Gastric Amyloidosis

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ABSTRACT

AA amyloidosis occurs as secondary to rheumatoid arthritis, inflammatory bowel disease and other diseases and also associated with familial Mediterranean fever. Outcomes are worse if there are cardiac or gastrointestinal manifestations. A 57 year-old female was admitted to our hospital with clinical manifestations of nausea, vomiting, epigastric pain, odynophagia, dysphagia and chronic diarrhea. She has also history of rheumatoid arthritis for 10 years. Upper gastrointestinal endoscopy revealed hyperemia in the whole region of gastric mucosa and lower gastrointestinal endoscopy showed hyperemia with erosion in colonic and ileal mucosa. Histopathologic examination of the gastric biopsy showed the deposition of amyloid materials in the mucosa. We report a case of gastric amyloidosis secondary to rheumatoid arthritis.

Keywords: *gastric amyloidosis, rheumatoid arthritis, dyspepsia*

INTRODUCTION

Amyloidosis is a unique metabolic storage disease that results from deposition of insoluble fibrillar proteins or aberrantly folded and assembled protein fragments in a variety of tissues, mainly in the extracellular spaces, and not metabolized or cleared by the body. As a conformational disease, amyloid fibrils can be deposited locally or may involve virtually every organ system of the body, may have no apparent clinical consequences or may be associated with severe pathophysiologic changes.[1-3]

There are distinct types of amyloidosis, which are classified according to the protein composition of the amyloid deposits and usually subdivided into systemic (generalized) and localized (tissue-spesific) forms. The clinical manifestations, prognosis, and therapy vary greatly depending on the specific type of amyloidosis (table 1).[4] In immunoglobulin-light-chain-related (AL) amyloidosis (also called primary amyloidosis), an underlying monoclonal plasma-cell disorder produces the constituents of the deposits, which are the variable regions of the immunoglobulin light chains. In AA (secondary) amyloidosis, by contrast, the amyloidogenic precursor is a normal acute-phase reactant called serum amyloid A (SAA), which is produced as the result of chronic infection or inflammation.[5,6]

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CASE REPORT

A 57 years old female, came to hospital complained of difficulty in swallowing that occurred since one month before. Actually, she had already felt pain on swallowing and difficult to eat for about 4 months accompanied by nausea, vomiting and epigastric pain. At first, she still could take liquid food but then it was progressively worsening. Finally, she felt hardly passage both liquid or solid food. She got a 20 kg unintentional weight loss in a year. There is also diarrhea since one month ago, with frequency of 2 - 3 defecations per day.

There is history of rheumatic disease since about 10 years, regularly control to rheumatologic division and take methylprednisolone and ranitidine, but she had stopped taking these drugs since one month ago. She also had already stopped taking captopril for her hypertension since then.

On examination, her blood pressure is 170/100 mmHg, height 155 cm and weight 35 kg. There is lymph node enlargement in the left neck around

Table 1. Treatment of systemic amyloidosis.[4]

Type of amyloidosis	Amyloid protein component	Current therapy	Goal of therapy
AL or AH (primary)	Immunoglobulin light chain (AL) or (occasionally) heavy chain (AH)	Melphalan plus dexamethasone; alternative is autologous stem-cell transplantation in selected patients with limited organ involvement who are candidates for the procedure	Eradicate clonal plasma cells that are the source of immunoglobulin protein
AA (secondary to chronic inflammatory or familiar Mediterranean fever)	Serum amyloid A protein	Treatment of underlying infection or inflammation colchicines for familial mediterranean fever	Reduce level of serum amyloid A protein
Mutant ATTR (familial)	Mutant form transthyretin	Liver transplantation	Eliminate source of mutant transthyretin
Senile systemic amyloidosis	Wild-type form of transthyretin	No therapy	
Other forms of familial amyloidosis			
Fibrinogen α-chain	Mutant form of fibrinogen α-chain	Hepatorenal transplantation	Eliminate source of fibrinogen α-chain (liver) and replace affected organ (kidney)
Lysozyme	Lysozyme	Undefined	
Apolipoprotein	Apolipoproteins A-I and A-II	Renal transplantation	Replace affected organ

2 x 2 x 2 cm and deformities on extremities, Swan neck and Boutonniere deformities (figure 1). Laboratory results showed mild anemia (11.7 g/dL), elevated ESR (114 mm), high GGT (103 U/L), hypoalbuminemia (2.6 g/dL), low transthyretin level (6.9 mg/dL), hypokalemia (2.7 mmol/L), no albuminuria/proteinuria and no erythrocyte in urine, transferin level was low (51 mg/dL), TSHs and Free T4 were normal.

The problem lists of the patient at admission were difficult intake, chronic diarrhea, rheumatoid arthritis, malnutrition, hypertension and lymphadenopathy colli sinistra. She was then proceed upper and lower gastrointestinal endoscopic examination. Upper gastrointestinal endoscopy showed hyperemia in the whole region of gastric mucosa (figure 2) and histopathologic examination of the biopsy specimen showed the typical deposition of amorphous, homogeneous and acidophilic material in the gastric mucosa (figure 4A & 4B) with conclusion of amyloidosis gaster. Lower gastrointestinal endoscopy showed pancolitis and ileitis, there's appearance of hyperemia and erosion (figure 3) with histopathologic results of non-destructive chronic colitis (figure 5).

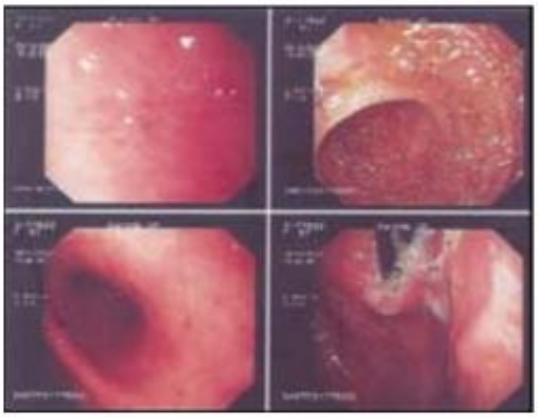

Figure 2. Gastric mucosal hyperemia

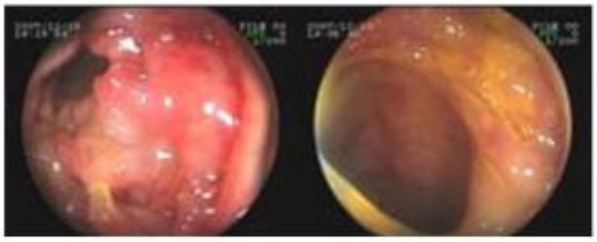

Figure 3. Hyperemia and erosion of colon

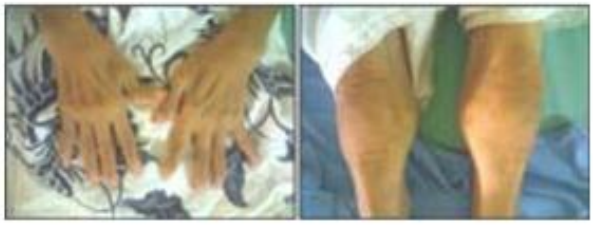

Figure 1a. Swan neck and boutonniere, b. Bilateral knees arthritis

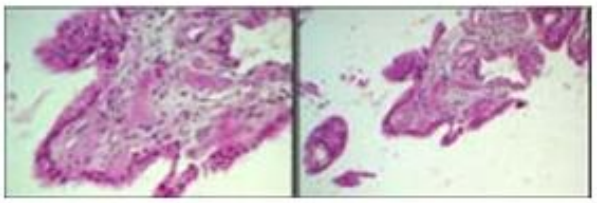

Figure 4. Gastric amyloidosis, deposition of amorphous, homogeneous and acidophilic material

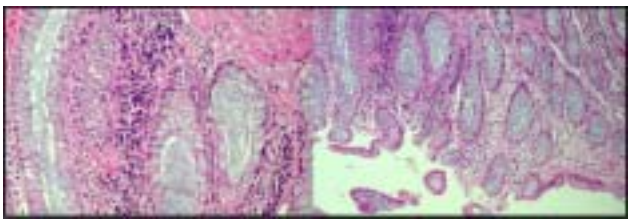

Figure 5. Chronic colitis

DISCUSSION

Amyloidosis may be classified in different forms characterized by the structure of deposited fibrillar proteinaceous amyloid. AL amyloidosis occurs in a primary form and as a complication to myelomatosis or Waldenstroms macroglobulinaemia. AA amyloidosis occurs as secondary to rheumatoid arthritis (like this patient), inflammatory bowel disease and other diseases and also associated with familial Mediterranean fever. Patients with amyloidosis may be treated with melphalan, prednisone and colchicine. Outcomes are worse if there are cardiac or gastrointestinal manifestations. In AL amyloidosis the median survival after diagnosis is 1-2 years. In renal amyloidosis dialysis or transplantation may improve survival.[7,8]

Amyloidal protein was further should be proven by positive Congo red stain appearing red microscopically in normal light (as shown in figure 4A & 4B) and will exhibit green birefringence under polarized light. Amyloid deposits could give positive reaction with AA-antibody using peroxidase technique. A more detailed evaluation of the amyloid composition was beyond the capability of our laboratory.[7]

In 1885, the term ''Congo'' red was introduced in Berlin at the Berlin West Africa Conference as the name for the first direct textile dye. At the time, European newspapers were filled with exciting stories of the exotic Congo River basin in Central Africada hot new geopolitical and potentially profitable area in which to invest or exert control. Hence, the name had marketing cache, just like another textile dye with an African name used in medicine: Sudan black. A patent on Congo red was issued to its inventor, Paul Bottiger, who subsequently sold its rights to a major German textile dyestuff company (AGFA), a firm that ultimately merged with others to form the IG Farben Company. A challenge to AGFA's Congo red patent subsequently led to a precedent-setting decision in intellectual property law. Congo red is rarely used today as a textile dye because it tends to change color when handled by sweaty fingers and stains the fabrics of other garments when washed together.

In the GI tract, amyloid may involve the vasculature, producing changes of ischemia; the mucosa, resulting in bleeding, malabsorption, and diarrhea; and the muscles, causing subsequent dysmotility and intestinal obstruction. Whitish ulcers, black necrosis, tan polyps made largely of amyloid, and blotches of reddish-purple may be seen. So many colors in the rainbow!.[9]

The amyloid found in the gastrointestinal system may be localized, or a part of systemic amyloidosis. In systemic amyloidosis, gastrointestinal involvement is common; however, local deposition of amyloid in the gastrointestinal system without systemic involvement is an uncommon form. As part of systemic amyloidosis, Gilat T, suggested two patterns of gastrointestinal amyloid deposition.[10] In the AA type, amyloid was deposited in the mucosa and the inner layer of the blood vessels. In the AL type, amyloid deposition was found in the muscular layer and the outer layers of the blood vessels. Yamada et al, confirmed these observations in their 21 autopsy cases with amyloidosis.[11]

Localized gastric amyloidosis is characterized by mucosal or submucosal amyloid deposition in the gastric wall. Subclinical gastrointestinal involvement in amyloidosis is common, occurring in up to 98% of patients. The clinical manifestations of the gastrointestinal amyloidosis were often uncharacteristic, and it is difficult to assess the incidence of clinical symptoms, which are said to occur in less than 20% of cases. The clinical manifestations are varied, including motility disorders, bleeding, malabsorption, obstruction, protein-losing enteropathy and perforation. As for localized gastric amyloidosis, a variety of common gastrointestinal symptoms such as epigastric discomfort, poor appetite, hematemesis, hematochezia and gastric perforation may occur in the process of this disease. Gastric amyloidosis shows association with gastric malignancies, such as carcinoma and stromal tumor. Hematologic malignancies including plasma cell dyscrasia and gastrointestinal lymphoma have occasionally been reported in association with amyloidosis.[6,7]

Amyloid-associated gastrointestinal dismotility can be manifested as intestinal pseudoobstruction, diarrhea, or achalasia. GI symptoms typically include anorexia, eating difficulty due to macroglossia, and altered bowel habits. Nausea may occur in up to 40% of patients with amyloidosis. Clinical gastroparesis occurs rarely in patients with amyloidosis; one study reported only 3 cases in 769 patients.[12,13] In this patient, the predominant symptoms are nausea, vomiting, epigastric pain, odynophagia and dysphagia. The possibility of amyloidosis may cause chronic diarrhea in this patient remain to be established, further histopathologic evaluation with the Congo red stain should be done to get certainty.

We have presented herein a case of gastric amyloidosis that was found associated with

rheumatoid arthritis. It showed morphological features identical to those previously described as a systemic amyloidosis and manifested as dyspepsia and difficult intake.

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