are rare, and in this case report, we describe how an unexpected source of choline salicylate in a common over-the-counter oral gel caused persistent gastric ulceration.

Case history

A 39-year-old Caucasian male presented with three years of dyspepsia followed by an episode of melaena on the background of aspirin usage. At direct access oesophagogastroduodenoscopy (OGD), he was found to have multiple gastric and duodenal ulcers with a negative rapid urease test for *Helicobacter pylori*. The biopsies showed evidence of a chemical gastropathy with no *Helicobacter*-like organisms seen. He was started on Omeprazole 40 mg once daily and was advised to stop aspirin. A repeat OGD three months later showed several persistent gastric ulcers whilst the duodenitis had resolved. Repeat biopsies were unchanged, and the Omeprazole was increased to 40 mg twice daily. He denied continued aspirin consumption or any other over-the-counter medication. He had a past history of asthma and no significant family history.

Computed tomography of the abdomen was normal as were fasting gut hormone levels and faecal *H. pylori* antigen (both taken off Omeprazole). From May 2010 to July 2011, he had undergone five OGDs with no resolution of the gastric ulcer, and surgical treatment was being considered for refractory, symptomatic gastric ulceration. At this stage, urine salicylate levels were checked and found to be positive. At the same time, he was admitted with a four-day history of melaena and normochromic anaemia with a haemoglobin of 8.1 g/dL. A repeat OGD during admission showed persistent gastric ulceration, but no endoscopic therapy was required. In view of the raised salicylate level, he was questioned more closely and, after instructions to closely examine the ingredients lists of any substances used at home, frequent use of a common ulcer soothing oral gel which contains choline salicylate 8.7% was identified as a potential cause. This was discontinued leading to symptom resolution, and a repeat OGD three months later demonstrated complete endoscopic healing (see Figures 1–3). He has now been followed up for a year without any recurrence of symptoms.

Discussion

Peptic ulcer disease is common and represents significant usage of healthcare resources with an annual prevalence rate of 1.5%.[1] Most cases are diagnosed and treated in the primary care setting although development of complex ulceration with gastrointestinal (GI) bleeding or gastric outlet obstruction can occur in the minority. Refractory cases are uncommon with 70% of peptic ulcers healing in four weeks and 96% by six weeks of treatment.[2] Proton pump inhibitors (PPIs) and *H. pylori* eradication are highly effective treatments and form the cornerstone of modern management with surgery now rarely required.

Nonsteroidal anti-inflammatory drugs (NSAID) and *H. pylori* are the two most common causative agents, and this was demonstrated in a recent UK hospital study where 57% of patients with endoscopic ulcers had exposure to NSAID and a similar proportion had *H. pylori* infection. GI ulceration was developed in 15–35% of patients using NSAID over long periods (≥3 months) but with rarely serious complications.[3] Important risk factors for NSAID-related GI ulcer complications include old age, previous

Figure 1. Initial OGD documenting multiple gastric ulcers.

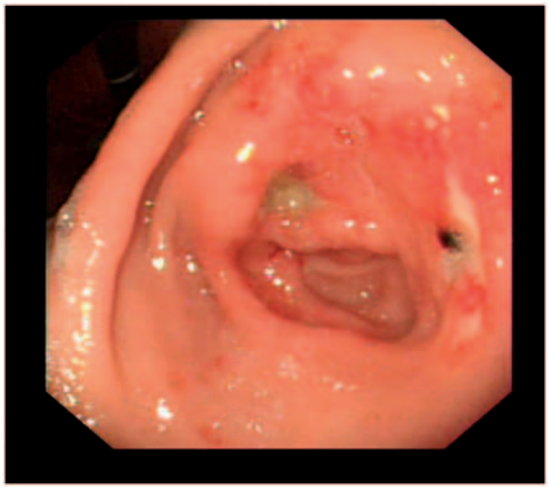


Figure 2. Non-healing ulcers despite high dose PPI.

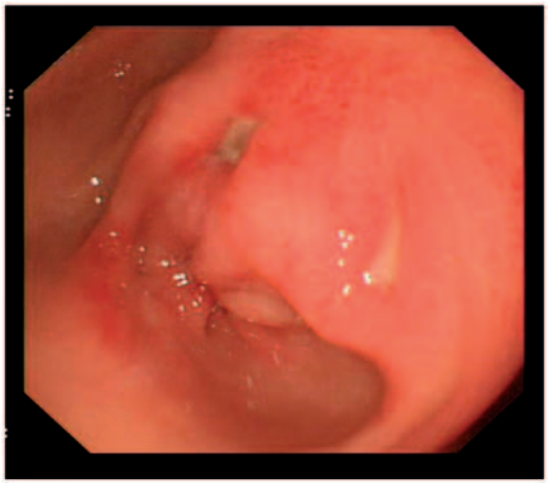
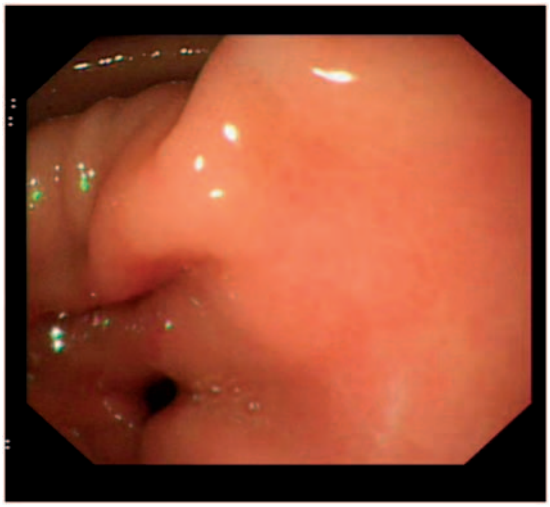


Figure 3. Complete healing following withdrawal of Bonjela.



history of bleeding, *H. pylori* presence, major organ impairment and concurrent use of steroids and anticoagulants.[4]

The exact mechanism of NSAID-induced GI damage is unclear and likely due to a combination of local and systemic effects. It acts as a direct irritant on the GI mucosa causing gastropathy and submucosal erosions. Systemically, it inhibits the cyclooxygenase enzyme and blocks the conversion of arachidonic acid to prostaglandin H2 and subsequently all other prostaglandins. These chemicals are important in mucosal homeostasis and formation of a protective lining in the stomach. Its loss impairs mucosal defence against local irritants and reduces mucosal ability to restore structure and function after injury.[5] If ulcers are already present, the impaired healing process leads to longer healing time and development of complex peptic ulceration.

In this report, the patient was worked up by excluding these two common causes through repeated history taking for any NSAIDs and assessment for *H. pylori* status through CLO testing and faecal antigen both of which were performed optimally off PPIs. However, despite high doses of treatment, the ulcers persisted.

Although NSAIDs are commonly elucidated during history taking, surreptitious or undisclosed NSAID consumption is recognised. In a prospective study of consecutive patients attending OGD where peptic ulcers were found, 66 patients were *H. pylori* negative and denied any NSAID consumption. However, serum thromboxane A2 was suppressed in 30.8% suggesting undisclosed usage.[6] In a separate study assessing small bowel injury with video capsule enteroscopy, urinalysis was positive for NSAIDs including salicylate in 10 patients of whom only one declared usage.[7]

In this time of widespread NSAID availability over the counter, assessment is further complicated by its many forms such as topical ointment and, in this case, oral gel. Topical NSAIDs applied to the skin are well studied and not associated with severe GI toxicity. A Cochrane review in 2010 showed no difference in the proportion of patients having a systemic adverse event compared to placebo (3.2% vs. 3.4).[8] Although this patient was directly questioned regarding the use of NSAIDs on several occasions,

he had not considered the oral gel to be a medication nor had he appreciated that it contained salicylates. While oral gel choline salicylate toxicity is yet to be reported in the adult population, it is recognised as a significant source of salicylate in the paediatric population following several cases of Reye's syndrome.[9] The manufacturers have withdrawn choline salicylate from its teething gel.

Our case is the first report of oral choline salicylate gel implicated in refractory gastric ulceration. The choline ester is suspected to have enhanced systemic absorption,[10] and the buccal route avoids first pass metabolism. Despite availability of modern investigative tools, this case highlights the importance of careful history taking and thoughtful assessment of these challenging patients.

Declarations

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