Upper Gastrointestinal Hemorrhage from Gastric Amyloidosis Associated with Non-Hodgkin Lymphoma

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Case Report

A 70-year-old woman was admitted to our hospital due to melena for 1 day. She had been in good health until 1 month before admission when she had experienced dyspnea on exertion and become anemic. She denied other symptoms e.g., abdominal pain, nausea, hematemesis, weight loss and fever. She did not smoke or drink alcohol. She had no history of tuberculosis, diabetes mellitus, collagen vascular diseases. No history of elicited drug use. Her family history was non-contributory.

On physical examination, the patient looked markedly pale. Her blood pressure was 110/70 mmHg and pulse rate was 78 beats per minute. Generalized lymphadenopathy was found including left cervical lymph node 2 cm, left supraclavicular lymph node 2.5 cm and left inguinal lymph node 3 cm in diameters. The abdomen was soft, not tender. Liver was enlarged with liver span 14 cm without palpable mass. Rectal examination revealed melena. Other examinations were unremarkable. Laboratory data at admission were as followed: Hemoglobin 2.6 g/dL, WBC count 7310/mm³ (N 65%, L 31%, M 2%, Eo 1%, B 1%), platelet count 4000/mm³, BUN 29 mg/dL, Cr 1.2 mg/dL, albumin 2.2 g/dL and total protein 4.5 g/dL. Other liver chemistry tests, coagulogram, and other routine biochemical tests were within normal ranges. Urinalysis had no proteinuria.

Esophagogastroduodenoscopy (Figure 1) revealed 0.8 cm ulcerative mass with adherent clot at gastric incisura. The nearby gastric mucosa showed granular nodularity and waxy-plaque appearance. Computed tomography of upper abdomen demonstrated multinodular low-density masses in segment 2 and 4 of liver and spleen. Multiple hepatic and paraaortic lymph node enlargement were seen. (Figure 2)

Histopathologic evaluation of gastric biopsy (Figure 3) demonstrated erosions and inflammatory cells infiltration but also a large amount of amyloid material deposits in the submucosal and muscle layers that exhibited apple-green birefringence on staining with Congo red. A diagnosis of gastric amyloidosis was made.

Biopsy of left cervical lymph node was performed...
Endoscopic views of the patient revealed 0.8 cm ulcerative mass (arrow). The nearby gastric mucosa showed granular, waxy plague-like appearance.

Contrast-enhanced CT of upper abdomen demonstrated multiple low density lesions in segment 2, 4 of liver and spleen with minimal contrast enhancement. Multiple hepatic and paraaortic lymphadenopathy was also seen.

Amyloidosis of the stomach. The lamina propria is expanded by amorphous glassy hyaline substance with accompanying mild chronic inflammation.

Congo Red-positive amyloid. The hyaline material shows orange-red appearance by Cong Red staining. Apple green birefringence is evident under polarized light (not shown).
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Figure 4  A Amyloidosis of the perinodal fat and lymph node. Amyloid substance is present in fibrous framework of lymph node and perinodal fat. The lymph node is diffusely replaced by lymphoma cells.
B Large lymphoma cells showing centroblastic feature
C CC20+ large lymphoma cells with membranous staining. The lymphoma cells are CD3- (not shown)

and histology showed diffuse proliferation of large lymphoma cells with centroblastic feature. Amyloid material deposit similar to that found in gastric biopsy was seen in perinodal fat, blood vessel walls, capsule and fibrous framework of the lymph node. The lymphoma cells demonstrated B-cell phenotype (CD20+, CD3-) (Figure 4 A-C). Bone marrow study demonstrated lymphoma with increased hemophagocytic activity. Liver biopsy was not performed after discussing with the patient about the risk and benefit of the procedure since it may not change the treatment. The masses were possible lymphoma. We planned to follow up their evolutions after treatment. The final diagnosis was gastric amyloidosis-induced gastrointestinal bleeding associated with non-Hodgkin lymphoma. After treatment with a course of chemotherapy including Cytarabine arabinoside, 6-Mercapuric acid, dexamethasone and vincristine, no further gastrointestinal bleeding was evident and the remainder of the patient’s hospital course was uneventful.

DISCUSSION

In this presented patient, gastrointestinal (GI) hemorrhage was from gastric amyloidosis by the evidence of amyloid substance depositing in the stomach. This led us to the differential diagnosis between primary and secondary amyloidosis. The finding of generalized lymphadenopathy that was finally confirmed to be non-Hodgkin’s lymphoma (NHL) suggested the diagnosis of the gastric lesion to be most likely secondary gastric amyloidosis in patient with systemic NHL.

It is well-known that GI tract is commonly involved in systemic amyloidosis but GI hemorrhage as in our patient was rarely reported as a sole presenting symptom of amyloidosis.\(^1\,2\) Bleeding caused by GI amyloidosis can range from a positive fecal occult blood test to massive hemorrhage. Several possible mechanisms of GI hemorrhage in intestinal amyloidosis have been proposed.\(^3\) First, bleeding may result
from diffuse mucosal oozing because of intestinal ischemia caused by diffuse deposition of amyloid in all layers of the intestinal wall or within the walls of the small blood vessels supplying the gut. Second, bleeding can arise from an ulcer that develops secondary to the heavily infiltration with amyloid. Third, amyloid deposits in mesenteric and submucosal vessel walls may lead to arterial or venous changes and fragility, with resulting massive bleeding. Last, coagulation factor deficiencies associated with amyloidosis are thought to contribute to massive GI bleeding. The mechanisms of GI hemorrhage in gastric amyloidosis were unknown but likely to be similar.

Many endoscopic findings of GI amyloidosis have been reported, including a fine granular appearance, multiple yellowish-white polypoid protrusions, prominent folds, small mucosal hemorrhages, shallow ulcers, erosions, waxy plaques, and mucosal friability.\(^{(4,5)}\)

Amyloidosis is a rare consequence of NHL. There are few reported cases of both localized and systemic amyloidosis in NHL.\(^{(6-9)}\) Most of those had AL amyloidosis and to our knowledge, only 2 cases of AA amyloidosis have been reported.\(^{(10,11)}\) Unfortunately, we could not specify the type of amyloid protein in our case. The co-existent between gastric amyloidosis and gastric lymphoma is even very rare.\(^{(12)}\) In our case, we could not demonstrate lymphoma in the gastric biopsy.

Although GI hemorrhage from gastric amyloidosis is uncommon, it should be strongly suspected in patients with known amyloidosis and, like the presented case, patient with NHL, particularly when compatible endoscopic lesions were found. When the diagnosis of gastric amyloidosis was made, NHL, in spite of their rare association, should be considered as one of the possible diagnosis.

**REFERENCES**