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# Gastrointestinal AA Amyloidosis following Recurrent SARS-CoV-2 Infection: A Case Report

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been associated with the overproduction of serum amyloid A protein, resulting in systemic AA amyloidosis. In this report, we describe a case of gastrointestinal (GI) AA amyloidosis following SARS-CoV-2 infection. A 75-year-old male presented to the emergency department with upper abdominal pain 6 weeks post kidney transplantation. He had a history of SARS-CoV-2 infection 4 weeks prior. On day 7 of hospitalization, while receiving conservative management, the patient developed symptoms of cough and fever, leading to a diagnosis of SARS-CoV-2 reinfection. The patient's abdominal pain persisted, and hematochezia developed on day 30 of hospitalization. Esophagogastroduodenoscopy and colonoscopy revealed multiple ulcers in the stomach and colon, with histologic findings revealing the presence of amyloid A. The patient was managed conservatively and was also given remdesivir for the SARS-CoV-2 infection. His clinical symptoms subsequently improved, and endoscopic findings demonstrated improvement in multiple gastric ulcers. GI amyloidosis may be a subacute complication following SARS-CoV-2 infection in immunocompromised patients.

**Key Words:** Gastrointestinal amyloidosis, kidney transplantation, SARS-CoV-2

## INTRODUCTION

Gastrointestinal (GI) amyloidosis is a disorder of insoluble extracellular protein deposition which interferes with the structure and function of the GI tract.[1] It can be either acquired or genetic and localized or systemic according to the location of amyloid precursor proteins.[1] The most common types of amyloidosis are light chain (AL), secondary (AA), amyloid transport protein transthyretin, and dialysis-related [β-2-microglobulin ($\beta_2$-M) type]. AL amyloidosis is characterized by the accumulation of plasma cells that produce misfolded amyloidogenic light chains, which are subsequently deposited in the different organs, whereas AA amyloidosis is caused by chronic inflammations, infections, or neoplasms.[2] GI involvement can occur in both subtypes. Currently, information on GI amyloidosis is limited given its rare occurrence.

Recent studies have suggested that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been associated with the overproduction of serum amyloid A protein, leading to systemic AA amyloidosis.[3-5] Herein, we present a case of a 75-year-old male diagnosed with GI AA amyloidosis following SARS-CoV-2 reinfection within 2 months of kidney transplantation (KT).

## CASE REPORT

A 75-year-old male presented to the emergency department with upper abdominal pain persisting for 5 days. He had undergone a living-donor KT 6 weeks prior. The patient's medical history included polycythemia vera and a 15-year history of

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diabetes. Notably, he had no history of chronic hepatitis, pulmonary tuberculosis, or other malignant diseases. He had received treatment for SARS-CoV-2 4 weeks ago. Pre-transplant screening esophagogastroduodenoscopy (EGD) and colonoscopy conducted 3 months prior had been unremarkable (Fig. 1A). Upon admission, laboratory tests, including viral and tumor markers, as well as an abdominal CT had revealed no significant abnormalities. During admission, the patient developed new onset of symptoms that included fever and cough, and on day 7 of hospitalization, he was diagnosed with SARS-CoV-2 reinfection for which he received 3 days of intravenous remdesivir. However, the patient continued to experience abdominal pain and worsening watery diarrhea, without evidence of positive cytomegalovirus polymerase chain reaction (PCR) results in serum or without evidence of Clostridium difficile infection including culture, toxin, and PCR in stool. Despite conservative management, the patient's abdominal pain persisted, and he developed hematochezia on day 30 of hospitalization. Laboratory findings at that time were unremarkable, except for elevated high sensitivity C-reactive protein (hsCRP, 12.24 mg/dL). EGD revealed friable mucosa and multiple new small, round coalescing ulcerative lesions in the lower gastric body and antrum (Fig. 1B). Histopathological examination of the gastric ulcers showed deposition of amorphous, acellular, and eosinophilic material in the mucosal layer, with positive Congo Red staining, indicating the presence of diffuse amyloid A intermixed with loosely arranged collagen fibers (Fig. 2). Colonoscopy also revealed multiple ulcerations in the terminal ileum (Fig. 3A) and throughout the colon (Fig. 3B and C). Histologic examination also confirmed the presence of amyloid A. Subsequent testing showed normal serum levels of free κ-AL [13.23 mg/L (normal range: 3.3–19.4)], free λ-light chain [17.06 mg/L (normal range: 5.71–26.3)], and κ/λ ratio [0.7755 (normal range: 0.26–1.65)], suggesting a diagnosis of AA amyloidosis. The patient's abdominal pain gradually subsided, and a follow-up EGD 2 weeks later showed slight improvement in the mucosal lesions of the stomach (Fig. 1C). Despite resolution of his hematochezia and normalization of hsCRP levels to 0.03 mg/dL, the patient continued to experience intermittent abdominal pain and loose stools. He was eventually discharged after 64 days of hospitalization.

## DISCUSSION

Amyloidosis encompasses a rare group of diseases characterized by the extracellular deposition of abnormal proteins known as amyloids. This condition most frequently arises from chronic inflammatory disorders, hematologic malignancies, and end-stage renal disease, in which the development of amyloidosis correlates with inflammatory markers, including hsCRP and serum amyloid A protein.[6] In the present case, GI AA amyloidosis developed following a SARS-CoV-2 infection in a patient with a history of diabetic kidney disease who had recently undergone KT. Although KT is a treatment option for dialysis-related amyloidosis,[1] it can also recur or manifest after many years of solid organ transplantation, particularly in patients with ongoing inflammatory conditions such as rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, pulmonary tuberculosis, or recurrent urinary tract infections.[7,8] In this case, the patient was asymptomatic and had no abnormal findings on diagnostic tests for amyloidosis prior to KT. Therefore, this newly developed amyloid deposition may not have been associated with a chronic inflammatory condition. Recent studies have suggested that a SARS-CoV-2 protein facilitates serum amyloid A formation,[9] and patients with COVID-19 infection exhibit significantly elevated levels of serum amyloid A. This protein can promote inflammatory responses through the activation of cytokines and induction of chemotaxis,[10] and is associated with disease severity and poor prognosis.[5] Djafari, et al.[11] reported a case in which a 68-year-old female was diagnosed with secondary bladder amyloidosis after developing

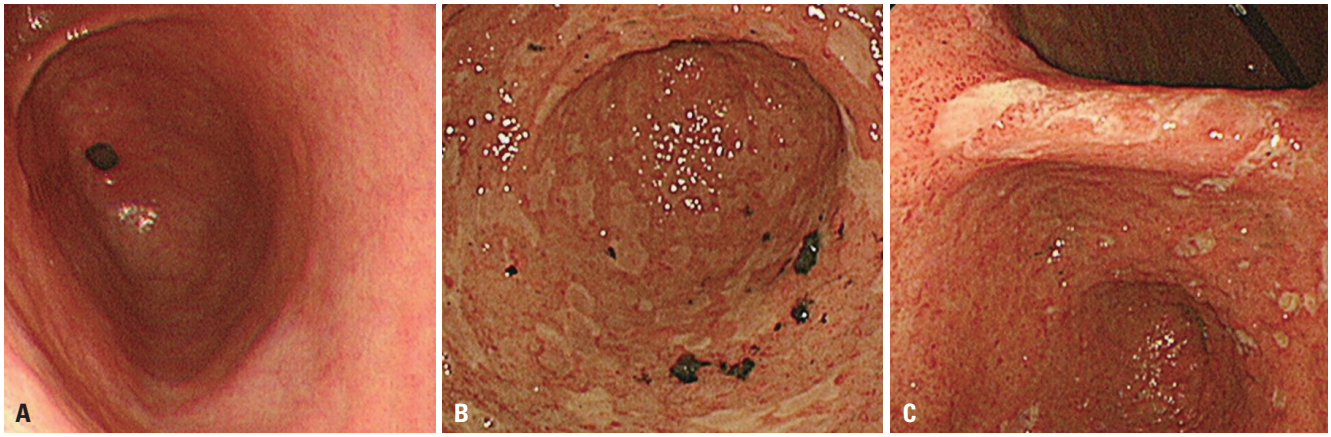


**Fig. 1.** Esophagogastroduodenoscopy (EGD). Pre-transplant EGD showed no specific abnormal findings in the stomach (A). On the day 30 of hospitalization, EGD showed friable mucosa with newly observed multiple, small-round coalesced ulcers in the lower body and stomach antrum (B). Follow-up EGD at 2 weeks revealed improvement in the mucosal lesions of the stomach (C).

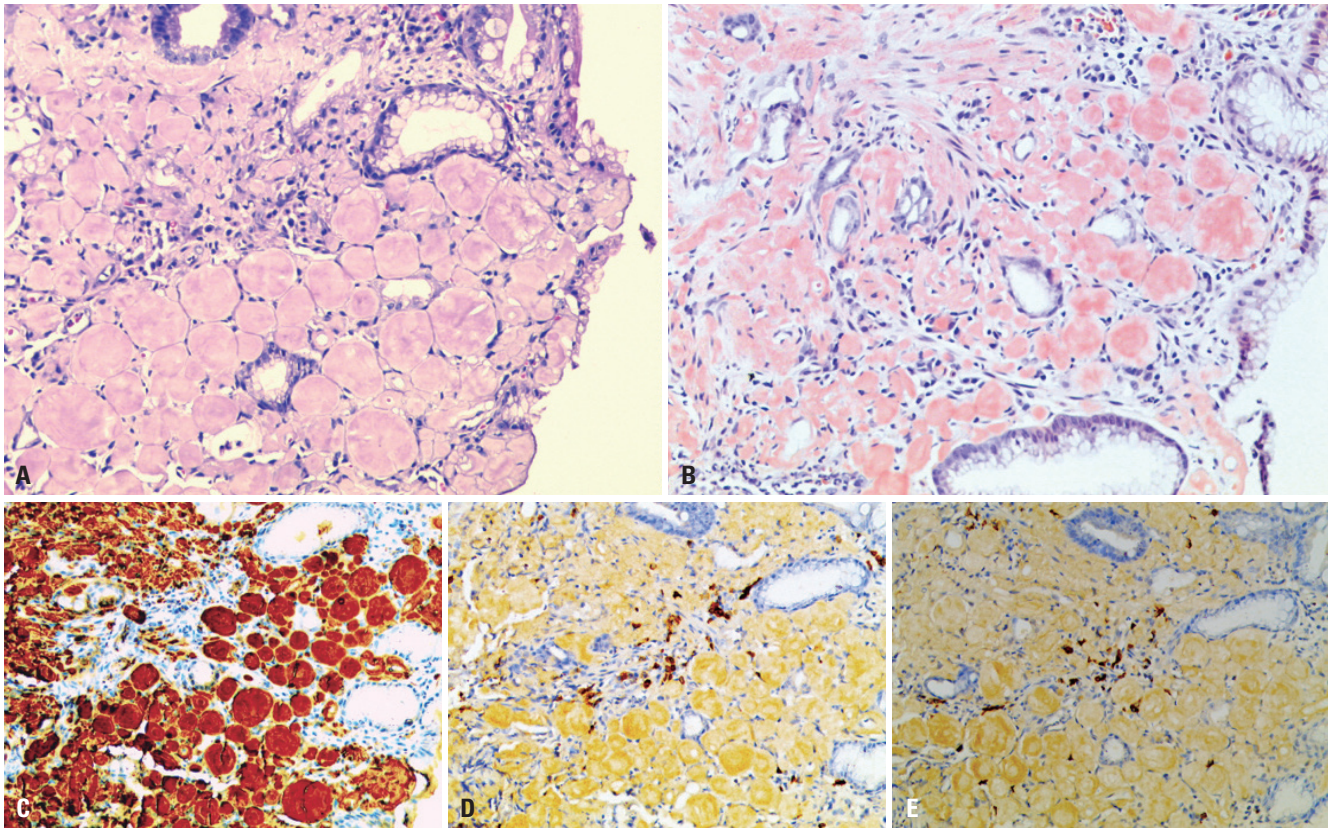


**Fig. 2.** Histopathologic examination. (A) Representative photomicrographs of the histopathologic examination showing chronic gastritis with intestinal metaplasia and deposition of amorphous eosinophilic substance in the mucosal layer (H&E, 200×). (B) Staining of the eosinophilic material in the mucosal layer (Congo red, 200×). (C) Interstitial AA amyloid deposits in the mucosal layer (Amyloid AA, 200×). (D) Monoclonal staining with λ-light chain in mucosal layer (λ-light chain, 200×). (E) Monoclonal staining with κ-light chain in mucosal layer (κ-light chain, 200×).

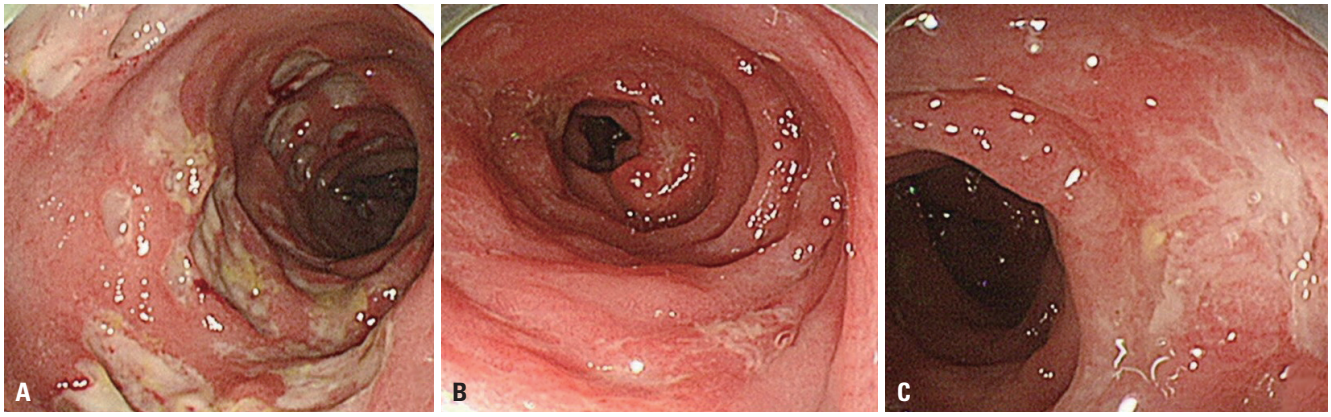


**Fig. 3.** Colonoscopy findings. Colonoscopy showed multiple ulcers in terminal ileum (A) and descending colon (B and C).

gross hematuria during hospitalization for COVID-19 infection. In this case, considering that the abdominal pain, diarrhea, and hematochezia manifested after the SARS-CoV-2 reinfection, it is possible that immune and inflammatory responses induced by this reinfection contributed to gastric amyloid deposition.

The primary approach to managing amyloidosis involves treating the underlying disorder responsible for the increase in amyloid precursors. In AL amyloidosis, plasma cells accumulate and produce misfolded amyloidogenic light chains, which are deposited in various organs. Suppressing the production of monoclonal immunoglobulin light chains is crucial in AL amyloidosis. Consequently, autologous stem cell transplantation has become the standard care for plasma cell dyscrasia.[12] On the other hand, AA amyloidosis is an ongoing inflammatory process,[6] in which controlling the underlying pathologies is vi-


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tal for reducing the continuous production of inflammatory precursors or serum amyloid A protein.[1]

The prognosis of GI AA amyloidosis depends on several factors, including the extent and severity of amyloid deposition, the underlying cause of amyloidosis, and the presence of associated conditions. Generally, systemic amyloidosis, characterized by amyloid deposition in multiple organs, is linked to a poorer prognosis compared to localized amyloidosis limited to the GI tract.[13] The median survival of patients with AL amyloidosis has been found to be 7.9 months for those with GI involvement, which is shorter than the 15.8 months for patients without GI involvement.[14] In the current case, the patient's gastric mucosal lesions and GI symptoms improved due to the early management of the SARS-CoV-2 reinfection. The patient is expected to have a relatively favorable prognosis, since AA amyloidosis is limited to the GI tract without systemic involvement, while considering the patient's age and comorbid conditions, such as hypertension, diabetes, and chronic kidney disease, appropriate conservative management with regular follow-up should be considered.

In conclusion, GI amyloidosis can be considered a potential subacute complication following SARS-CoV-2 infection in immunocompromised patients. Clinicians should take GI amyloidosis into account when considering differential diagnoses in patients exhibiting atypical GI symptoms following COVID-19 infection.

## AUTHOR CONTRIBUTIONS

Conceptualization: Seon-Young Park. Data curation: Hyung-Min Park, Seon-Young Park, Myung-Giun Noh, and Tae-bum Lee. Resources: Yong-wook Jung and Soo Jin Na Choi. Supervision: Seon-Young Park. Visualization: Hyung-Min Park and Myung-Giun Noh. Writing—original draft: Hyung-Min Park and Seon-Young Park. Writing—review & editing: Seon-Young Park. Approval of final manuscript: all authors.

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