Localized Gastric Amyloidosis

by Ashutosh Niraj, Nolan E. Perez, Nabiha Sakr-Khoury, Volkan Adsay, Olca Basturk, Martin Tobi and Nadeem Ullah

Amyloidosis is usually observed in the systemic form with only 10% 20% of cases being localized. Although stomach and gastrointestinal tract involvement is a common feature of systemic amyloidosis, localized gastric involvement is an exceedingly rare event. Herein, we report a case of localized gastric amyloidosis—found at endoscopy and confirmed by biopsies—which caused excessive bleeding requiring endoscopic therapy. A methodical evaluation excluded systemic amyloidosis.

INTRODUCTION

Amyloidosis involving the gastrointestinal (GI) tract can cause mild to severe bleeding (1–6). Gastrointestinal bleeding in amyloidosis results from local factors or coagulation factor deficiency (4,7). Local mechanisms include wall ischemia, ulcer formation due to transmural amyloid infiltration, and mucosal fragility due to amyloid infiltration of blood vessels (4). In order to provide timely therapy and minimize complications, it behooves the endoscopist to be able to identify this entity. Amylodosis manifests as irregular and thickened GI mucosa and may be confused with (scirrous) gastric carcinoma when found in the stomach (8).

Amyloidosis results from the extracellular deposition of fibrils composed of low molecular weight subunits of a variety of serum proteins. The accumulation of these protein subunits leads to a myriad of clinically relevant disorders. Amyloid proteins have a pathognomonic apple-green birefringence in polarized light after Congo red staining (9).

There are many forms of amyloidosis, including primary amyloidosis (AL), which occurs in the setting of multiple myeloma or other plasma cell dyscrasias, secondary or reactive amyloidosis (AA), which occurs in chronic inflammatory diseases (such as rheumatoid arthritis) and with long-term hemodialysis, familial amyloidosis (AF), and senile systemic amyloidosis (SSA) (10–13).

Amyloidosis is usually observed in the systemic form with only 10%–20% of cases being localized (14). Although stomach and gastrointestinal tract involvement is a common feature of systemic amyloidosis (15), localized gastric involvement has been reported rarely, with only 15 cases worldwide (16–28). We report the third case of localized gastric amyloidosis in the United States and the first among Caucasians.

CASE REPORT

A 60-year-old white man was referred to our GI clinic after an incidental finding of “thickened gastric folds” on an abdominal computed tomography (CT), which was ordered to evaluate chronic anemia and rule out polycystic kidney disease (Figure 1). He reported occa-

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A CASE TO REMEMBER

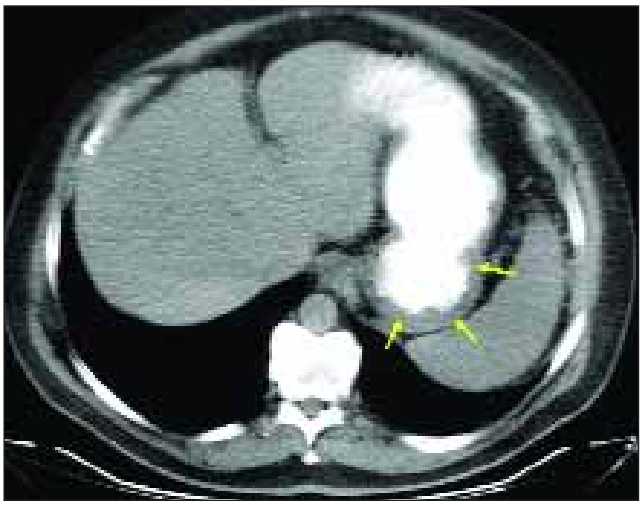


Figure 1. Computed tomography (CT) showing thickened gastric folds (arrows).

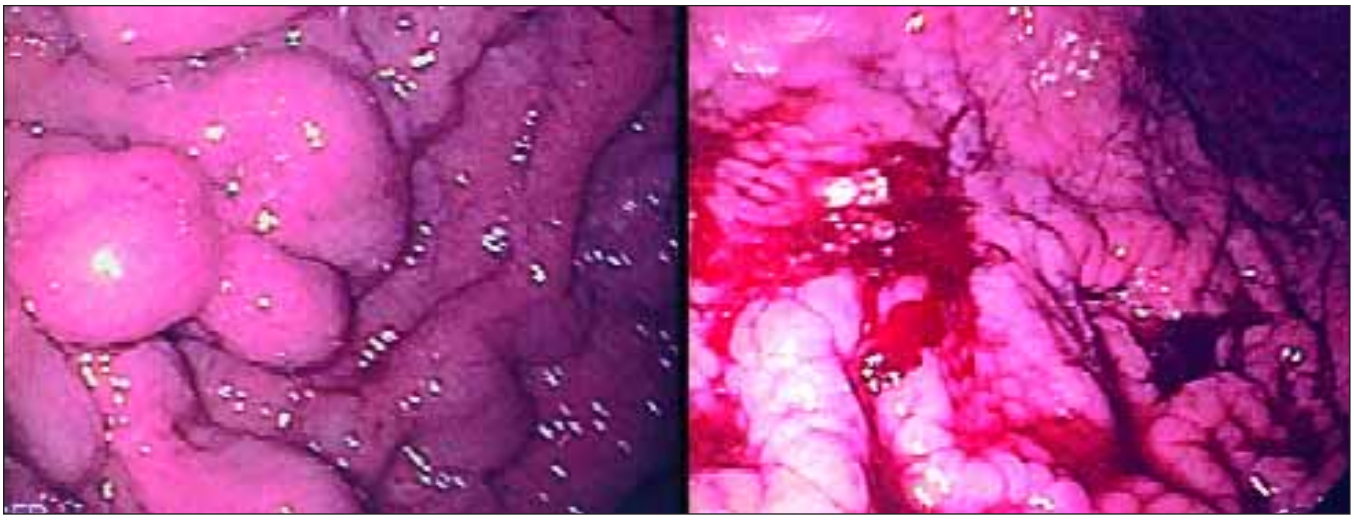
sional heartburn but denied any other gastrointestinal symptoms. His medical history included type 2 diabetes mellitus for over 20 years, hypertension, nephrotic syndrome, peripheral vascular disease, hypothyroidism, and hypertriglyceridemia with a history of pancreatitis.

On physical examination, vitals signs were normal and he was obese. The abdomen was soft to palpation with normal bowel sounds, and there were no masses or organomegaly. There were no signs of systemic amyloidosis such as macroglossia or periorbital purpura.

Laboratory work up was significant for ESR of 58 mm/hr, hemoglobin 11 g/dL, MCV 84 cu mm, triglycerides 732 mg/dL, creatinine 1.7 mg/dL, BUN 46 mg/dL, and 7,525 mg/day of protein in the urine. The rest of the extensive laboratory work-up was unremarkable, including liver tests, electrolytes, amylase, lipase, C reactive protein, prothrombin time, partial thromboplastin time, folate and B_{12} levels, fecal occult blood test, rheumatoid factor, *H. pylori* serology, ANA and anti-ds DNA antibody, and hepatitis viral serologies.

Esophagogastroduodenoscopy (EGD) revealed many "grape-like" lesions in the gastric fundus and many thickened, nodular and erythematous folds in the gastric body (Figure 2). There was significant bleeding after biopsies of the gastric body were obtained, and injection of epinephrine was required to achieve hemostasis. We did not biopsy the "grape-like" lesions in the fundus because of the concern of these being gastric varices. Indeed, at a later date, he underwent upper endoscopic ultrasound (EUS) which did reveal gastric fundal varices and a grade 1 esophageal varix.

Pathology results from the gastric body biopsies revealed evidence of chronic gastritis with deposits of eosinophilic fibrillary staining material which tested negative on PAS and mucin staining. On further



A B

Figure 2. Endoscopic images showing many "grape-like" lesions in the gastric fundus (varices) (2A), and many thickened, nodular and erythematous folds in the gastric body (amyloidosis) (2B). There was significant bleeding after biopsies were obtained from the gastric body.

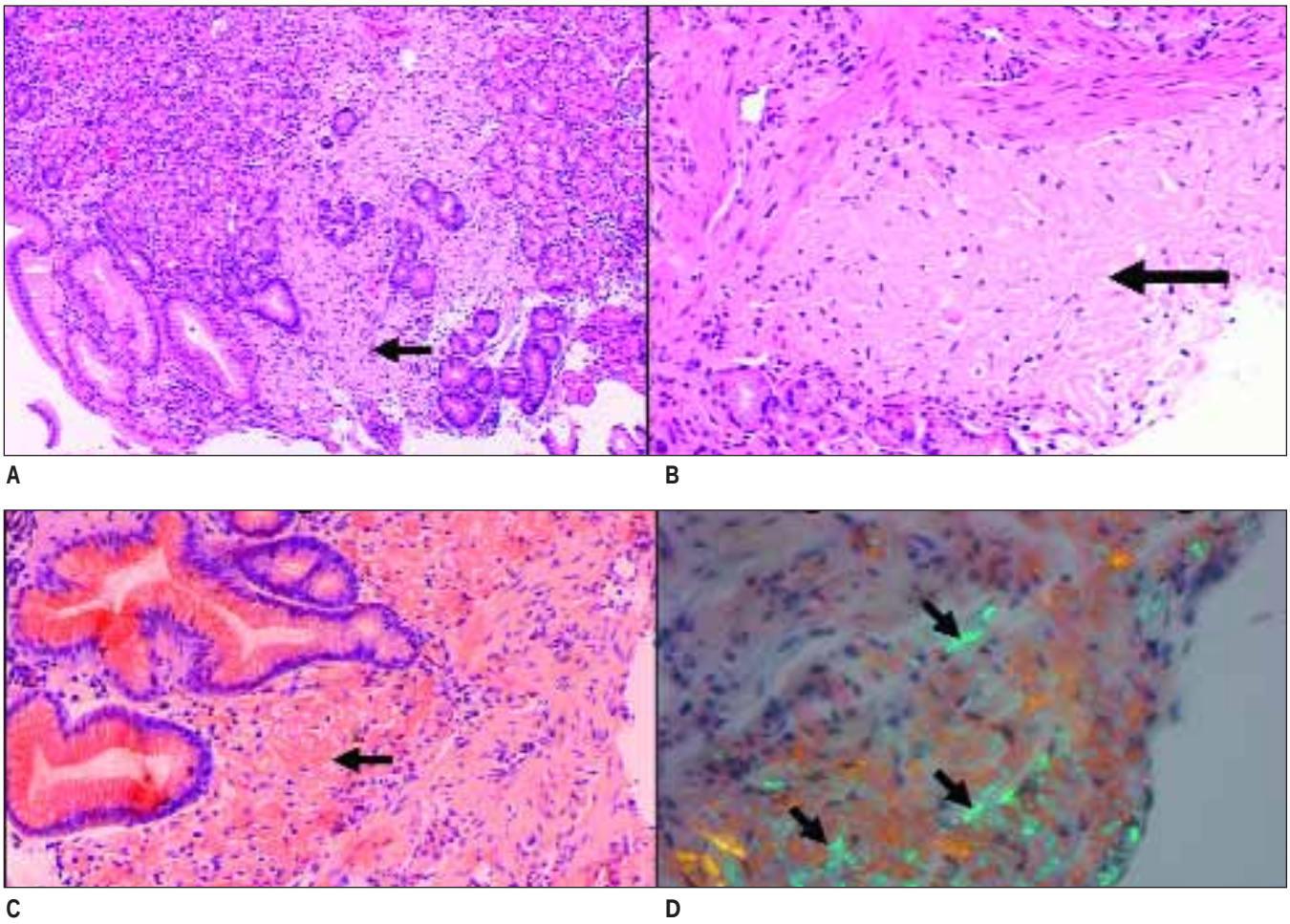


Figure 3. Amyloid deposits (arrows) in gastric biopsy specimens: Biopsy specimen on hemotoxin and eosin (H&E) staining shows amorphous eosinophilic material infiltrating the gastric mucosa and wall (3A and 3B) in the background of chronic gastritis changes. Amyloid deposits were confirmed by Congo red staining (3C) revealing characteristic "apple-green" birefringence in polarized light (3D).

special staining, the eosinophilic material was Congo red stain positive with characteristic apple-green birefringence under polarized light consistent with the classic appearance of amyloid deposits (Figure 3).

The patient was evaluated by a nephrologist and underwent percutaneous kidney biopsy to exclude amyloidosis as a cause for his nephrotic syndrome. Renal histology was consistent with diabetic glomerulonephropathy. Congo red and Thioflavin T stains, electron microscopy and immunofluorescence were all negative, thus ruling out renal amyloidosis. His nephrotic-range proteinuria (secondary to diabetes mellitus) was managed with diuretics.

He was then investigated for multiple myeloma and other monoclonal gammopathies, and protein and immunofixation electrophoresis (IFE) were negative for protein bands on both serum and urine specimens.

The patient was followed for over two years with no signs or symptoms of systemic amyloidosis noted. In addition, no evidence of other organ involvement was found after extensive work-up including liver enzymes, urine analysis for Bence-Jones proteins, CT scans of the abdomen and thorax, electrocardiogram (ECG), echocardiography and MRI of the brain. Thus, a methodical evaluation excluded systemic amyloidosis.

A CASE TO REMEMBER

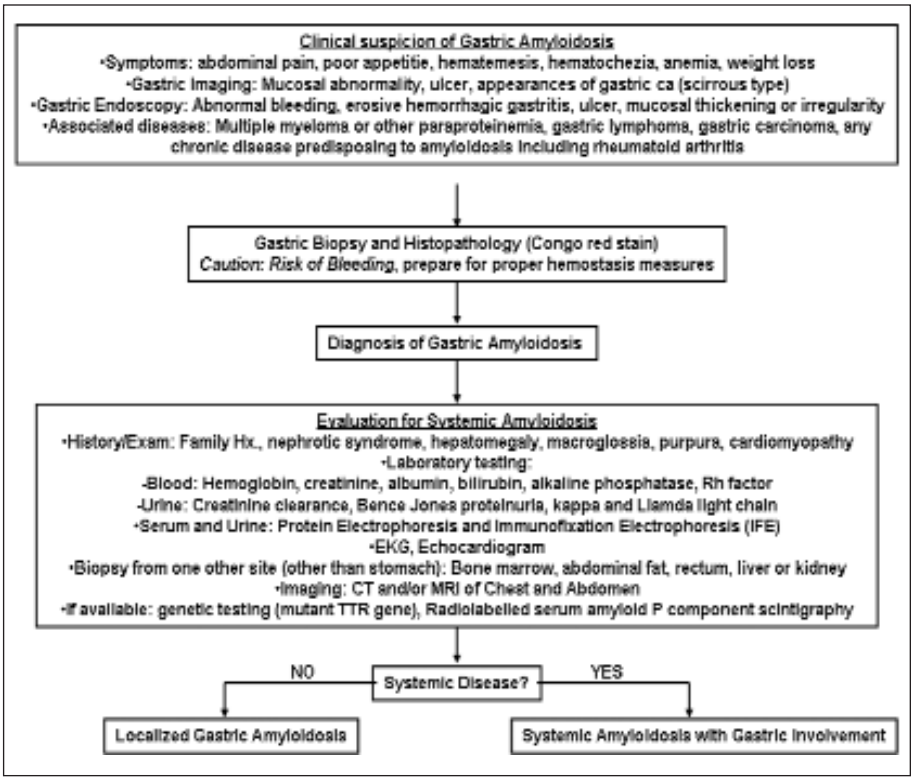


Figure 4. Diagnostic algorithm for localized gastric amyloidosis.

DISCUSSION

The diagnosis of localized gastric amyloidosis requires a complete and methodical investigation to exclude systemic amyloidosis (12,29,30). Correct classification is important, as systemic chemotherapies can effectively treat patients with primary amyloidosis (AL) (13,31–33). On the other hand, localized amyloidosis does not require systemic therapy because long-term prognosis is excellent (13).

Organs such as bone marrow, kidney, heart, bowel, lung, and joints are nearly always involved in systemic amyloidosis, and as such, systemic amyloidosis can practically be ruled out if histopathology fails to demonstrate amyloid in any one of these organs or tissues (30). In addition, it has been suggested that for the diagnosis of localized amyloidosis, paraproteinemia should be excluded through immunifixation electrophoresis (IFE), which has been shown to be the most sensitive test in detecting serum monoclonal proteins (34). We propose an algorithm for the diagnosis of localized gastric amyloidosis (Figure 4).

Gastrointestinal tract involvement is a common feature of systemic amyloidosis (15), and may present as intestinal dysmotility (35–37), malabsorption (due to mucosal infiltration or bacterial overgrowth) (38), protein-losing gastroenteropathy (39) or intestinal obstruction (40). On the other hand, localized gastric amyloidosis has been reported very rarely, with 15 cases reported worldwide and only 2 in the United States (US) (16–28). Unlike our case, both of the previous US cases were in African-Americans and had paraprotenemia (16,17).

Symptoms of gastric amyloidosis are usually non-specific and include abdominal pain, anorexia and weight loss. Gastric amyloidosis can also present with gastric perforation (41), gastro-colic fistula (42) and with gastric malignancies (25,43,44). Even the benign forms have been confused with gastric cancer due to their endoscopic and radiographic appearance. Therefore, biopsy with histologic confirmation is necessary to confirm the diagnosis (45–47).

In conclusion, amyloidosis must be considered in the differential diagnosis of irregular, nodular and/or thickened GI mucosa seen on imaging or at endoscopy. It can be asymptomatic or present with overt gastrointestinal bleeding, and it may cause significant hemorrhage after biopsy. With this in mind, caution should be exercised when performing gastrointestinal biopsies in a patient with suspected amyloidosis, and the endoscopist should be prepared to control the hemorrhage that may ensue. The diagnosis of localized amyloidosis requires a methodical investigation to exclude systemic amyloidosis. ■

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