Clinicians should be aware of proton pump inhibitor–related changes in the gastric mucosa

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See “Association between occurrence of multiple white and flat elevated gastric lesions and oral proton pump inhibitor intake” by Rino Hasegawa, Kenshi Yao, Takao Kanemitsu, et al., Endosc 2023;56:000–000.

Since the clinical introduction of omeprazole in the early 1990s, proton pump inhibitors (PPIs) have been used worldwide to prevent gastroduodenal mucosal injuries caused by aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), as well as to treat acid-related diseases such as peptic ulcers and gastro-esophageal reflux disease (GERD). In particular, many patients with GERD (especially those with Barrett’s esophagus) and individuals who use NSAIDs require long-term PPI therapy.1-3 An important problem associated with long-term PPI therapy is hypergastrinemia secondary to the homeostatic response of antral G cells to decreased gastric acidity. Histopathologically, long-term PPI therapy induces protrusion of parietal cells into the lumen of glands, cystic dilatation of the fundic glands of the stomach, and hyperplasia of foveolar epithelial cells.4 Long-term PPI therapy has been associated with the formation of gastric mucosal lesions, including fundic gland polyps, hyperplastic polyps, multiple white and flat elevated lesions (MWFELs), cobblestone-like mucosa, and black spots (Table 1).4 Fundic gland polyps, cobblestone-like mucosa, and black spots are attributed to parietal cell protrusion and cystic dilatation of the fundic glands, whereas hyperplastic polyps and MWFELs result from foveolar epithelial hyperplasia.

MWFELs are defined as circumscribed, white, flat, protruding mucosal lesions with serrated borders on endoscopy.5 These are usually detected in the upper gastric corpus and fundus, and regular tubular structures can be seen on their surface on close observation. Recently, image-enhanced endoscopy techniques, such as narrow-band imaging (NBI), have increased the detection rate of MWFELs, with a reported incidence of 14% to 26% in PPI users.4 Several observational studies have reported that MWFELs are significantly associated with PPI use (odds ratio [OR], 3.58), moderate to severe atrophic gastritis (OR, 2.63), Helicobacter pylori eradication therapy (OR, 2.11), female sex (OR, 1.92), and aging (OR, 1.05).4,6 In the current issue of Clinical Endoscopy, Hasegawa et al.8 reported a significantly higher incidence of MWFELs in PPI users than in non-PPI users (49.3% vs. 10.9%, p<0.01; OR, 5.78 in multivariable analysis) and an association between MWFELs and hypergastrinemia. These results confirm the strong association between PPI use and MWFELs suggested in previous studies.

In practice, MWFELs can be misdiagnosed as intestinal metaplasia, especially by endoscopists who lack knowledge about MWFELs. The main differentiating features are as follows: MWFELs are detected in the upper corpus and fundus;
Table 1. Histopathological and endoscopic features of proton pump inhibitor–related changes in the gastric mucosa

<table>
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<th>Histopathological features</th>
<th>Endoscopic findings</th>
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<td>Parietal cell protrusion and cystic dilatation of fundic glands</td>
<td>Fundic gland polyps</td>
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<td>Cobblestone-like mucosa</td>
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<td>Foveolar epithelial hyperplasia</td>
<td>Hyperplastic polyps</td>
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<td>Multiple white and flat elevated lesions</td>
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intestinal metaplasia in the antrum usually appears as whitish elevated patches, whereas intestinal metaplasia in the corpus is usually seen as flat areas. In addition, MWFELs exhibit a ridged or papillary surface structure that lacks the light-blue crest sign on magnifying endoscopy with NBI.49

Because long-term PPI use has increased in response to the increasing prevalence of chronic disorders in aging societies, endoscopic identification of PPI-related gastric mucosal lesions is essential. Therefore, endoscopists should be aware of the occurrence of these lesions among PPI users and avoid providing unnecessary or worrisome information to patients. In addition, when these lesions are observed during endoscopy, the clinician should ask the patient about the use of PPIs.

Conflicts of Interest

Gwang Ha Kim is currently a deputy editor at Clinical Endoscopy; however, he was not involved in the peer reviewer selection, evaluation, or decision process for this article. The author has no other potential conflicts of interest.

Funding

None.

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REFERENCES