

[ CASE REPORT ]

## A Rare Case of Localized Esophageal Amyloidosis

Taku Fujiya<sup>1</sup>, Waku Hatta<sup>1</sup>, Tomoyuki Koike<sup>1</sup>, Yohei Ogata<sup>1</sup>, Masahiro Saito<sup>1</sup>, Xiaoyi Jin<sup>1</sup>, Kenichiro Nakagawa<sup>1</sup>, Takeshi Kanno<sup>1</sup>, Kiyotaka Asanuma<sup>1</sup>, Kaname Uno<sup>1</sup>, Naoki Asano<sup>1</sup>, Akira Imatani<sup>1</sup>, Fumiyoshi Fujishima<sup>2</sup>, Nagaaki Katoh<sup>3</sup>, Tsuneaki Yoshinaga<sup>3</sup> and Atsushi Masamune<sup>1</sup>

### Abstract:

A 72-year-old man without any symptoms was referred to our hospital. Esophagogastroduodenoscopy revealed an elevated esophageal lesion that was covered with normal mucosa. The examination of biopsy specimens from the lesion revealed amyloid light-chain (AL) ( $\lambda$ ) type amyloid deposits, but there were no amyloid deposits elsewhere in the gastrointestinal tract. Further examinations did not indicate systemic amyloidosis. Thus, this case was diagnosed as a localized esophageal amyloidosis. As the clinical outcome of localized amyloidosis is favorable, this case was scheduled for close follow-up. Localized amyloidosis should be considered in the differential diagnosis of esophageal submucosal tumors.

**Key words:** esophagus, amyloidosis

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### Introduction

Amyloidosis is a rare disease caused by deposits of rigid non-branching protein fibrils that lead to various pathophysiological changes. Amyloidosis can occur in virtually any organ system in the body, and histological involvement of the gastrointestinal (GI) tract is very common among patients with systemic amyloidosis (1). However, an amyloid deposit confined to a single organ or tissue is uncommon and localized amyloidosis in the GI tract is relatively rare (2). Localized esophageal amyloidosis is an extremely rare condition. We herein report a case of localized esophageal amyloidosis that showed a submucosal tumor (SMT)-like appearance without symptoms.

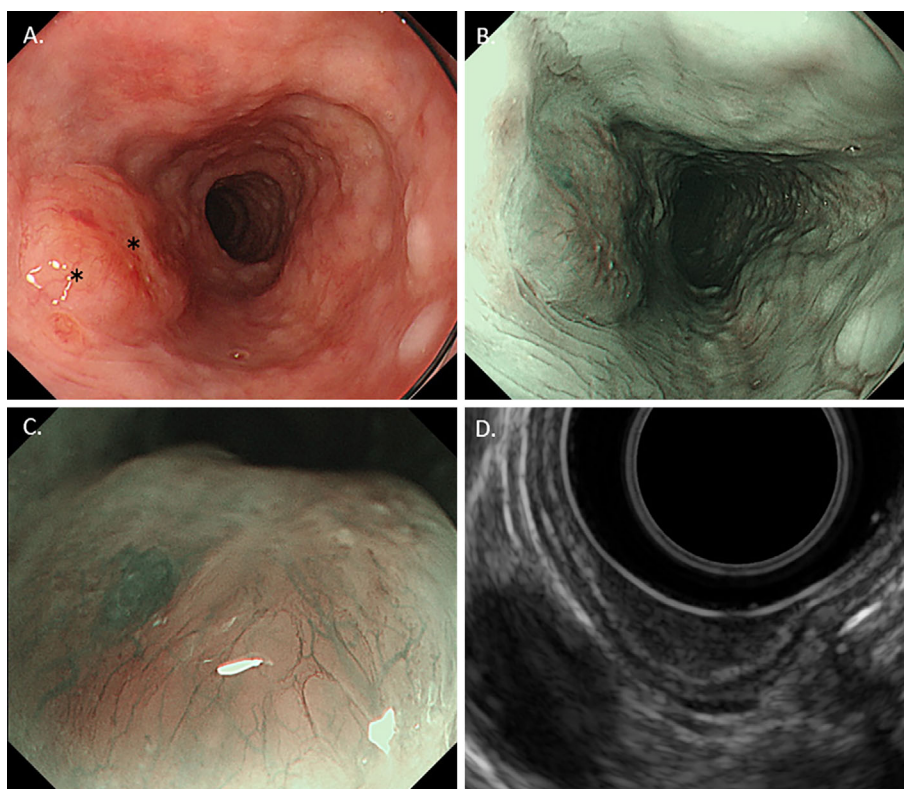
### Case Report

A 72-year-old man was referred to our hospital with suspected esophageal amyloidosis, which was identified during a medical check-up at another hospital. His past history included diabetes and he was an inactive hepatitis B carrier.

He did not present dysphagia or abdominal pain. His family history was unremarkable. A physical examination revealed no remarkable findings in the chest, heart or abdomen. No abnormal neurological findings were present.

There were no abnormalities in the patient's laboratory data (complete blood count, chemistry including serum alkaline phosphatase and immunoglobulin levels, urinalysis, coagulation). Esophagogastroduodenoscopy (EGD) showed a reddish elevated lesion with a maximum diameter of approximately 15 mm located on the upper part of the esophagus, which was covered with a normal mucosa (Fig. 1A, B). Magnifying endoscopy with narrow-band imaging (NBI) revealed dilated green-colored blood vessels but small vascular changes with irregularity were not apparent (Fig. 1C). Endoscopic ultrasonography (EUS) revealed a hypoechoic mass localized in the second and third layer, corresponding to the lamina propria mucosa to the submucosa, but no abnormal findings were observed in the fourth layer (Fig. 1D), which suggested that this lesion was located on the lamina propria mucosa to the submucosa. Biopsy specimens showed eosinophilic amorphous material in the lamina propria mucosa (Fig. 2A). Congo red staining of the material was posi-

<sup>1</sup>Division of Gastroenterology, Tohoku University Graduate School of Medicine, Japan, <sup>2</sup>Department of Pathology, Tohoku University Graduate School of Medicine, Japan and <sup>3</sup>Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Japan  
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Correspondence to Dr. Waku Hatta, waku-style@festa.ocn.ne.jp



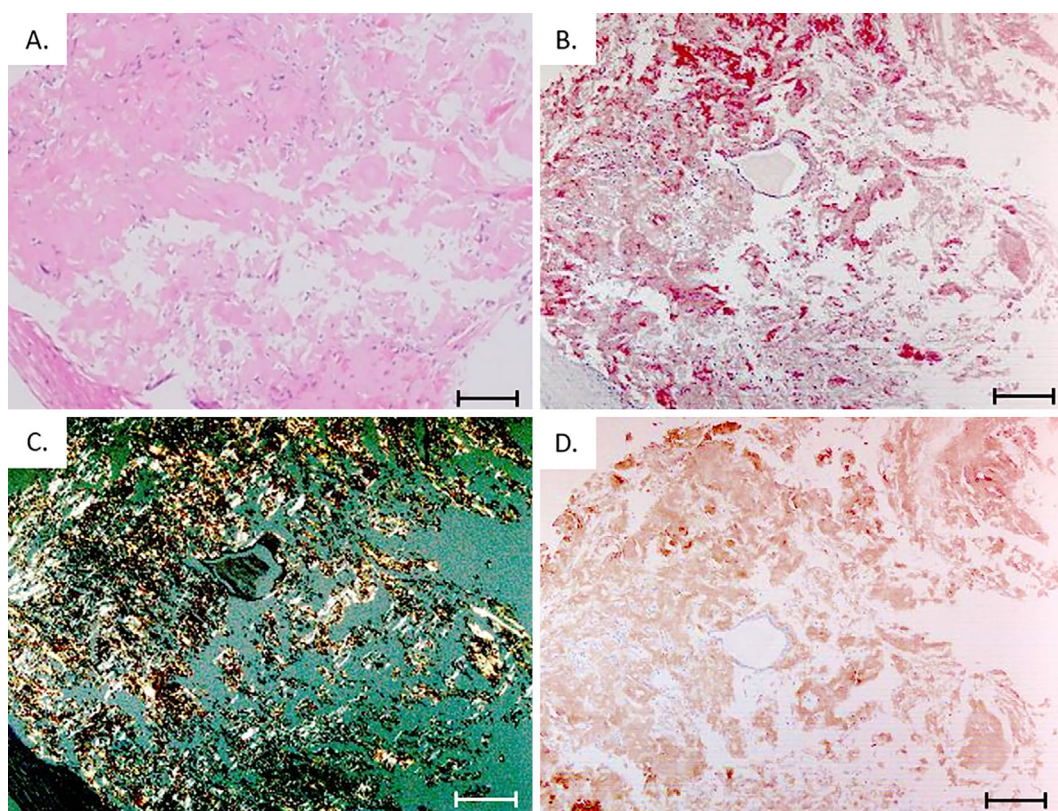
**Figure 1.** Endoscopic images of a case of localized esophageal amyloidosis. The reddish lesion is covered with a normal mucosa (A, B). Magnifying endoscopy with NBI shows green-colored dilated blood vessels (C). In EUS, a hypoechoic mass is localized in the second and third layers (D). \*Biopsy specimens were acquired from these parts. NBI: narrow-band imaging, EUS: endoscopic ultrasonography

tive (Fig. 2B) and green birefringence was observed by polarized light microscopy (Fig. 2C). Immunohistochemical staining revealed that the amyloid protein was the amyloid light chain (AL)-type, and that it was derived from immunoglobulin  $\lambda$  light chain (Fig. 2D). The specimen was negative for immunoglobulin  $\kappa$ , amyloid A and transthyretin light chain. No other sites of suspected amyloid deposition were found by EGD, colonoscopy, or capsule endoscopy, and biopsy specimens from the stomach (six specimens), duodenum (two specimens), ileum (four specimens), colon (four specimens), and esophagus (distal to the lesion; one specimen) indicated no amyloid deposits. Computed tomography and positron emission tomography-computed tomography showed no remarkable findings. A urine specimen was negative for Bence-Jones protein and the serum immunoglobulin levels were normal. The serum-free light-chain levels and ratio, electrocardiography, and echocardiography were also normal. Bone marrow aspiration was negative for multiple myeloma and monoclonal gammopathy of undetermined significance. Based on these findings, systemic amyloidosis was excluded. Thus, this case was diagnosed as localized esophageal amyloidosis characterized by AL ( $\lambda$ ) type amyloid deposition. The patient was scheduled for close follow-up. No progression was observed during 9-months of follow-up.

## Discussion

GI involvement is common in systemic amyloidosis (1), and esophageal involvement of amyloidosis is sometimes observed in patients with systemic amyloidosis (3). Tada et al. reported that 72% (21/37) of cases of amyloidosis involving the GI tract had biopsy-proven amyloid in the esophagus but that only 16% (6/37) had any endoscopic findings (4). An old study revealed that 22% (16/73) of patients with any type of amyloidosis on autopsy had amyloid deposition in the esophagus (5). On the other hand, GI involvement is rare in localized amyloidosis. The most frequent organ of involvement of localized GI amyloidosis is the stomach (3), but cases in which amyloid deposits are only detected in the esophagus are extremely rare.

We searched the PubMed database for all relevant studies published until August 31, 2020 using the following search term: [localized], [esophagus] OR [esophageal], AND [amyloidosis] OR [amyloidoma]. The findings of this search and relevant references only yielded three reported cases of localized esophageal amyloidosis (6-8) (Table). The present case is the first asymptomatic case; two of the previous cases presented severe symptoms. One case had sudden, severe chest pain and underwent resection of the distal esophagus and proximal stomach, which revealed perfora-



**Figure 2.** The microscopic findings in a case of AL ( $\lambda$ )-type localized esophageal amyloidosis. Hematoxylin and Eosin staining of the biopsy specimen revealed eosinophilic amorphous material in the lamina propria mucosa (A). Congo red staining of the material was positive (B) and green birefringence was observed by polarized light microscopy (C). Immunohistochemical staining for immunoglobulin  $\lambda$  light chain was positive (D). Bar=200  $\mu$ m. AL: amyloid light chain

**Table.** Reported Cases of Localized Esophageal Amyloidosis.

Author, year	Age/sex	Symptom	Location of esophagus	Endoscopic finding	Type	Treatment
Ref. 6)	68/M	Hematemesis, chest pain	Distal part	Edema (ulcerated mass <sup>†</sup> )	Unknown	Surgery <sup>‡</sup>
Ref. 7)	48/F	Dysphagia, appetite loss	Distal part	Pale mucosa (black mass <sup>¶</sup> )	Unknown	Surgery <sup>§</sup>
Ref. 8)	47/M	Dysphagia	Distal part	SMT	AL ( $\kappa$ )	No treatment
Present case	72/M	None	Upper part	SMT	AL ( $\lambda$ )	No treatment

<sup>†</sup> In the specimen of surgery.

<sup>‡</sup> Resection of distal esophagus and proximal stomach.

<sup>¶</sup> Under the view in the thoracotomy.

<sup>§</sup> Colon transplant was performed because excision of the mass was not possible due to the close adherence to the thoracic aorta and the left pulmonary ligament.

MT: submucosal tumor, AL: amyloid light chain

tion (6). The other case with severe symptoms showed appetite and weight loss due to stenosis of the esophagus by a mass of amyloidosis, and was treated with colon transplantation, because excision of the mass was not possible due to its tight adherence to the thoracic aorta and left pulmonary ligament (7). In comparison to these cases, one recent case showed relatively mild symptoms and selected no treatment (8). In our case, no treatment was selected because the patient was asymptomatic. Such a therapeutic approach is

generally selected for localized amyloidosis because most such cases do not progress to systemic disease (9). On the other hand, two of three previous cases required surgery, although all of them were old cases and the changes in the examination and classification of amyloidosis may have caused discrepancies in the symptoms between the old and recent cases. The further accumulation of cases is necessary for deciding the therapeutic approach for localized esophageal amyloidosis; however, careful observation is required

when no treatment is selected.

Endoscopic images were presented in two cases, one case by Kahi et al. (8) and the present case. Both cases exhibited an SMT-like appearance in conventional white light endoscopy. The present case was also examined by magnifying endoscopy with NBI and EUS. Magnifying endoscopy with NBI showed dilated blood vessels, which may have been affected by the subepithelial mass. Although we did not compare the EUS findings with the corresponding histology, because only biopsy was performed, EUS showed a regular hypoechoic mass in the second and third layers, corresponding to the lamina propria mucosa to the submucosa. According to the reports about localized gastric amyloidosis, localized amyloidosis has various EUS findings; however, the present study is significant in that it is the first to report the EUS findings of localized esophageal amyloidosis.

In systemic amyloidosis, the precursor of the fibril protein is expressed at one site, such as the liver. It is released into blood plasma in soluble form, distributed via circulation, and is finally deposited in different organs as amyloid fibrils (10). Regarding localized amyloidosis, Hamidi et al. hypothesized that localized AL amyloidosis occurs due to local production of light chains by a clone of plasma cells residing in the target organ (11). Westermarck suggested the "suicide neoplasm" hypothesis for the pathogenesis of localized AL amyloidosis (10). In this hypothesis, a plasma cell clone is formed at one organ after prolonged antigenic stimulation, and a toxic effect on plasma cells of self-produced pre-amyloid might play a role in controlling the plasma cell clone. However, the detailed mechanism underlying the development of localized amyloidosis-including that in the present case of esophageal amyloidosis-remains unclear and further studies are needed.

In summary, we described an extremely rare case of AL ( $\lambda$ )-type localized esophageal amyloidosis that showed an SMT-like appearance. Hence, localized amyloidosis should

be considered in the differential diagnosis of esophageal SMTs.

**The authors state that they have no Conflict of Interest (COI).**

## References

1. Sattianayagam PT, Hawkins PN, Gillmore JD. Systemic amyloidosis and the gastrointestinal tract. *Nat Rev Gastroenterol Hepatol* **6**: 608-617, 2009.
2. Hirata K, Sasaguri T, Kunoh M, et al. Solitary "amyloid ulcer" localized in the sigmoid colon without evidence of systemic amyloidosis. *Am J Gastroenterol* **92**: 356-357, 1997.
3. Cowan AJ, Skinner M, Seldin DC, et al. Amyloidosis of the gastrointestinal tract: a 13-year, single-center, referral experience. *Haematologica* **98**: 141-146, 2013.
4. Tada S, Iida M, Iwashita A, et al. Endoscopic and biopsy findings of the upper digestive tract in patients with amyloidosis. *Gastrointest Endosc* **36**: 10-14, 1990.
5. Briggs GW. Amyloidosis. *Ann Intern Med* **55**: 943-957, 1961.
6. Heitzman EJ, Heitzman GC, Elliott CF. Primary esophageal amyloidosis. Report of a case with bleeding, perforation, and survival following resection. *Arch Intern Med* **109**: 595-600, 1962.
7. Solanke TF, Olurin EO, Nwakonobi F, et al. Primary amyloid tumour of the oesophagus treated by colon transplant. *Br J Surg* **54**: 943-946, 1967.
8. Kahi CJ, Vakili S, Liepnieks JJ, et al. Amyloidoma of the esophagus. *Am J Gastroenterol* **102**: 910-911, 2007.
9. Biewend ML, Menke DM, Calamia KT. The spectrum of localized amyloidosis: a case series of 20 patients and review of the literature. *Amyloid* **13**: 135-142, 2006.
10. Westermarck P. Localized AL amyloidosis: a suicidal neoplasm? *Ups J Med Sci* **117**: 244-250, 2012.
11. Hamidi Asl K, Liepnieks JJ, Nakamura M, et al. Organ-specific (localized) synthesis of Ig light chain amyloid. *J Immunol* **162**: 5556-5560, 1999.

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