Different Outcomes of Three Localized Primary Gastric Amyloidosis Cases

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Case Report

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Abstract

Background: Localized primary gastric amyloidosis is a rare disorder characterized by the extracellular deposition of insoluble fibrillary protein confined to the stomach, which can mimic various diseases, including gastrointestinal stromal tumors, gastric cancer and ulcers in endoscopic examination.

Case presentation: Here, we report a series of 3 cases of localized gastric amyloidosis mimicking gastric mucosa-associated lymphoid tissue (MALT) lymphoma by endoscopic examination that were evaluated over the past ten years in our hospital. The different times of detection of this rare disease resulted in three totally different outcomes, indicating the significant importance of the early detection, diagnosis and treatment of this rare disease. The difficulty of making an accurate diagnosis and differential diagnosis is highlighted, and this report may provide more clinical experience for the diagnosis of localized primary gastric amyloidosis.

Conclusions: Localized gastric amyloidosis is a rare metabolic disease that can look like MALT lymphoma. Early detection, diagnosis and treatment of this rare disease results in an excellent prognosis.

Background

Localized gastric amyloidosis is a rare disorder characterized by extracellular deposition of insoluble fibrillary protein confined to the stomach [1]. The clinical manifestations of localized gastric amyloidosis are often uncharacteristic and subclinical [2]. Gastric endoscopic findings include redness, erosion, ulcers, submucosal tumor-like features, and scirrhous-like features, among others [3]. Although imaging studies such as computed tomography (CT), radiographic contrast, endoscopic ultrasound (EUS), and upper endoscopy are helpful in the initial assessment of patients, determining the correct clinical diagnosis remains difficult. Previous reports have indicated that the main diseases considered alongside localized gastric amyloidosis for differential diagnosis include gastrointestinal stromal tumors [4, 5], gastric cancer [3] and healing gastric ulcers [6]. Herein, we report 3 cases of localized gastric amyloidosis with different outcomes over the past ten years at our hospital. In these cases, the disease mimics gastric MALT lymphoma under upper endoscopy, suggesting the importance of early detection, clinical and pathological diagnosis and treatment.

Case Presentation

Case report 1

A 36-year-old woman visited our hospital because of epigastric pain for approximately 1 month. Esophagogastroduodenoscopy (EGD) revealed a faint red reddish flat-elevated lesion of 15 x 16 mm in size with multiple nodules on the surface in the great curvature of the antrum adjacent to the corpus (Figure 1A). The lesion presented a defined green area under narrow band imaging (NBI) (Figure 1B). Magnifying endoscopy with NBI (ME-NBI) showed expanded normal glands with changed polarity as well as dilated and tortuous vessels, suggesting that something other than epithelial tumors was located in

the lamina propria mucosae or deeper (Figure 1C). Based on morphology, *Helicobacter pylori* (Hp) negative MALT lymphoma was considered first, but further examination by H&E staining and Giemsa staining of multiple gastric biopsies showed that the samples were negative for *Helicobacter pylori* and that the histology of the lesion indicated only nonspecific inflammation. Therefore, after informed consent was obtained from the patient, diagnostic endoscopic submucosal dissection (ESD) was successfully performed. Histologically, massive and cord-like pink substances were deposited in the mesenchyme and inside the blood vessel wall at the bottom of the lamina propria mucosa, muscularis mucosae and superficial submucosal layer, with cystic dilated gastric glands suggesting cystic gastritis (Figure 1D). Additionally, Congo red staining with the pretreatment of potassium permanganate confirmed the light chain amyloid (AL) type, which was reconfirmed by polarized light microscopy with the observation of apple-green birefringence in the lesions (Figure 1E, F). Ultrasonography and CT revealed a normally functioning heart and normal-sized liver and kidneys, and no amyloid deposition was histologically seen anywhere in A final diagnosis of primary localized gastric amyloidosis with cystic gastritis was established. The patient was discharged uneventfully after ESD, and no local or systemic recurrence was seen at 2 months, 6 months or 1 year of follow-up. This case report presents endoscopic features and associated histology of a confirmed gastric amyloidosis with cystic gastritis by ESD sample of the lesion, which contributes to endoscopic detection of primary localized gastric amyloidosis.

Case report 2

A 28-year-old woman was admitted to our hospital due to 6 months of epigastric pain. Physical examination and routine laboratory investigations were unremarkable. Conventional endoscopy identified red and white area in the gastric antrum, mainly white lesions, accompanied with active gastritis as well as multiple atrophy, nodules and erosion lesions (Figure 2A). NBI showed a defined light brownish area (Figure 2B), and ME-NBI showed expanded normal glands with changed polarity and tree-like vessels. The first suspected diagnosis was Hp positive MALT lymphoma (Figure 2C); however, pathological examination demonstrated gastric amyloidosis in the mucosa, and no malignant tumor was found (Figure 2D, E). CT showed no abnormalities. Urine immunoelectrophoresis was negative for Bence-Jones protein, and serum immunoglobulin levels were normal. Due to the large sizes of the lesions and the lack of gastric outlet obstruction, ESD was not performed. The pain of this patient was relieved after Hp eradication for active gastritis, and she was followed up for 4 years. There were no changes in the relevant lesions.

Case report 3

A 72-year-old man was referred to our hospital due to intermittent epigastric pain and vomiting for 2 years. The situation worsened this time; he could not eat at all and had severe vomiting. Before this visit, he had never been to hospital for any examination. Conventional endoscopy demonstrated that the whole gastric mucosa was congestive, edematous and mainly red. Enlarged and thickened irregular gastric folds in the whole stomach with sporadic and large sheet erosions were detected. Moreover, gastric antrum peristalsis disappeared, and gastric outlet obstruction occurred due to narrowing of the antrum

(Figure 3A). EUS showed that the mucosa and submucosa layer were thickened, but the muscle and serosal layers were intact (Figure 3B). MALT lymphoma and gastric cancer were highly suspected. To relieve his discomfort, we dissected some tissue to remove obstruction, and a gastric tube was placed into the antrum to support nutrition (Figure 3C). CT showed that the pyloric wall was thickened, and submucosal enhancement was not obvious. There were no signs of amyloidosis in the liver, spleen, or heart, and no amyloid deposition was histologically seen elsewhere in the whole GI tract. Finally, H&E staining showed abundant amyloid deposition in the mucosal and submucosal layers (Figure 3D, E), and these were positive for Congo red staining. No bone destruction was found in the lumbar spine, pelvis or skull by CT examination, immunoelectrophoresis was negative for Bence-Jones protein, and serum immunoglobulin levels were normal. Primary gastric focal amyloidosis was diagnosed. Unfortunately, due to a lack of financial assistance, the patient gave up further treatment and died 2 weeks later due to severe malnutrition.

Discussion

Amyloidosis is characterized by extracellular deposition of abnormal proteins in organs, including six types: primary, secondary, hemodialysis-related, hereditary, senile, and localized [1]. Primary amyloidosis is associated with monoclonal light chains in serum and/or urine, with 15% of patients having multiple myeloma. Secondary amyloidosis is associated with inflammatory, infectious, and neoplastic diseases, and these two types of amyloidosis are the most common type in clinical practice. Generally, amyloid deposits are distributed along the gastrointestinal (GI) tract, liver, kidney, and spleen, and sometimes is associated with the onset of inflammatory bowel disease (IBD) [1]. The duodenum and stomach are the most common sites for protein deposition. GI involvement is common in cases of systemic amyloidosis, and the majority of cases of gastric amyloidosis are related to systemic involvement of amyloidosis. Nausea, vomiting, hematemesis, and epigastric pain are the symptoms, and purpura, macroglossia, joint swelling, congestive heart failure and hepatomegaly are the typical characteristics of physiological examination of systemic amyloidosis.

For localized primary amyloidosis in the GI tract, the most common location is the stomach [7], followed by the esophagus [8], small bowel [9], and colon [10]. Localized gastric amyloidosis is a rare disorder characterized by the extracellular deposition of insoluble fibrillary protein confined to the stomach [4]. The clinical presentation of localized gastric amyloidosis ranges from no symptoms to nausea, vomiting hematemesis, melena, abdominal pain, a gastric mass or tumor, inflammation, erosions, healing ulcers, and even perforation [11, 12]. Epigastric pain is one of the most common symptoms, and gastric outlet obstruction may be due to submucosal tumors [13], polyps, or antral narrowing [14]. In our study, all lesions were located in the gastric antrum, one of which spread to the whole stomach, and the gastric mucosal background displayed active gastritis. Among the 3 cases, epigastric pain was a prominent symptom, with no typical signs of systemic amyloidosis by physiological examination, strongly suggesting local gastric amyloidosis.

Conventional endoscopic findings, including thickened irregular gastric folds [15], gastric outlet obstruction [14], loss of rugal folds [1, 14], gastric ulcers with clean bases or irregular edges [14, 16, 17], arteriovenous malformations [18], granular-appearing mucosa [19], plaque-like lesions [20], ulcerative gastritis [21], submucosal tumor-like features [4], healing gastric ulcer [6] and gastroparesis [22], have been reported in gastric amyloidosis. Three cases had different lesions, including a faint red flat-elevated lesion with multiple nodules on the surface; a white-yellowish circular area with the appearance of multiple nodules and active gastritis; and redness, sporadic erosion, thickened irregular gastric folds and gastric outlet obstruction. Therefore, there was no specific feature of localized primary amyloidosis during endoscopic examination under white light. With the development of endoscopic technology, NBI and ME-NBI are becoming increasingly useful in detecting early gastric cancer. Thus, it is important to exclude cancers such as undifferentiated adenocarcinoma or MALT lymphoma because localized gastric amyloidosis commonly appears as a cancerous lesion or mass. In our observations, it was difficult to distinguish MALT lymphoma by NBI and ME-NBI imaging in these cases, we observed expanded normal glands with changed polarity, mucosal irregularities, and round small vascular changes such as dilated vessels without variable caliber on the surface and tree-like vessels, which were considered characteristics of MALT lymphoma [23]. Moreover, despite the reported utility of EUS in diagnosing gastric amyloidosis [24], specific EUS features were not well defined. In our 3 cases, the EUS images of localized primary amyloidosis showed thickening of the gastric wall with homogenous lesions in the first and second layers only. Therefore, it is still difficult to distinguish gastric amyloidosis from other lesions, such as gastric cancer and MALT lymphoma, by EUS. However, it is very important for endoscopists to consider this rare disease when performing endoscopic diagnoses.

Pathological analysis is the gold standard for the diagnosis of gastric amyloidosis, and biopsy with pathology assessment and staining are very helpful for determining the correct diagnosis. In AL amyloidosis, there is greater deposition of amyloid in the muscularis mucosa, submucosa, and muscularis propria, in contrast to AA amyloidosis, which does not involve deeper layers of the gastric wall [3] but instead manifests as mucosal lesions that can be visualized by endoscopy and biopsied. Thus, it is necessary to perform a biopsy to reach the muscularis mucosa. In these 3 cases, H&E staining showed abundant amyloid deposition in the mucosal or submucosal layers. Congo red staining with the pretreatment of potassium permanganate confirmed the light chain AL type, which was reconfirmed by polarized light microscopy with the observation of apple-green birefringence in the lesions. Additionally, serum and urine immunoelectrophoresis showed no monoclonal immunoglobulin or free light chain. k and l light chains in serum or urine were all in the normal range. These are the typical pathological findings for primary amyloidosis.

For patients with a diagnosis of amyloidosis, it is important to determine whether they have systemic or localized disease because the treatment and prognosis are different for each disease entity. For instance, treatment for systemic AL amyloidosis is chemotherapy and stem cell transplantation [1], but localized GI amyloidosis without evidence of systemic involvement has an excellent prognosis.

From our experience, in the first case, because the lesion was less than 2 cm, ESD was recommended for not only the diagnosis but also treatment and resulted in a good prognosis and minimal recovery time. This kind of treatment is also recommended when mucosal biopsies are negative [6]. For the second case, because a circular area in the gastric antrum and the patient had no gastric outlet obstruction due to narrowing of the antrum, we performed Hp eradication to reduce her pain, which was successful. She was followed up for 4 years, and there were no changes in the relevant lesions. However, at this stage, in addition to close follow-up, no other good treatment was recommended. These clinical observations suggested that patients with localized primary amyloidosis should be monitored and treated symptomatically because they rarely experience progression to systemic disease, and their survival is excellent. The outcome of the third case was unfortunate; due to late detection, amyloidosis was deposited in the whole stomach, particularly in the gastric antrum, resulting in low gastric motility, obstruction and gastric retention. Time for effective treatment was lost.

Conclusion

In conclusion, localized gastric amyloidosis is a rare metabolic disease that can look like MALT lymphoma. Early detection, diagnosis and treatment of this rare disease results in an excellent prognosis. In this study, the difficulty in making an accurate diagnosis and differential diagnosis is highlighted, which may provide more clinical experience for the diagnosis and treatment of localized primary gastric amyloidosis.

Abbreviations

AL: Amyloid; CT: Computed tomography; EGD: Esophagogastroduodenoscopy; ESD: Endoscopic submucosal dissection; EUS: Endoscopic ultrasound; GI: Gastrointestinal; Hp: Helicobacter pylori; IBD: Inflammatory bowel disease; MALT: Mucosa-associated lymphoid tissue; ME-NBI: Magnifying endoscopy with NBI; NBI: Narrow band imaging.

Declarations

Ethics approval and consent to participate

After ethical review, this study was approved by the Ethics Committee of Affiliated Hospital of Zunyi Medical University. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

XML and LJD are the first author of this report and performed the endoscopic in these cases. They also analyzed the data and wrote the manuscript. JXZ, XLW, HPL and HCW performed experiment and pathological diagnoses. BGT has read and approved the final manuscript.

Authors' information (optional)

Not applicable.

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Figures

Figure 1

Endoscopic and Histological data of case 1. A: EGD revealed a fainted reddish flat-elevated lesion of 15 x 16 mm in size with multiple nodules on the surface in the great curvature of the antrum adjacent to the corpus; B: NBI showed a defined green area; C: ME-NBI showed expanded normal glands with changed polarity as well as dilated and tortuous vessels; D: H&E staining showed cystic dilated gastric glands; E: Massive and cord-like pink substances were deposited in the mesenchyme and inside the blood vessel wall at the bottom of the lamina propria mucosa, muscularis mucosae and superficial submucosal layer; F: Polarized light microscopy found apple-green birefringence in the lesions. Yellow arrows indicate amyloidosis deposited substance.

Figure 2

Endoscopic and Histological data of case 2. A: Conventional endoscopy showed red and white area in the atrophic gastric antrum with active gastritis; B: NBI showed a defined light brownish area; C: ME-NBI showed expanded normal glands with changed polarity and tree-like vessels; D: H&E staining showed abundant cord-like red substance in the mucosal layers; E: These were positive for Congo red staining. Yellow arrows indicate amyloidosis deposited substance.

Figure 3

Endoscopic and Histological data of case 3. A: Conventional endoscopy demonstrated that the whole gastric mucosa was congestive, edematous and mainly red; B: EUS showed that the mucosa and submucosa layer were thickened (blue arrow), but the muscle and serosal layers were intact; C: A gastric tube was placed into the antrum to support nutrition; D: H&E staining showed abundant brick red substance in the mucosal and submucosal layers; E: These were positive for Congo red staining; Yellow arrows indicate amyloidosis deposited substance.

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