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Single Case

Side Effects of Stem Cell Transplant Mimicking Symptoms of Known Amyloidosis

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AL amyloidosis · Immunoglobulin light chain amyloidosis · Esophageal ulcer · Odynophagia

Abstract
Introduction: AL amyloidosis can involve the gastrointestinal (GI) tract in a sporadic manner, affecting certain anatomical areas while sparing others. ***Case Presentation:*** Our patient with AL amyloidosis and confirmed colonic involvement was found to have new odynophagia, GI bleeding, and imaging findings that might suggest AL amyloidosis. However, negative pathology results from esophageal biopsies suggested the patient's new ulcerations were more likely a side effect of her autologous stem cell transplant (SCT) and chemotherapy meant to target amyloidosis, as opposed to an effect of amyloid infiltration itself. ***Conclusion:*** GI involvement of amyloidosis requires a high degree of clinical suspicion and should be considered in patients with systemic diseases affecting the kidney, heart, and GI tract; however, when satisfactory biopsies obtained from endoscopy results are negative, other causes should be considered.

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Introduction

Amyloidosis is a systemic disease with widely variable presentations. AL amyloidosis comprises 75% of total cases of systemic amyloidosis [1]. However, epidemiologic data are still lacking as this condition is exceedingly rare with an incidence of approximately 12 cases per million persons [2]. Although uncommon, AL amyloidosis can be associated with significant morbidity and mortality.

AL amyloidosis involves excessive production and extracellular deposition of monoclonal light chains; in the GI tract, this can lead to ischemia due to total occlusion of blood supply. Consequently, ulceration, bleeding, and pseudo-obstruction can occur at any point. GI-involved amyloidosis – when compared with cardiac or renal amyloidosis – rarely leads to death but can cause significant morbidity. Poor prognostic features of GI amyloid include intractable diarrhea, hyperbilirubinemia from liver involvement, and progressive colonic pseudo-obstruction [3].

The use of SCT, steroids, and chemotherapy drugs, such as bortezomib and melphalan, can improve hematologic response rate and overall survival in AL amyloidosis [4]. We report a rare case of a patient with known colonic involvement from AL amyloidosis who developed upper GI bleeding from esophageal ulceration. Interestingly, esophageal biopsies were negative for amyloid, which indicated that the esophageal symptoms were more likely a side effect of the medical treatments intended to treat the amyloidosis than a primary effect from amyloid infiltration itself.

Case Presentation

A 67-year-old female with a history of hypertension, rheumatoid arthritis, and biopsy-confirmed AL amyloidosis, known to involve the heart, kidneys, and GI tract, was admitted electively for chemotherapy and SCT to treat AL amyloidosis. Of note, the patient was found to have biopsy-positive colonic involvement of her amyloidosis on a screening colonoscopy 1 year prior to admission.

On admission, initial vital signs were within normal limits. Laboratory data were significant for a white blood cell count of 5×10^9/L, hemoglobin 11 g/dL, platelets 268 k/mm^3, and creatinine 0.75 mg/dL. High-dose melphalan chemotherapy (200 mg/m^2) was initiated on hospital day (HD) 1. On HD 4, the patient received an autologous stem cell transplant and shortly thereafter began to complain of new odynophagia. Computed tomography of the thorax with contrast was obtained on HD 7 that demonstrated esophagitis and ulceration involving the proximal esophagus. On HD 9, the patient had new episodes of black-colored diarrhea. She remained hemodynamically stable, but her hemoglobin dropped from 11.0 g/dL on admission to 7.6 g/dL. The patient had no episodes of hematemesis or coffee-ground emesis.

On HD 9, the patient underwent esophagogastroduodenoscopy. A new, large dark brown raised irregular lesion extending from 15 cm to 25 cm from the incisors was seen in the esophagus. Other notable findings in the stomach included erythematous mucosa in the antrum, fundus, cardia, pre-pyloric region, and stomach body. No overt bleeding was found. Biopsies were taken from the esophagus, stomach, and duodenum. Esophageal biopsies showed fibrinopurulence but were negative for amyloid on Congo red stain (shown in Fig. 1). On the other hand, gastric and duodenal biopsies were positive for amyloid on Congo red stain (Fig. 2, 3). The patient was treated with supportive care, and she remained clinically stable with no further evidence of bleeding and was discharged home on HD 11.

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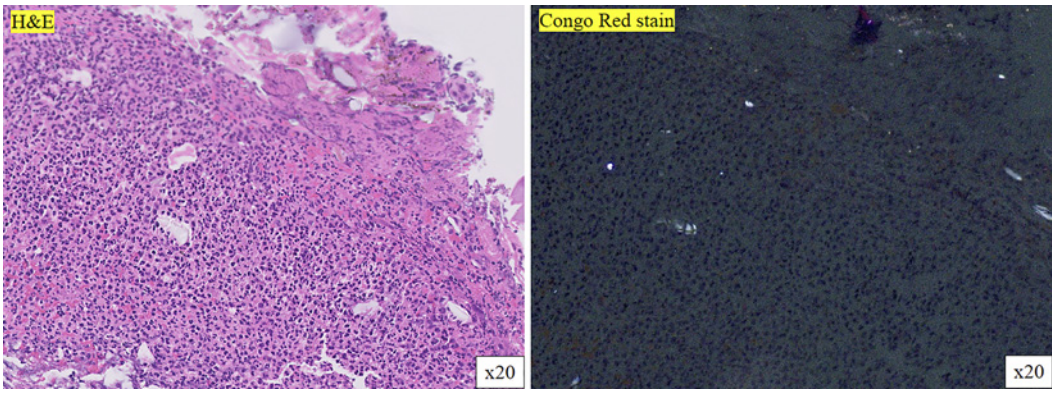

Fig. 1. Esophageal biopsy: small blood vessels were present, but no Congo red-positive material was identified.

Discussion

Although our patient's presentation caused original suspicion of her known AL amyloidosis, it appears more likely that her esophageal lesions arose because of SCT and chemotherapy. However, it is important to note that small vessels were present at the esophageal biopsy site, but there was no viable mucosa (Fig. 4). Given the extensive fibrinopurulence and the lack of underlying mucosa at the esophageal biopsy site, amyloid presence in the esophagus cannot be ruled out definitively.

Melphalan and SCT have long been understood to lead to GI bleeding and early mortality, especially during the peri-transplant period. Comenzo and Gertz [2002] found GI bleeding in 22% of patients who had autologous SCT and had received the standard dose of 200 mg/m^2 melphalan, just as our patient did [5]. This illustrates the importance of close monitoring for GI bleeding at the time of SCT. Further, our patient had a platelet count of 127 at the time of GI bleed. It is important to consider that EHA-ISA guidelines recommend that patients with amyloidosis are transfused to a platelet goal of greater than 50 because of the risk of GI bleed [6]. Although our patient had amyloid renal involvement, she did not have renal insufficiency, another risk factor for GI bleeding.

Interestingly, our patient indeed had evidence of amyloid involvement in new areas of the GI tract besides the esophagus, as evidenced on stomach and duodenal biopsies. Although the amyloid had not yet been detected in the stomach, it had likely existed there since the time of presentation. Amyloid deposits can affect any part of the GI tract but preferentially target certain areas more often than others. Cowan et al. [7] [2013] revealed that AL amyloidosis-positive biopsies were most common in the small bowel (50%), followed by the stomach (44%), colon (32%), esophagus (12%), rectum (8%), and gallbladder (2%) [7]. Pathologic and endoscopic investigation can help determine location and severity of involvement in patients with AL amyloidosis; however, the information obtained does not necessarily correlate with the presence or absence of GI symptoms. One study demonstrated that only 45% of amyloidosis patients with GI symptoms ultimately had biopsy-proven GI involvement of their amyloidosis after esophagogastroduodenoscopy or colonoscopy [8]. Our patient's main endoscopic abnormality in her esophagus did not stain positively for amyloid on biopsy. Conversely, our patient's gastric and duodenal biopsies returned amyloid involvement, despite the lack of clinically apparent sequelae. Despite effective treatment, there are no medications, which can be used to eliminate amyloid from tissues in which it is already present. Further research should be performed to develop such medications.

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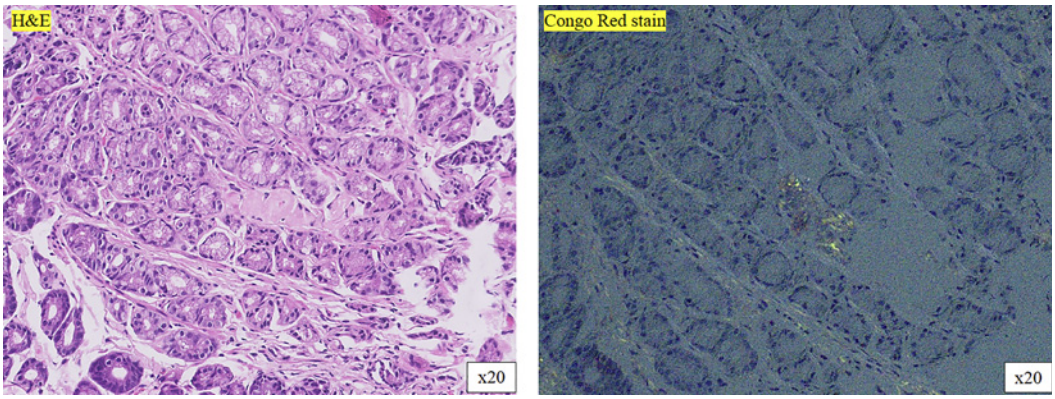

Fig. 2. Stomach biopsy: the amorphous paucicellular eosinophilic material (amyloid) can be seen around blood vessels.

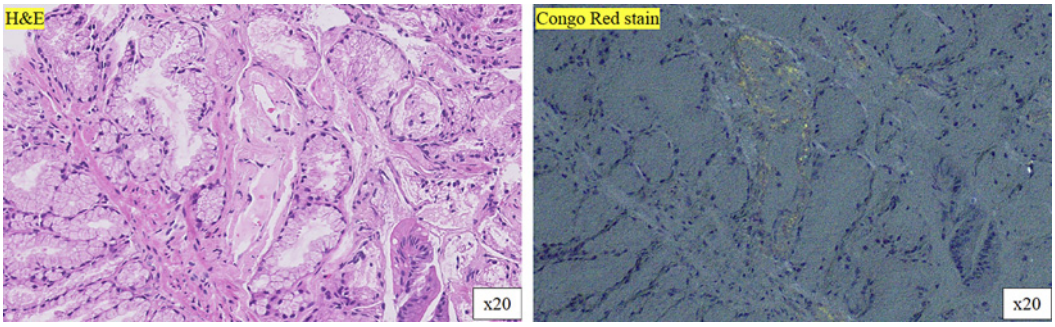

Fig. 3. Duodenal biopsy: amyloid present around blood vessel wall.

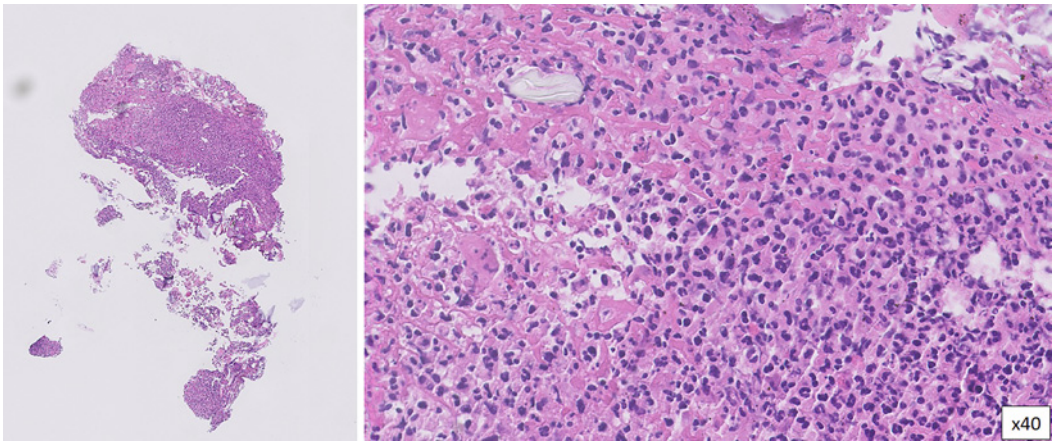

Fig. 4. Esophageal tissue: there is no viable squamous mucosa, only necrotic and fibrinopurulent tissue with acute and chronic inflammation.

Despite approved therapies shown to improve both morbidity and mortality, amyloidosis remains underdiagnosed [2]. Our case demonstrates that GI bleeding can be either a symptom of amyloidosis or a side effect of the treatment of amyloidosis. GI involvement in amyloidosis demands a heightened clinical awareness, especially in patients with renal, cardiac, and gastrointestinal disease. However, if endoscopy biopsies yield negative results, alternative causes should be explored. The CARE Checklist has been completed by the authors of this case report and is attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000538947).

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Gabriel Heering: drafting the work and revising it critically for important intellectual content. Zilan X. Lin and Michael Rosman: substantial contributions to the conception of the work and editing. Nao Hara and Fouzia Shakil: substantial contributions to the conception of the work and editing and clarification and reevaluation of biopsy findings and the implications of these findings. Dimitrios Georgostathis: editing assistance and final approval of the version to be published.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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