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CASE REPORT

Light-chain amyloidosis presenting with rapidly progressive submucosal hemorrhage of the stomach

Song-Yi Kim [a,c], Suk-Bae Moon [a,c], Seung Koo Lee [b], Seong Kweon Hong [a], Yang Hee Kim [a], Gi Bong Chae [a], Sung-Bae Park [a,*]

[a] *Department of Surgery, Kangwon National University Hospital, Kangwon National University School of Medicine, Chuncheon, South Korea*
[b] *Department of Pathology, Kangwon National University Hospital, Kangwon National University School of Medicine, Chuncheon, South Korea*

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Summary The gastrointestinal tract is frequently in involved light-chain (AL) amyloidosis, but significant hemorrhagic complications are rare. A 71-year-old man presented to our hospital with dyspepsia and heartburn for 1 month. Gastroscopy revealed a large submucosal hematoma at the gastric fundus. Two days later, a follow-up gastroscopy indicated extensive expansion of the hematoma throughout the upper half of the stomach. The hematoma displayed ongoing expansion during the endoscopic examination, suggesting that rupture was imminent. Emergency total gastrectomy was performed, and amyloidosis was confirmed after examining the surgical specimen. Bone marrow examination revealed multiple myeloma, and serum immunoglobulin assay confirmed the diagnosis of myeloma-associated AL amyloidosis. At manuscript submission, the patient was doing well and was undergoing chemotherapy.

* Corresponding author. Department of Surgery, Kangwon National University Hospital, 156 Baekryoung-ro, Chuncheon 200-722, South Korea.
E-mail address: bsb1971_kr@kangwon.ac.kr (S.-B. Park).
[c] S.-Y.K. and S.-B.M. contributed equally to this work.

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1. Introduction

Amyloidosis describes a group of diseases that result from the extracellular deposition of protein fibrils in tissues and organs. Light-chain (AL) amyloidosis, also called primary systemic amyloidosis, is usually caused by a clonal expansion of plasma cells in the bone marrow. These cells secrete a clonal immunoglobulin that deposits as amyloid fibrils in tissues.[1] Diagnosis of AL amyloidosis is straightforward when a clonal plasma cell dyscrasia can be demonstrated. However, diagnosis may be delayed until organ-specific symptoms raise the suspicion of amyloidosis. The gastrointestinal tract is one of the most commonly affected organs, but gastric involvement causing substantial bleeding has rarely been reported in AL amyloidosis.[2] In this study, we describe a case of rapidly progressive gastric submucosal hemorrhage and consequent total gastrectomy in a patient with AL amyloidosis.

2. Case report

A 71-year-old man presented to our hospital with dyspepsia and heartburn that had developed 1 month previously. His family and medical histories were unremarkable. Physical examination and laboratory tests revealed no significant findings. Upon gastroscopy, a very large submucosal hematoma was noted from the fundus to the anterior wall of the high body. The overlying mucosa was intact, and no active bleeding was observed. Two days later, a follow-up gastroscopy revealed an extensive submucosal hematoma involving the upper half of the stomach (Fig. 1A and B). Ongoing hematoma expansion was noted during the endoscopic examination, implying impending rupture. Biopsy was not attempted to avoid hematoma rupture and catastrophic bleeding. Celiac angiography revealed diffuse extravasation throughout the upper stomach and no foci for embolization were identified. Although the patient was hemodynamically stable at that time, surgery was recommended to prevent further bleeding and sudden rupture of the hematoma. Upon performing laparotomy, it was noted that the submucosal hematoma had spread to the entire gastric wall, and total gastrectomy was inevitable. Pathological examination indicated the presence of amyloid fibrils and AL protein deposition in vessel walls, suggesting an AL amyloidosis (Fig. 2A and B). The concentrations of serum immunoglobulin kappa and lambda light chains were 7.91 and 552.65 mg/L, respectively, resulting in a kappa-to-lambda ratio of 0.01. Bone marrow biopsy confirmed multiple myeloma, and the patient was diagnosed with primary lambda-AL amyloidosis associated with multiple myeloma. At his 8-month postoperative follow-up, the patient was doing well and undergoing chemotherapy.

3. Discussion

The gastrointestinal tract can be affected by any type of amyloidosis, and biopsies identify gastric involvement in 8% of amyloidosis cases. Only 1% of amyloidosis patients present with gastrointestinal symptoms, which include nausea, vomiting, epigastric pain, and gastric outlet obstruction.

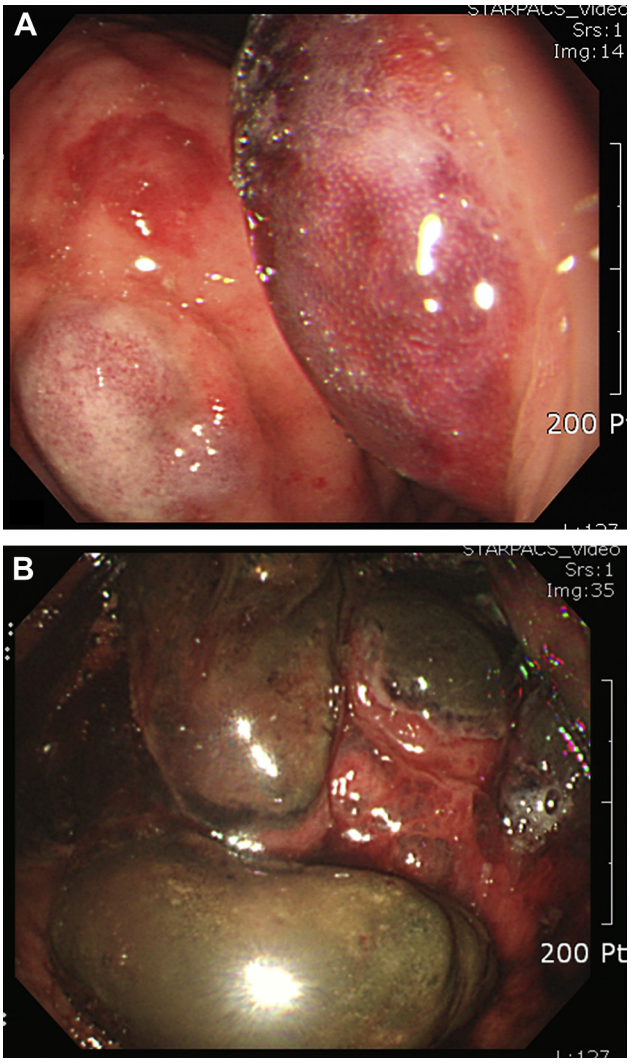

Figure 1 (A) Initial gastroscopy indicated a very large submucosal hematoma from the gastric fundus to the anterior wall of the high body. (B) Follow-up gastroscopy showed an extensive submucosal hematoma covering the entire upper half of the stomach.

Hemorrhagic complications of amyloidosis with gastric involvement are rare.[3] Iijima-Dohi et al[4] and Usui et al[5] reported two cases of massive gastric bleeding in AL amyloidosis; both patients were treated by emergency total gastrectomy. As in the present study, those patients had no predisposing factors for spontaneous bleeding, such as coagulopathy, trauma, or peptic ulcer disease.

In gastrointestinal amyloidosis, the amyloids usually deposit in the submucosa, and the mucosal architecture remains normal until massive deposits of amyloid accumulate and destroy all mucosal structures.[6,7] Yoshii et al[8] suggested that colonic submucosal hematoma is a highly suggestive finding of AL amyloidosis in the absence of other endoscopic pathologies. Therefore, in patients with spontaneous gastric submucosal hemorrhage who are otherwise healthy and without mucosal abnormalities, AL amyloidosis with gastric involvement should be considered as a differential diagnosis.

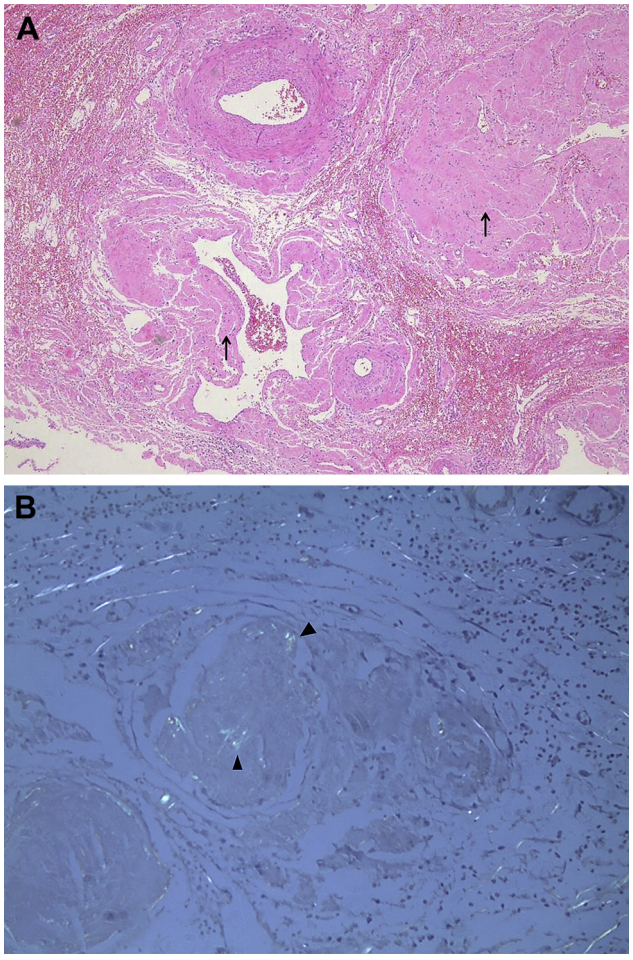

Figure 2 Surgical specimen: (A) amorphous pinkish hyaline deposits were observed in vessel walls (arrows; hematoxylin and eosin stain, 400×); (B) polarizing microscopy indicated a greenish birefringence corresponding to hyaline deposits in the same layer as (A) (arrowheads; Congo red stain, 400×).

Because the submucosal hematoma is susceptible to touch bleeding, when AL amyloidosis is suspected, diagnostic tests should be individualized to avoid imprudent endoscopic biopsy and significant bleeding. AL amyloidosis is a systemic disease, and amyloid can be deposited in any tissue of the body, although it most commonly deposits in the fat of the abdominal wall.[9] We performed total gastrectomy under emergent conditions without a clear diagnosis. However, considering the morbidity and invasiveness of major gastrectomy, definite diagnosis should be made preoperatively whenever possible.

The mainstay of AL amyloidosis treatment is the use of drugs with a focus on targeting plasma cell diseases. However, confronted with hemorrhagic complications, the first-line treatment should be selected cautiously. Although the exact pathogenesis of submucosal bleeding in AL amyloidosis remains unclear, the deposition of AL amyloid fibrils within the intima or adventitia of the vessels contributes to fragility and spontaneous bleeding beneath the lamina propria.[10] Because amyloid deposition within tissues is irreversible and cannot be cleared by medical treatment and because the natural course of AL amyloidosis is rapidly progressive and fatal if untreated,[1] we propose that hemorrhagic complications in AL amyloidosis should be managed promptly by surgical intervention in cases with massive hemorrhage.

In summary, we described a patient with AL amyloidosis presenting with a rapidly progressive gastric submucosal hemorrhage. An extensive submucosal hematoma necessitated total gastrectomy, and the diagnosis was determined postoperatively. It is important to differentiate AL amyloidosis in the setting of spontaneous submucosal hemorrhage without predisposing factors, and prompt diagnostic and therapeutic interventions should be initiated.

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