学 位 論 文 の 要 旨

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学 位 論 文 名　Specific Locations of Linear Furrows in Patients With Esophageal Eosinophilia.

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論 文 内 容 の 要 旨

INTRODUCTION

Eosinophilic esophagitis (EoE) is a clinicopathological condition characterized by symptoms of esophageal dysfunction, typical endoscopic findings, and dense esophageal eosinophilia (EE), which is defined as more than 15 eosinophils per high-power field (HPF) in at least one esophageal biopsy specimen. The clinical features of EoE are non-specific and can overlap those of gastroesophageal reflux disease (GERD), making it difficult to distinguish between those conditions in clinical settings. In addition, gastroesophageal reflux may play an important role in the development of EE, as gastric acid suppression by giving proton pump inhibitor is effective in more than half of patients with EE.

Recent study shows that over 90% of patients with EE have abnormal endoscopic findings, such as linear furrows, which is the most common findings. However, the precise endoscopic features remain to be fully elucidated. In the present study, we sought to clarify the endoscopic features of EE, essential for the diagnosis of EoE, by focusing on the specific locations of linear furrows in a Japanese population.

MATERIALS AND METHODS

We retrospectively enrolled 70 patients with EE who were diagnosed at Shimane University Hospital between July 2005 and January 2016. Information regarding endoscopic findings and clinical parameters was obtained and reviewed. To clarify the endoscopic features of EE, we focused on the specific locations of linear furrows. In cases with linear furrows, their specific locations, including circumferential location, longitudinal distribution, and position in relation to esophageal longitudinal folds (ridge or valley), were noted. As a control group, another 108 consecutive patients with reflux esophagitis (RE), Los Angeles grade A or B, who were endoscopically diagnosed at our hospital between January and May 2015 were also enrolled. Position of mucosal breaks in relation to esophageal longitudinal folds was also evaluated in the same manner as linear furrows in the EE patients. Finally, the relationship between linear furrows and eosinophilic infiltration was evaluated. Biopsy specimens were obtained from linear furrows in valleys as well as mucosa on adjacent ridges between valleys, and peak eosinophil count/HPF was compared between those locations. The study protocol was approved by the Ethics Committee of Shimane University.

RESULTS AND DISCUSSION

The 70 enrolled patients consisted of 57 males and 13 females, with a mean age of 48.1 ± 14.4 years (range 17-85 years). EE was frequently observed in middle-aged patients with a peak age of occurrence in the 40s and 71% had concurrent allergic diseases. As for endoscopic findings, linear furrows, whitish exudates, and rings were frequently observed, and at least one of those findings was seen in every cases. Of these, linear furrows (n=63) were the most frequently found endoscopic abnormality in patients with EE.

Linear furrows were found to be longitudinally widespread throughout the lower to middle or upper esophagus in 51 (81%), whereas these were localized in the lower esophagus in 12

(19%). As for circumferential location, linear furrows were seen in all circumferential directions in a radial pattern in each of these patients. In addition, all of the linear furrows were found in esophageal longitudinal mucosal fold valleys, whereas none appeared on ridges. Our findings indicate that particular attention should be paid to mucosa in longitudinal fold valleys for detection of linear furrows, especially in the lower esophagus.

In contrast, the vast majority (93%) of mucosal breaks in RE cases were located on mucosal fold ridges and mainly found on the right anterior wall of the esophagus. These findings were consistent with those of our previous studies, and showed that localization of mucosal breaks was apparently different from that of linear furrows in EE patients, suggesting that acid reflux is not directly associated with formation of linear furrows in those patients.

Finally, we obtained biopsy specimens from 15 patients with linear furrows to determine the relationship between linear furrows and eosinophilic infiltration. Increased eosinophilic infiltration was significantly more frequent in linear furrows in the valleys (93%) as compared to mucosa on adjacent ridges (60%) ($P < 0.05$), indicating that fewer biopsies from linear furrows should be sufficient for an accurate diagnosis.

CONCLUSION

Our analysis included the largest number of EE cases reported in Japan. All had abnormal endoscopic findings, such as linear furrows, which was the most common. Linear furrows were detected in a radial pattern and were widespread throughout the lower to middle or upper esophagus. Furthermore, they were found only in the longitudinal mucosal fold valleys but not on the ridges, which is a completely different location as compared to mucosal breaks in RE cases. Eosinophilic infiltration $\geq$ 15/HPF was also more frequently found in linear furrows located in the valleys as compared to mucosa on adjacent ridges. More detailed investigation of these characteristics, especially by focusing on linear furrows in esophageal mucosal fold valleys, may provide important clues for more accurate diagnosis of EoE.