

学位論文の要旨

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- 学位論文名 Reliability of Symptoms and Endoscopic Findings for Diagnosis of Esophageal Eosinophilia in a Japanese Population
- 発表雑誌名 Digestion (90: 49-57, 2014)
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論文内容の要旨

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic inflammatory immune-mediated disease characterized by esophageal dysfunction and eosinophil-predominant infiltration in the esophageal epithelium. Pathologically, the hallmark of EoE is esophageal eosinophilia (EE), commonly defined by more than 15 eosinophils per high power field (HPF) in at least 1 esophageal biopsy specimen. EoE has become increasingly prevalent over the past decade, especially in Western countries. Although cases are also increasingly reported in Asian countries, the disease is thought to be rare in those countries and its clinical characteristics have not fully evaluated. Race may influence the clinical presentation and have a role in the phenotypic expression of EoE. Therefore, we aimed to investigate the diagnostic utility of EE, based on symptoms and endoscopic findings in Japanese individuals.

MATERIALS AND METHODS

We prospectively enrolled subjects who complained of esophageal symptoms suggesting EoE at least once during the last week when esophagogastroduodenoscopy (EGD) was scheduled, and/or those with endoscopic findings of suspected EoE at the outpatient clinics of 12 hospitals between August 2011 and August 2012. Those less than 15 years of age, or who received glucocorticoid administration, or had a high risk of bleeding from a biopsy were excluded. The patients who had organic causes of the symptoms, such as endoscopically proven reflux esophagitis, gastroduodenal ulcers, and upper gastrointestinal malignant tumors, were also excluded.

Endoscopic findings suspicious of EoE included longitudinal linear furrows, multiple concentric rings, whitish exudates, and reddening. At least two biopsy samples were taken from the upper and lower esophagus. Histological diagnosis of EE was defined as the presence of more than 15 eosinophils per HPF.

Standard dose of proton pump inhibitor (PPI) was prescribed for 4-8 weeks to symptomatic patients with EE. Positive response to PPI was defined as a case in which administration of PPI improved symptoms and intraepithelial eosinophilic infiltration ($<5/\text{HPF}$). PPI-resistant cases with EE were defined as cases with EoE.

The diagnostic utility of subjective symptoms and endoscopic findings was compared between the EE and non-EE groups using logistic regression analysis.

The protocol of this study was approved by the ethical committee of Shimane University School of Medicine, and written informed consent was obtained from all subjects prior to enrolment.

RESULTS AND DISCUSSION

During the study period of 13 months, EGD was performed in 17,324 patients, of whom 349 (163 men, 186 women; mean age 60.6 years) were enrolled in this study. Of the 349 enrolled patients, 319 had symptoms suggesting EoE, while 30 had no symptoms but endoscopic findings

suggesting EoE. Of those with symptoms, 8 (2.5%) had EE, and 3 were finally diagnosed with EoE. Dysphagia was the most common symptom observed in symptomatic patients, and none of the patients had a history of food impaction, a common symptom associated with EoE in Western individuals, especially Caucasians, suggesting racial differences with regard to EoE-related symptoms. Although the ratio of dysphagia was higher in our patients with EE (62.5%) than in those without EE (30.4%), subjective symptoms including dysphagia, heartburn, and chest pain were not specific enough to make a diagnosis of EE.

Eleven (18.3%) of 60 patients with endoscopic findings were diagnosed as EE, and linear furrows were seen in 10 (90.9%), while other findings were not so frequent. Interestingly, only a single patient (0.35%) was diagnosed with EE among those with symptoms but no endoscopic findings (n=289). Therefore, the presence of abnormal endoscopic findings was significantly more important to predict EE. Among the endoscopic findings, linear furrows was the most reliable (OR=41.583) as shown by logistic regression analysis. The sensitivity for linear furrows was modest at 83%, whereas specificity was 95%. These findings contradict the routine esophageal biopsies for the purpose of detecting EE in patients without abnormal endoscopic findings suggesting EoE.

CONCLUSION

EE remains a rare condition among Japanese patients with chest and epigastric symptoms as compared with Western populations. Presenting symptoms including dysphagia do not lend support to a diagnosis of EE. As for endoscopic findings, the presence of linear furrows was the most frequent and useful for EE diagnosis.

論文審査及び最終試験又は学力の確認の結果の要旨

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論文審査の結果の要旨			
<p>好酸球性食道炎は欧米において急激な有病率の増加を示している。近年、本邦においても報告例が増加しているが、日本人における臨床的特徴は十分に評価されていない。申請者らは、好酸球性食道炎の主要な病理所見である食道好酸球浸潤の診断に有用な症状および内視鏡所見を明らかにすることを目的に臨床研究を行った。当院および関連施設で上部消化管内視鏡検査を施行した 17,324 例のうち、食道関連症状を有する 319 例および無症状だが好酸球性食道炎を疑う内視鏡所見を有する 30 例の合計 349 例を対象に、食道からの生検で好酸球浸潤の有無を評価し、食道好酸球浸潤の診断に関連する症状および内視鏡所見についてロジスティック回帰分析を用いて解析した。その結果、食道関連症状を有した 319 例のうち、内視鏡所見を伴った 30 例では 7 例 (23.3%) に食道好酸球浸潤を認めたのに対して、内視鏡所見のない 289 例で食道好酸球浸潤を認めたのは 1 例 (0.35%) のみであった。また、症状がないものの内視鏡所見を有した 30 例中 4 例 (13.3%) に食道好酸球浸潤を認めた。内視鏡所見では縦走溝が最も頻度が高く、診断に関連する有用な因子 (OR=41.583) として抽出された。一方、嚥下困難などの症状については有意な関連性は認められず、食道関連症状のみで内視鏡所見を伴わない場合、食道好酸球浸潤を認める頻度はかなり低い (0.35%) ことが明らかとなった。これらの結果は、本邦における好酸球性食道炎の診療において有用な成果と考えられる。</p>			
最終試験又は学力の確認の結果の要旨			
<p>申請者は、17,324 例の内視鏡施行例から食道好酸球浸潤症例 12 例(内、好酸球性食道炎 3 例)を組織学的に診断し、その臨床的特徴と診断における内視鏡検査所見の有用性を明らかにした。この結果は、本邦における好酸球性食道炎診断ガイドラインの作成にも重要な示唆を与えるものである。学位審査における質疑応答も適確で、関連分野の知識も豊富であり、学位授与に値すると判断した。(主査:田島 義証)</p>			
<p>申請者は、好酸球性食道炎の病態・診断・治療に関する臨床病理学的検討を行い、内視鏡検査での特徴的な所見や生検による病理学的診断が確定診断に重要であることを、統計学的手法により、証明した。本疾患の臨床に被益する研究であり、学位に値すると判断した。(副査:川内 秀之)</p>			
<p>申請者は、17,000 例あまりの内視鏡施行例から症状および内視鏡所見を通じて好酸球性食道炎を疑う 349 例を抽出し、その中に食道好酸球浸潤例 12 例(そのうち好酸球性食道炎確定例 3 例)を見いだして、その臨床的特徴を解析した。これは、今後この疾患の診断技術向上に資する優れた結果である。背景の知識も豊富であり質疑応答も適確であったことから、学位授与に値すると判断した。(副査:並河 徹)</p>			

(備考) 要旨は、それぞれ 400 字程度とする。