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CASE REPORT | ESOPHAGUS

Antitumor Necrosis Factor-Refractory Esophageal Lesions in Crohn's Disease Successfully Treated With Upadacitinib

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ABSTRACT

A 39-year-old man with a 5-year history of ileocolonic Crohn's disease received treatment with 6-mercaptopurine and adalimumab. A computed tomography scan was performed due to a persistent cough, revealing esophageal wall thickening. Esophagogastroduodenoscopy identified multiple longitudinal ulcers throughout the esophagus. Despite infliximab treatment, the esophageal lesions deteriorated, leading to the initiation of upadacitinib for antitumor necrosis factor-refractory esophageal lesions. Consequently, all esophageal lesions were healed, and serum biomarkers returned negative results. Although upadacitinib is effective for patients with ileocolonic Crohn's disease, this is the first case demonstrating its efficacy for refractory esophageal lesions.

KEYWORDS: upadacitinib; Crohn's disease; refractory esophageal lesion; longitudinal ulcer

INTRODUCTION

Upper gastrointestinal (UGI) lesions in Crohn's disease (CD) are increasingly diagnosed in patients undergoing esophagogastroduodenoscopy (EGD) as part of their routine diagnostic evaluation. The prevalence of UGI lesions was reported to be 13%–15%, with esophageal lesions accounting for 11%.[1,2] Nevertheless, there is a lack of a definitive therapeutic approach for esophageal lesions, and information regarding the therapeutic efficacy and optimal utilization of biologics is scarce.

Upadacitinib (UPA) is a selective JAK1 inhibitor approved for the treatment of CD, with the advantages of oral administration and a rapid response. The efficacy of UPA for ileocolonic CD lesions has been reported; however, there have been no reports regarding the efficacy of UPA for esophageal CD lesions.[3,4] This case report highlights the successful use of UPA in managing esophageal CD lesions that were refractory to antitumor necrosis factor therapy.

CASE REPORT

A 39-year-old man diagnosed with ileocolonic CD (Montreal Classification: L3B1p) with a 5-year history of the disease. He was treated with 5-aminosalicylic acid at a dosage of 3 g per day, mercaptopurine at 30 mg per day, adalimumab at 80 mg every 2 weeks, and vonoprazan at 20 mg per day.

Ten months before, EGD revealed no UGI lesions. Computed tomography was conducted to investigate the persistent cough. Although no lesions were detected in the bronchi or lungs, thickening of the esophageal wall was observed. EGD identified multiple longitudinal ulcers along the entire esophagus (Figure 1). Pathological examination indicated inflammatory cell infiltration without granulomas. Despite the findings, medical management remained unchanged as the cough resolved spontaneously.

One year later, adalimumab was changed to infliximab (5 mg/kg) due to an anal fistula and abdominal symptoms. Subsequently, the dosage was increased to 10 mg/kg after 3 months because of persistent symptoms. After 5 months, the patient experienced chest pain,

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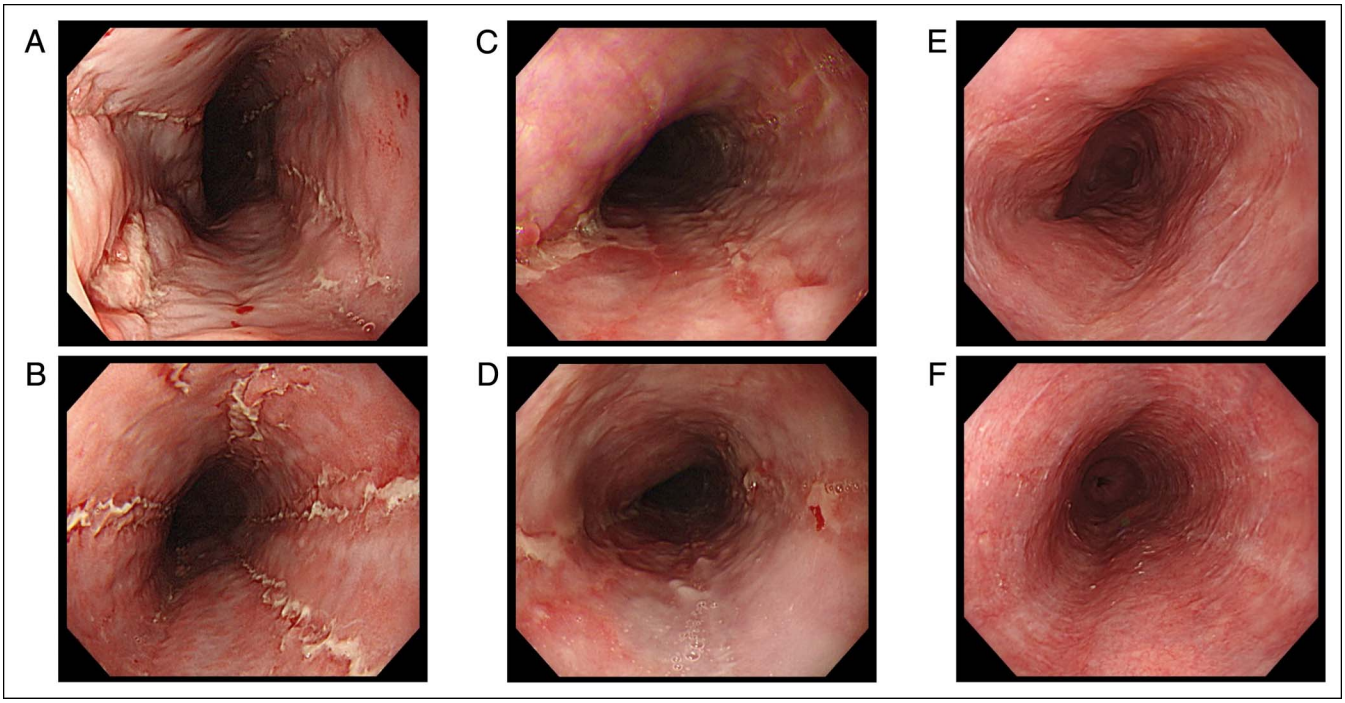

Figure 1. Esophagogastroduodenoscopy images of the esophagus: (A and B) initial examination, (C and D) second examination, and (E and F) third examination.

and esophageal ulcers were still present (Figure 1). Consequently, a daily dose of 45 mg of UPA was initiated to address antitumor necrosis factor (TNF)-refractory esophageal CD lesions. Nine months after the commencement of UPA treatment, endoscopic examination revealed scarring of all ulcers (Figure 1). Furthermore, serum biomarkers, including leucine-rich alpha-2-glycoprotein, erythrocyte sedimentation rate, and C-reactive protein, showed negative results. Throughout this period, 3 colonoscopies were performed, confirming remission in the terminal ileum and colon. The patient's clinical progression is illustrated in Figure 2.

DISCUSSION

This report is the first to demonstrate the efficacy of UPA for refractory esophageal lesions. These lesions developed during treatment with adalimumab and a potassium-competitive acid blocker and worsened despite treatment with infliximab.

Clinicians may not readily identify asymptomatic patients with CD and UGI lesions. These lesions serve as crucial indicators of disease activity, progression, and relapse.[5–7] Therefore, conducting EGD to evaluate UGI lesions is imperative in clinical settings.

Although granuloma was not detected, longitudinal ulcerations that were refractory to maximum dose of vonoprazan were observed and UPA was effective for those lesions. Inflammatory markers such as leucine-rich alpha-2-glycoprotein and C-reactive protein clearly decreased and normalized after UPA was started. These results suggested that esophageal lesions in this case were associated with CD.

At present, there is no clear therapeutic strategy for treating esophageal lesions in patients with CD. The European Crohn's and Colitis Organization guidelines recommend proton pump inhibitors for mild esophageal lesions and systemic corticosteroids or anti-TNF agents for severe or refractory lesions.[8] Several reports have highlighted the efficacy of anti-TNF agents, anti-integrin agent, and anti-interleukin 12/23 agents.[9–12] However, data on the therapeutic efficacy and optimal use of biologics are limited. Although several advanced therapies have been developed for patients with CD, we considered that UPA might be more effective than other advanced therapies, such as vedolizumab or ustekinumab for anti-TNF experienced CD patients. Therefore, we selected UPA for this case. To the best of our knowledge, there have been no reports on the efficacy of UPA for esophageal lesions. Therefore, UPA could be considered as a treatment option for patients with refractory diseases. Our findings will be valuable for future clinical practice, and it is essential to gather treatment reports using UPA for esophageal lesions in patients with CD.

DISCLOSURES

Author contributions: M. Naganuma conceived the study. N. Nakamura and Y. Honzawa designed the main concept of this study. N. Nakamura and M. Naganuma participated in clinical information acquisition. N. Nakamura and M. Naganuma drafted and wrote the manuscript. All authors contributed to

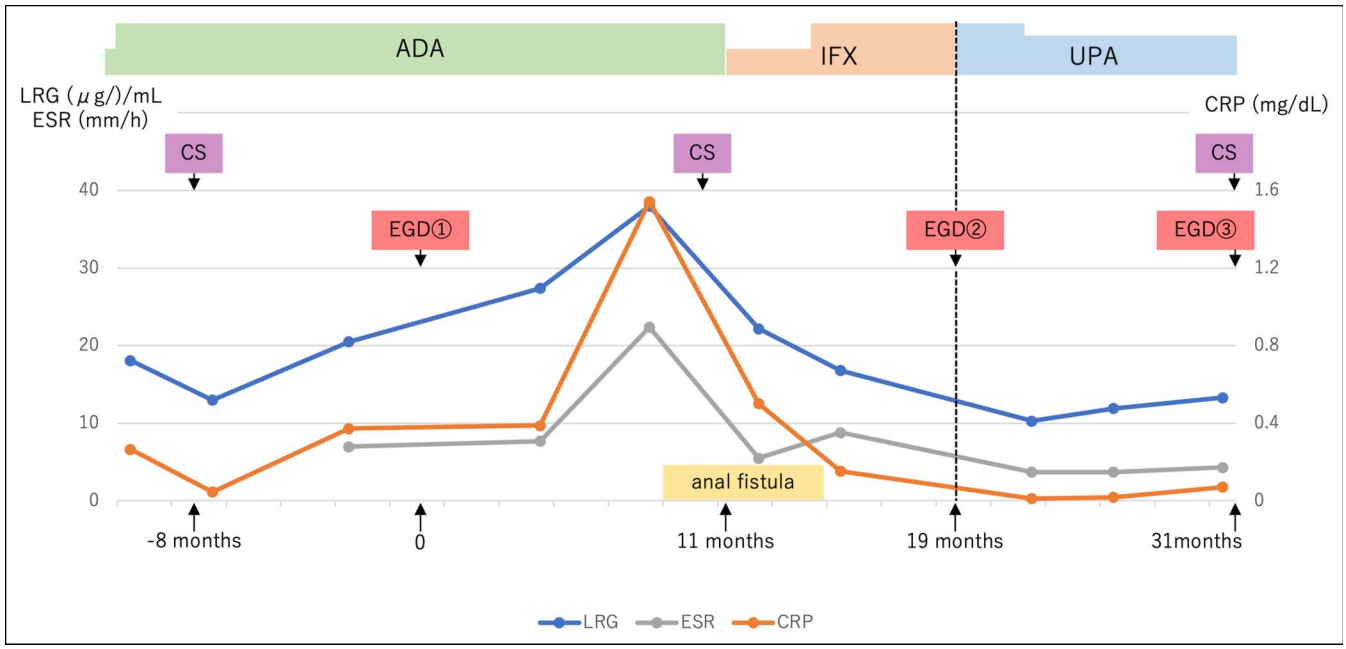

Figure 2. Clinical course of the case, including treatment and diagnostic modalities. ADA, adalimumab; CRP, C-reactive protein; CS, colonoscopy; EGD, esophagogastroduodenoscopy; ESR, erythrocyte sedimentation rate; IFX, infliximab; LRG, leucine-rich alpha-2-glycoprotein; UPA, upadacitinib.

critical review and approved the final draft. M. Naganuma is the article guarantor.

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