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Strategic Role of Immunohistochemical Staining in Detection of *Helicobacter pylori*

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Helicobacter pylori infection affects more than half of the global population and is linked to chronic gastritis, peptic ulcers, mucosa-associated lymphoid tissue lymphoma, and gastric adenocarcinoma.[1] The diagnosis of *H. pylori* infection is crucial in treating various gastrointestinal diseases. Diagnostic methods are classified as either invasive or noninvasive, and each has limitations based on the clinical situation and laboratory setting. During endoscopic procedures, common methods for detecting *H. pylori* include invasive tests such as the rapid urease test or histological analysis.[2] Histology, which is often incorporated into *H. pylori* detection, can be enhanced by combining specific stains such as Giemsa with hematoxylin–eosin staining for increased accuracy. Histologic examination of *H. pylori*, along with the subsequent histologic diagnosis, is preferred when incorporating histochemical staining.[3-5] However, the reliability of histochemical tests for *H. pylori* may vary based on factors such as the bacterial distribution, instrument quality, and pathologist expertise. To improve the accuracy of *H. pylori* detection, biopsies should ideally be taken from both the antrum and body of the stomach. When only one site is biopsied, areas with minimal atrophic gastritis or intestinal metaplasia should be selected.[4,6]

Immunohistochemistry (IHC) is highly effective for distinguishing *H. pylori* from other bacteria, especially in cases of low bacterial counts or when coccoid bacteria are present.[3,7-9] This is particularly important for patients taking proton pump inhibitors, which can induce *H. pylori* to change into coccoid forms and move deeper into the gastric foveolae. In complex cases requiring a definitive diagnosis, IHC staining proves crucial. Additionally, when histochemical methods fail to detect *H. pylori* in patients with chronic gastritis, IHC staining serves as an important ancillary test. It not only accelerates the detection process in low-density bacterial environments but also shows less variability in the interpretation of results compared with histochemical stains. Hence, IHC staining is particularly recommended in patients with chronic gastritis, in patients with atrophic gastritis with extensive intestinal metaplasia, and during post-eradication treatment follow-up when histochemical staining does not reveal the bacteria.[10]

In this issue of the *Korean Journal of Helicobacter and Upper Gastrointestinal Research*, Hall et al.[11] compared the effectiveness of IHC stains and histochemical stains such as cresyl violet (CV) in diagnosing *H. pylori* from gastric biopsies. They found that IHC staining had higher sensitivity and specificity (85.2% and 97.7%, respectively) than CV (64.5% and 90.6%, respectively). IHC staining proved particularly efficient in detecting low *H. pylori* loads and inactive gastritis. Notably, in 14 cases, *H. pylori* was missed in CV-stained samples but detected in IHC-stained samples. Of these 14 cases, 12 had a low *H. pylori*

load and 2 exhibited coccoid bacteria. The study also revealed the time-saving benefit of IHC staining, with average detection times being significantly shorter than those of CV staining.

The author recommends the use of IHC staining as a primary or confirmatory test for *H. pylori*, especially in complex cases. IHC staining, despite its higher cost, provides significant advantages over traditional staining methods. It is more reliable in detecting *H. pylori* in challenging cases such as patients with low bacterial loads or inactive gastritis. According to the current guidelines, however, histochemical staining remains the standard method for assessing *H. pylori* gastritis.[2,3] IHC staining is recommended as an additional test in specific cases, such as patients with chronic active gastritis in whom *H. pylori* is not detected through histochemistry. Importantly, IHC staining is generally not advised in cases of normal histology. Instead, IHC staining serves as a supplementary diagnostic tool, particularly when standard histochemical methods are insufficient. Additionally, in clinical practice, factors such as cost, availability, and the need for specialized laboratory equipment and expertise cannot be overlooked. The choice of a diagnostic method often depends on an appropriate balance among these factors.

This study revealed the effectiveness of IHC staining in diagnosing *H. pylori*, particularly in detecting low bacterial loads, inactive gastritis, and coccoid forms of the bacterium. IHC staining is best suited for specific cases in which its diagnostic superiority is crucial and when noninvasive tests or traditional stains yield inconclusive results. However, the practicality of its widespread use is challenged by high costs and equipment requirements. Therefore, the application of IHC staining should be tailored to cases in which its diagnostic superiority justifies the additional expense and resource requirements.

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