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## Acid suppressive therapy improved symptoms due to circumferential cervical inlet patch with proton pumps (H<sup>+</sup>/K<sup>+</sup>-ATPase)

Takanori Yamada, Atsushi Tsuji, Shunya Onoue, Masanao Kaneko, Fumihiko Tanioka, Satoshi Osawa, Yasuhiko Saida

Takanori Yamada, Atsushi Tsuji, Shunya Onoue, Masanao Kaneko, Yasuhiko Saida, Department of Gastroenterology, Iwata City Hospital, Iwata 438-8550, Japan

Fumihiko Tanioka, Division of Pathology, Iwata City Hospital, Iwata 438-8550, Japan

Satoshi Osawa, Department of Endoscopic and Photodynamic Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-3192, Japan

ORCID number: Takanori Yamada (0000-0001-6964-2931); Atsushi Tsuji (0000-0002-7362-9024); Shunya Onoue (0000-0001-5478-3299); Masanao Kaneko (0000-0003-4391-9837); Satoshi Osawa (0000-0003-3414-1808); Yasuhiko Saida (0000-0001-7642-1037).

**Author contributions:** Yamada T wrote the paper; Tsuji A treated the patient and performed endoscopy; Onoue S, Kaneko M, Osawa S and Saida Y contributed to the paper design and coordination; Tanioka F contributed to the pathological examination.

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**Correspondence to:** Takanori Yamada, MD, PhD, Department of Gastroenterology, Iwata City Hospital, 512-3 Okubo, Iwata 438-8550, Japan. [tky@hospital.iwata.shizuoka.jp](mailto:tky@hospital.iwata.shizuoka.jp)  
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**Fax:** +81-538-385050

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### Abstract

Cervical inlet patch (CIP), also referred to as esophageal heterotopic gastric mucosa, is regarded as the residue of columnar epithelium of the embryonic esophagus. Narrow band imaging increases the detection rate of CIP. Herein, we present a 55-year-old man with symptomatic circumferential inlet patch. He exhibited globus and dysphagia, and esophagogastroduodenoscopy found circumferential CIP, where immunohistochemistry revealed the existence of proton pumps (H<sup>+</sup>, K<sup>+</sup>-ATPase). His throat symptoms were relieved by acid suppressive therapy with pump inhibitors. This case indicated that CIP should be considered as a differential diagnosis for the cause of globus symptoms in rare cases.

**Key words:** Cervical inlet patch; Proton pump inhibitor

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**Core tip:** Cervical inlet patch (CIP) is the esophageal heterotopic gastric mucosa in the cervical esophagus. We present a 55-year-old man exhibiting circumferential CIP with globus and dysphagia. Proton pump inhibitors relived these throat symptoms. Immunohistochemistry revealed existence of proton pumps in the CIP lesion. The throat symptoms were suggested to be related with CIP and acid secretion.

Yamada T, Tsuji A, Onoue S, Kaneko M, Tanioka F, Osawa S, Saida Y. Acid suppressive therapy improved symptoms due to circumferential cervical inlet patch with proton pumps ( $H^+/K^+$ -ATPase). *World J Clin Cases* 2017; 5(11): 403-406 Available from: URL: <http://www.wjgnet.com/2307-8960/full/v5/i11/403.htm> DOI: <http://dx.doi.org/10.12998/wjcc.v5.i11.403>

## INTRODUCTION

Esophageal heterotopic gastric mucosa (HGM), also referred to as cervical inlet patch (CIP), is considered to be the residue of columnar epithelium of the embryonic esophagus<sup>[1,2]</sup>. The diagnosis rate of CIP is increasing because of the recent development and spread of image-enhanced endoscopy, including narrow band imaging (NBI)<sup>[3,4]</sup>. Patients with CIP rarely require treatment as most cases of CIP are asymptomatic. However, some reports indicated complications associated with acid secretion from CIP<sup>[5-7]</sup>. Herein, we present a patient with circumferential CIP in whom proton pump inhibitors (PPI) were effective and proton pump existence was confirmed by immunohistochemistry.

## CASE REPORT

A 55-year-old man visited the department of otolaryngology exhibiting globus and dysphagia without heartburn or epigastric pain. His past medical history only included an operation for appendicitis. Physical examination and laboratory findings were unremarkable. Laryngoscopy did not reveal the cause of the throat symptoms. He was then introduced to the department of gastroenterology and esophagogastroduodenoscopy (EGD) was performed to determine the cause. EGD revealed circular HGM in the cervical esophagus, the HGM was 19 to 21 cm from the incisor. The lesion appeared reddish by white light imaging (Figure 1A), whereas by NBI, it appeared as a dark brown lesion clearly distinguished from light green squamous epithelium (Figure 1B). There was only mild reflux esophagitis (Los Angeles grade A), but no esophageal hiatus hernia at the esophagogastric junction. His throat symptoms improved quickly by acid suppression therapy with PPI.

Endoscopic biopsy from the circumferential CIP lesion demonstrated foveolar epithelium and

fundic glands (Figure 2A). Furthermore, to confirm the relationship between the throat symptoms and acid secretion from the CIP, we performed immunohistochemistry and found proton pump,  $H^+$ ,  $K^+$ -ATPase alpha subunits. Immunohistochemical staining was concentrated in the glands of CIP (Figure 2B).

## DISCUSSION

CIP, also referred to as cervical esophageal HGM, is generally regarded as a congenital condition that results from an incomplete replacement by squamous epithelium, and the differentiation of persistent columnar-lined mucosa into cervical HGM<sup>[1,2]</sup>. The incidence of CIP was reported as 0.1% to 13.8%<sup>[3,8]</sup>. Using NBI endoscopy, there was increase in the detection of CIP<sup>[4]</sup>.

Some reports demonstrated acid secretion from CIP using pH monitoring<sup>[5-7]</sup>. Here, we demonstrated the existence of proton pumps ( $H^+$ ,  $K^+$ -ATPase) in CIP in a symptomatic patient by immunohistochemistry. The efficacy of PPI also supports the theory that acid secretion from proton pumps in CIP is the cause of throat symptoms. In the present case, the patient had mild esophagitis. Although there is a possibility that gastroesophageal reflux disease was one of the causes of the globus symptoms, we considered cervical CIP to be the main cause of his globus symptoms because of the existence of proton pumps in the large CIP and the previous reports of the relationship between throat symptoms and acid secretion from CIP. However, this case report did not directly show the relationship between existence of proton pumps and their acid secretion function in CIP. Further studies are needed to demonstrate the usefulness of immunohistochemistry for proton pump to predict PPI efficacy in patients with symptomatic CIP.

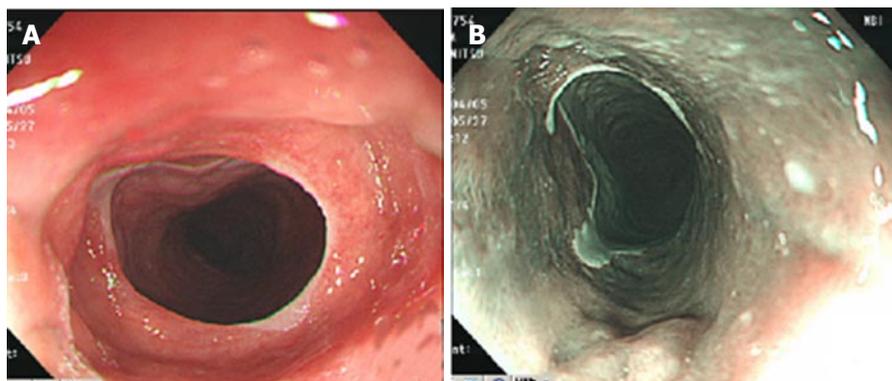
Recently, argon plasma coagulation and radio-frequency ablation were reported to be effective for symptomatic CIP<sup>[9-11]</sup>. However, these endoscopic ablation techniques are not available in all countries, including Japan. PPI treatment is more widely available than endoscopic ablation. PPI should be selected first in such situations. Furthermore, the detection of proton pumps by immunohistochemistry may predict the efficacy of PPI for throat symptoms in patients with CIP.

In summary, we reported a 55-year-old man with circumferential CIP where immunohistochemistry revealed proton pump existence. His throat symptoms were relieved by acid suppressive therapy with PPI. This case indicated that CIP should be considered as a differential diagnosis for the cause of globus symptoms in rare cases.

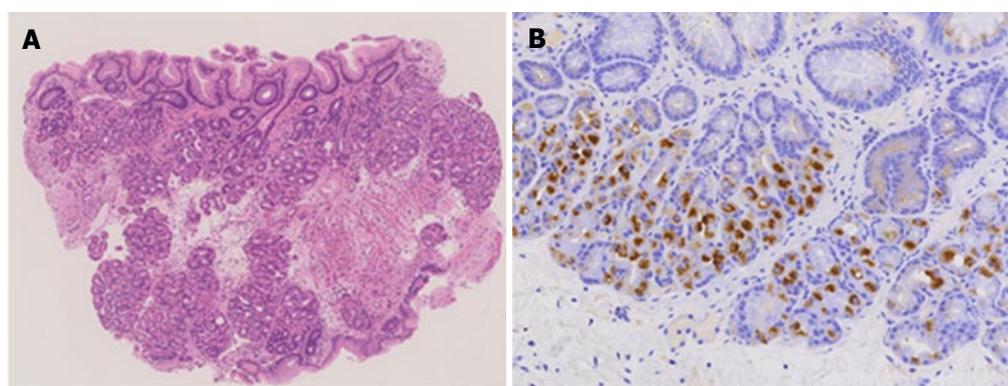
## COMMENTS

### Case characteristics

A 55-year-old man visited to complaint globus and dysphagia without heartburn



**Figure 1** Endoscopic image of circumferential cervical inlet patch. A: White light image showing circular reddish cervical inlet patch (CIP) mucosa; B: On narrow band imaging, CIP is the circular dark brown area and squamous mucosa is light green. This sharp contrast of color helps to detect CIP.



**Figure 2** Histopathological findings of biopsy specimen. A: Endoscopic biopsy of cervical inlet patch (CIP) showing foveolar epithelium and fundic gland (Hematoxylin and eosin staining); B: Immunohistochemistry for proton pump alpha subunit demonstrated concentration of staining in glands of CIP (X 400).

or epigastric pain.

### Clinical diagnosis

Endoscopy revealed circumferential cervical inlet patch (CIP).

### Differential diagnosis

Gastroesophageal reflux and globus hystericus.

### Imaging diagnosis

Esophagogastroduodenoscopy revealed circumferential CIP, where appeared reddish by white light imaging and appeared as a dark brown clearly distinguished from light green squamous epithelium by narrow band imaging.

### Pathological diagnosis

Immunohistochemistry for proton pump alpha subunit demonstrated concentration of staining in glands of CIP.

### Treatment

Acid suppressive therapy with proton pump inhibitors (PPI) improved globus and dysphagia in a patient with CIP.

### Related reports

Although some reports demonstrated acid secretion from CIP using pH monitoring, this is the first report that demonstrated the existence of proton pumps (H<sup>+</sup>, K<sup>+</sup>-ATPase) in CIP in a symptomatic patient by immunohistochemistry. The relationship should be elucidated between the existence of proton pump and acid secreting function in CIP.

### Term explanation

CIP is esophageal heterotopic gastric mucosa, which is considered to be the

residue of columnar epithelium of the embryonic esophagus.

### Experiences and lessons

CIP should be considered as a differential diagnosis for the cause of globus symptoms in rare cases.

### Peer-review

This case report clearly presented a case of CIP which expressed the proton pump and was successfully treated by PPI.

## REFERENCES

- 1 von Rahden BH, Stein HJ, Becker K, Liebermann-Meffert D, Siewert JR. Heterotopic gastric mucosa of the esophagus: literature-review and proposal of a clinicopathologic classification. *Am J Gastroenterol* 2004; **99**: 543-551 [PMID: 15056100 DOI: 10.1111/j.1572-0241.2004.04082.x]
- 2 Chong VH. Clinical significance of heterotopic gastric mucosal patch of the proximal esophagus. *World J Gastroenterol* 2013; **19**: 331-338 [PMID: 23372354 DOI: 10.3748/wjg.v19.i3.331]
- 3 Hori K, Kim Y, Sakurai J, Watari J, Tomita T, Oshima T, Kondo C, Matsumoto T, Miwa H. Non-erosive reflux disease rather than cervical inlet patch involves globus. *J Gastroenterol* 2010; **45**: 1138-1145 [PMID: 20582442 DOI: 10.1007/s00535-010-0275-8]
- 4 Cheng CL, Lin CH, Liu NJ, Tang JH, Kuo YL, Tsui YN. Endoscopic diagnosis of cervical esophageal heterotopic gastric mucosa with conventional and narrow-band images. *World J Gastroenterol* 2014; **20**: 242-249 [PMID: 24415878 DOI: 10.3748/wjg.v20.i1.242]
- 5 Galan AR, Katzka DA, Castell DO. Acid secretion from an esophageal inlet patch demonstrated by ambulatory pH monitoring. *Gastroenterology* 1998; **115**: 1574-1576 [PMID: 9834287 DOI: 10.1016/S0016-5085(98)70038-1]

- 6 **Kim EA**, Kang DH, Cho HS, Park DK, Kim YK, Park HC, Kim JH. Acid secretion from a heterotopic gastric mucosa in the upper esophagus demonstrated by dual probe 24-hour ambulatory pH monitoring. *Korean J Intern Med* 2001; **16**: 14-17 [PMID: 11417299 DOI: 10.3904/kjim.2001.16.1.14]
- 7 **Korkut E**, Bektaş M, Alkan M, Ustün Y, Meco C, Ozden A, Soykan I. Esophageal motility and 24-h pH profiles of patients with heterotopic gastric mucosa in the cervical esophagus. *Eur J Intern Med* 2010; **21**: 21-24 [PMID: 20122608 DOI: 10.1016/j.ejim.2009.10.009]
- 8 **Maconi G**, Pace F, Vago L, Carsana L, Bargiggia S, Bianchi Porro G. Prevalence and clinical features of heterotopic gastric mucosa in the upper oesophagus (inlet patch). *Eur J Gastroenterol Hepatol* 2000; **12**: 745-749 [PMID: 10929900 DOI: 10.1097/00042737-200012070-00005]
- 9 **Meining A**, Bajbouj M, Preeg M, Reichenberger J, Kassem AM, Huber W, Brockmeyer SJ, Hannig C, Höfler H, Prinz C, Schmid RM. Argon plasma ablation of gastric inlet patches in the cervical esophagus may alleviate globus sensation: a pilot trial. *Endoscopy* 2006; **38**: 566-570 [PMID: 16802267 DOI: 10.1055/s-2006-925362]
- 10 **Bajbouj M**, Becker V, Eckel F, Miehke S, Pech O, Prinz C, Schmid RM, Meining A. Argon plasma coagulation of cervical heterotopic gastric mucosa as an alternative treatment for globus sensations. *Gastroenterology* 2009; **137**: 440-444 [PMID: 19410576 DOI: 10.1053/j.gastro.2009.04.053]
- 11 **Dunn JM**, Sui G, Anggiansah A, Wong T. Radiofrequency ablation of symptomatic cervical inlet patch using a through-the-scope device: a pilot study. *Gastrointest Endosc* 2016; **84**: 1022-1026.e2 [PMID: 27373671 DOI: 10.1016/j.gie.2016.06.037]

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