



# A Case of Early Barrett's Adenocarcinoma With Eosinophilic Esophagitis

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## ABSTRACT

A 61-year-old man presented with epigastric pain and underwent upper gastrointestinal endoscopy. A strongly erythematous area was found in the short segment of the Barrett's esophagus, and a biopsy revealed well-differentiated adenocarcinoma. Linear furrows were observed in the lower esophagus, and a biopsy of the lesion revealed eosinophil infiltration of 30 eosinophils per high-power field. Therefore, a diagnosis of Barrett's adenocarcinoma with eosinophilic esophagitis was made. Although rare, the incidence of Barrett's adenocarcinoma and eosinophilic esophagitis has been increasing in Japan in recent years, and the number of cases may increase in the future.

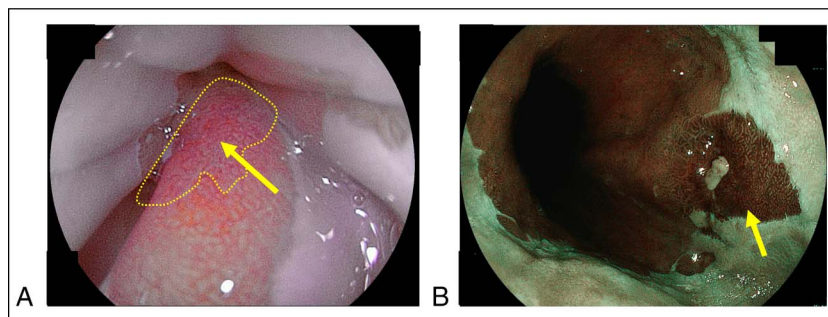
**KEYWORDS:** Barrett's adenocarcinoma; eosinophilic esophagitis; Barrett's esophagus; *Helicobacter pylori*

## INTRODUCTION

Risk factors of Barrett's esophagus (BE) and Barrett's adenocarcinoma (BA) include male sex, smoking, obesity, and non-*Helicobacter pylori* infections.<sup>1-3</sup> Furthermore, risk factors of eosinophilic esophagitis (EoE) include male sex, non-*H. pylori* infection, and history of allergy.<sup>4,5</sup> Because male sex and non-*H. pylori* infections are common risk factors of both diseases, occurrence of concurrent BA and EoE is expected to rise given the current decline in the rate of *H. pylori* infection; however, to our knowledge, no such cases have been reported. This may be because of the low complication rate of cancer among patients with allergic diseases.<sup>6,7</sup> We report an extremely rare case of BA occurring with EoE.

## CASE REPORT

A 61-year-old man presented with epigastric pain and underwent an upper gastrointestinal endoscopy. He was admitted to the hospital for the treatment of lifestyle-related diseases such as hypertension, hyperlipidemia, hyperuricemia, and diabetes. Although currently a nonsmoker, he had a 19-year history of smoking. In the upper gastrointestinal endoscopy, a strongly erythematous area was found 40 cm from the incisors in the short segment of the BE (Figure 1). Pathological examination of biopsy specimens obtained from the lesion revealed a well-differentiated adenocarcinoma. Background endoscopic findings of the lower esophagus showed linear furrows and fragile protruded mucosal lesion sandwiched between the linear furrows, similar to caterpillar tracks (Figure 2).<sup>8</sup> A biopsy of the lesions showed hypereosinophilia with marked 30 eosinophils/high-power field (Figure 3). Blood tests revealed elevated eosinophil counts at 310.5/ $\mu$ L (white blood cells, 5,750/ $\mu$ L; eosinophil rate, 5.4%), and the serum anti-*H. pylori* immunoglobulin G antibody level was <3.0 U/mL. Therefore, a diagnosis of EoE was made based on clinical symptoms and endoscopic and pathological



**Figure 1.** Endoscopic image of BA in the lower esophagus with (A) linked color imaging and (B) narrow-band imaging. The strongly erythematous area of the BA lesion in the short segment of the BE (yellow dotted area and arrow). The white area in the center of the erythematous patch in Figure 1B shows the postbiopsy scar. BA, Barrett's adenocarcinoma; BE, Barrett's esophagus.

findings. Lymph node metastasis was not detected on computed tomography, and early cancer was suspected based on endoscopic findings. Therefore, endoscopic submucosal dissection (ESD) of the lesion was performed. The final histological diagnosis of the resected ESD specimen revealed well-differentiated adenocarcinoma with mucosal invasion and no lymphovascular involvement (Figure 4). The specimen was free of tumor cells in the lateral/vertical histological margin. The pathological diagnosis after ESD for BA was 12 × 9 mm, Ae, Type0-IIb, tub1, pT1a-LPM, pHM0, pVM0, INFA, ly0, and v0 (Figure 4).<sup>9</sup> Two years after ESD, there were no changes or cancer recurrence. In addition, EoE manifested no symptoms such as epigastric pain due to vonoprazan administration.

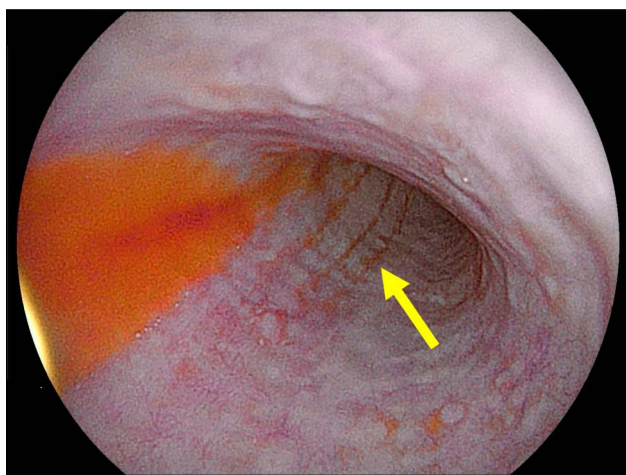
## DISCUSSION

We report a case of early BA occurring concurrently with EoE. To our knowledge, this is the first report of a patient with both BA and EoE.

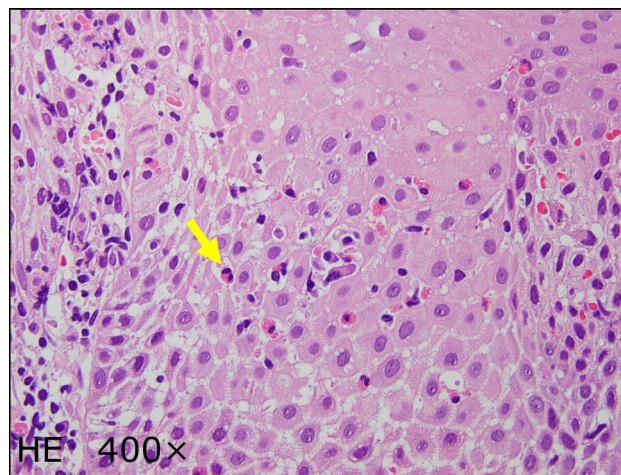
In 3 previous studies investigating the relationship between esophageal cancer and EoE, a negative relationship was

reported.<sup>10–12</sup> However, there have been several reports on the relationship between BE and EoE, which is the cause of BA.<sup>10,13,14</sup> Takashima et al<sup>13</sup> reported that the prevalence of BE was significantly lower in patients with EoE than in healthy individuals (2.1% vs 13.2%,  $P = 0.00528$ ). In addition, BE and EoE were negatively correlated in a multivariate analysis (odds ratio, 0.132; 95% CI: 0.0302–0.573;  $P = 0.00686$ ). Conversely, Lipka et al<sup>10</sup> reported that 13 patients with EoE were followed up for an average of 13.6 years (5–24 years), and 7 patients (53.8%) had BE. Lifestyle factors, such as obesity, eating habits, reflux esophagitis, and non-*H. pylori* infection, are well-known risk factors of BE and BA.<sup>1–3</sup> Risk factors of EoE include non-*H. pylori* infection and history of allergic diseases.<sup>4,5</sup> The incidence and prevalence of EoE, BE, and BA have increased in recent years because of decreasing *H. pylori* infection rates in Japan.<sup>15–17</sup>

Prolonged, low-grade, or smoldering inflammation is a hallmark of cancer. However, the relationship between allergies and cancers in various organs, including that in the esophagus, has been investigated, and most studies have detailed that cancer and allergies are inversely related.<sup>6,7</sup> Eosinophils have been

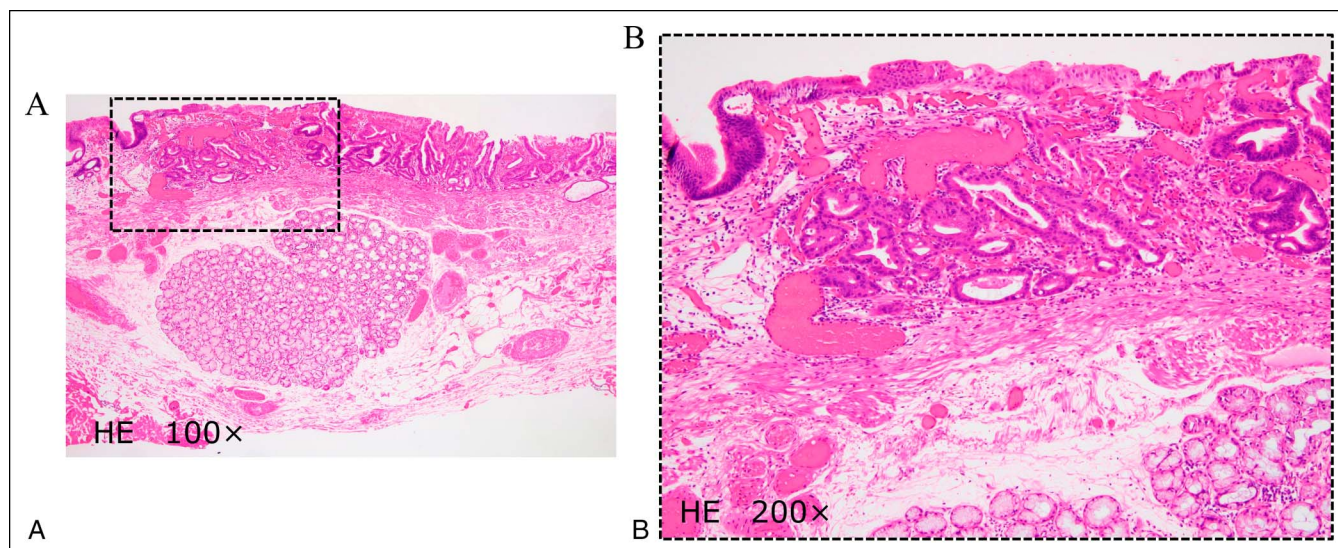


**Figure 2.** Endoscopic image of the lower esophagus with linked color imaging. Endoscopy reveals decreased vascularity, linear furrows, and fragile protruded mucosal lesion sandwiched between the linear furrows, representing a caterpillar sign (yellow arrow).



**Figure 3.** Pathological findings in an esophageal mucosal biopsy specimen from the endoscopic findings of linear furrows indicate eosinophilic infiltration with marked 30 eosinophils/high-power field (yellow arrow indicates eosinophils).





**Figure 4.** Pathological images of Barrett's adenocarcinoma of endoscopic submucosal dissection specimens. (A) Esophageal glands are observed at the depth of the tumor. (B) Well-differentiated adenocarcinoma lesion.

reported to be components of the immune microenvironment that regulate tumor initiation and progression.<sup>18,19</sup> In addition to exerting direct cytotoxic effects on cancer cells, eosinophils may also participate in the antitumor response of accessory and immunomodulatory cells.<sup>19</sup> By contrast, eosinophils produced by carcinogenesis and allergic reactions may play different roles. A previous study has reported multiple cases of gastric cancer complicated with eosinophilic gastroenteritis.<sup>20</sup> The pathogenesis was unclear. BE and EoE are common diseases among patients with non-*H. pylori* infection, and with the current decrease in the *H. pylori* infection rate in Japan, the number of similar cases may increase.

## DISCLOSURES

Author contributions: N. Sumi and K. Haruma conceived the idea, interpreted the data, and wrote the manuscript. N. Hisamoto, K. Inoue, K. Mabe, N. Manabe, Y. Kawahara, and H. Okada collected data and references. T. Takao reviewed the manuscript and provided critical intellectual input. All authors reviewed and approved the submitted version of the manuscript. N. Sumi is the article guarantor.

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