EDITORIAL

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Significance of duodenal mucosal lesions: can they be a clue to a systemic disease?

Seung Woo Lee

Division of Gastroenterology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

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Upper gastrointestinal endoscopy is widely used in Korea not only for hospitalized patients but also for check-ups of healthy individuals. Endoscopically, duodenitis is defined as inflammation of the duodenal mucosa. The endoscopic terms for duodenopathy are erosive, hemorrhagic, and hyperemic changes, according to the Minimal Standard Terminology of the World Endoscopy Organization [1]. Although endoscopists frequently encounter duodenal ulcers and duodenitis, the duodenum is frequently overlooked during endoscopy because duodenal malignancy is rare [2]. The most common causes of duodenal ulcers are *Helicobacter pylori* and nonsteroidal anti-inflammatory drugs (NSAIDs) [3]; therefore, an examiner might assume any duodenal mucosal lesions identified to be one of these two etiologies. According to the 2015 Kyoto consensus report, duodenitis has various causes [4]. The proposed etiologies of duodenitis are *H. pylori*, other bacteria (mycobacteria and *Tropheryma whipplei*), fungi, parasites, viruses, external causes (e.g., alcohol, radiation, and drugs), allergic reactions, eosinophilic disease, and other diseases (e.g., Crohn's disease, sarcoidosis, vasculitis, Henoch-Schonlein purpura, and celiac disease). Thus, the etiology of duodenitis is more complex than previously believed.

In the current issue of the Korean Journal of Internal Medicine, Han et al. [5] report a retrospective study of the characteristics of duodenitis and duodenal ulcers relating to primary and secondary duodenal lesions. They enrolled 475 patients hospitalized in a single institution due to duodenal mucosal lesions from 2011 to 2014. The authors categorized the primary and secondary causes of duodenal lesions according to underlying disease. The prevalence of *H. pylori* did not differ between the primary and secondary duodenal lesion groups; however, the number of users of NSAIDs or aspirin was significantly higher in the primary duodenal lesion group. Primary duodenal lesions were found in 454 patients (95.6%), and secondary duodenal lesions were found in 21 patients (4.4%). The most frequent secondary cause was inflammatory bowel disease (IBD). Other diseases were cytomegalovirus, Behcet's disease, Henoch-Shonlein purpura, radiation-induced duodenitis, candida, tuberculosis enteritis, eosinophilic enteritis, and parasitic infection. Han et al. [5] reported that age and the extent of duodenal lesions were significant predictors of secondary duodenal lesions.

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Correspondence to
Seung Woo Lee, M.D.
Division of Gastroenterology, Department of Internal Medicine, College of Medicine, Daejeon St. Mary's Hospital, The Catholic University of Korea, 64 Daeheung-ro, Jung-gu, Daejeon 34943, Korea
Tel: +82-42-220-9501
Fax: +82-42-252-6808
E-mail: leeseungw00@hanmail.net

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Kim et al. [6] reported that the prevalence of *H. pylori* in duodenal ulcers in the Korean population is 65.4%. Histologic duodenitis is associated with *H. pylori* in 75% to 82% of patients [7,8]. The duodenal bulb is the most common location of duodenal ulcers. In H. pylori-infected patients, a high gastric-acid output increases acid loading to the duodenum and results in gastric metaplasia in the duodenal bulb. Metaplastic epithelium can be infected with *H. pylori*, resulting in duodenitis, erosions, and ulcers. [3] Non-*H. pylori* and non-NSAID duodenal ulcers are reportedly associated with multiple ulcers; in contrast, *H. pylori*-related ulcers usually occur singly [9]. This result is similar to the finding of Han et al. [5].

NSAIDs are also important causes of gastroduodenal lesions. The prevalence of H. pylori-negative but NSAID-positive duodenal ulcers varies from 8.5% to 70% [10]. In Korea, the prevalence of duodenal and gastric ulcers is reportedly 12.3% and 23.6%, respectively, in patients taking NSAIDs. [6] Based on this study, duodenal ulcers are affected more markedly by *H. pylori* than by NSAIDs. The exact pattern of duodenal involvement of NSAID users is unknown. Because NSAIDs can influence the upper to lower gastrointestinal tract, instead of being confined to the bulb their effect may extend to the distal duodenum. In the study by Han et al. [5], although the primary duodenal lesion group contained a greater number of patients taking NSAIDs, the extent of duodenal mucosal lesions was greater in the secondary group. In previous studies, NSAIDs were found to affect the duodenal mucosa in only 13% of patients with *H. pylori*-negative duodenal ulcers [11], and histologic changes in the duodenum were negligible [12]. These results may explain the findings of Han et al. [5].

The duodenum is involved in 23% to 53% of IBD cases [13,14]; these are predominantly Crohn's disease, which can involve the entire gastrointestinal system. Histologic duodenitis was diagnosed in 28.2% and 2.7% of Crohn's disease and ulcerative colitis patients, respectively, and the prevalence of upper gastrointestinal tract involvement was higher in patients less than 18 years of age [15]. Han et al. [5] also reported that patients less than 30 years of age have predictive factors of secondary mucosal lesions due to systemic disease. The most common endoscopic findings of Crohn's disease are erythema, edema, ulcers, and erosion. Granuloma is the definitive histopathologic finding of upper gastrointestinal Crohn's disease, although its prevalence is low [16].

The indications for duodenal biopsy are evaluation of malabsorption, iron-deficiency anemia, gluten-sensitive enteropathy, neoplasia, and diarrhea, together with confirmation of ulceration induced by NSAIDs and bleeding from an unknown site [17]. Although identification of duodenal lesions by histopathologic findings is important, these are not strongly correlated with endoscopic findings [12,18]. Moreover, celiac disease is rare in Korea, unlike in Western countries, and duodenal biopsy for endoscopic duodenitis is reserved for cases with clinical suspicion of selected diseases.

This study is limited by its retrospective nature and the small number of patients with secondary duodenal lesions. Thus, the results could be biased if a particular disease predominated in patients with secondary duodenal lesions. Another limitation is that pathologic diagnosis was not performed in all cases, which might have introduced selection bias. Despite these limitations, this work is noteworthy because few studies have reported the extent of duodenal mucosal lesions. Endoscopists should consider causes other than *H. pylori* infection and NSAID use, and obtain biopsies in young patients with duodenitis beyond the second portion. Further large-scale studies should investigate the pattern of duodenal involvement in duodenitis of various etiologies.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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