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Localized gastric amyloidosis: A case report

Lokalize gastrik amiloidoz: Olgu sunumu

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Local deposition of amyloid without systemic involvement is rather uncommon and has been found in many organs. A 67-year-old man was admitted to our hospital presenting with weight loss, fatigue and poor appetite. Blood work and bone marrow examination revealed megaloblastic anemia. Upper gastrointestinal endoscopy reveeled e purple polypoid wass lesion of 5mm eliameter in the paracardiac region. Histopathologic examination of the gastric biopsy showed the deposition of amyloid materials in the mucosa. The patient had no evidence suggesting systemic amyloidosis. We report a rare case of localized amyloidosis of the stomach. The clinical and pathological features of this rare condition and association with megaloblastic anemia are discussed.

Key words: Gastric amyloidosis, megaloblastic anemia

Sistemik tutulum olmaksızın lokal amiloid depolanması, nispeten nadirdir ve birçok organda görülür. 67 yaşında erkek hasta kilo kaybı, halsizlik ve iştahsızlık ile hastanemize başvurdu. Kan ve kemik iliği incelemeleri megaloblastik anemiyi ortaya çıkardı. Endoskopide parakardiak bölgede 5mm çapında pembe polipoid lezyon görüldü. Vakanın mide biyopsisinin histopatolojik incelemesinde mukozada amiloid birikimi gözlendi. Hastada sistemik amiloidozu düşündüren bulgular izlenmedi. Nadir görülen bir lokalize gastrik amiloidoz olgusunu rapor ettik. Bu nadir durumun klinik, patolojik özellikleri ve megaloblastik anemi ile ilişkisi tartışıldı.

Anahtar kelimeler: Gastrik amiloidoz, megaloblastik anemi

INTRODUCTION

The term amyloidosis refers to a group of disorders characterized by the extracellular accumulation of insoluble, fibrillar proteins in various organs and tissues (1). Generally amyloidosis is more commonly manifested as systemic involvement. Local deposition of amyloid is a rather uncommon form, and amyloidal deposit confined to the stomach is extremely scarce in the previous literature (2, 3, 4). The clinical manifestations of gastric amyloidosis were often uncharacteristic and subclinical (5, 6).

No previous reports exist of megaloblastic anemia in patients with localized gastric amyloidosis. The pathologic findings of such an unusual association and a review of the literature are presented.

CASE REPORT

A 67-year-old male presented to the Hematology Department with the complaints of weight loss, fatigue and poor appetite of four-months' duration. On admission, physical examination was unremarkable except for pallor and jaundice. Blood work showed hemoglobin concentration as 5.7 g/dl with a hematocrit of 17% and reticulocyte of 0.04%, leukopenia with leukocyte count of $3.2x10^9$/L, and thrombocytopenia with platelet count of $129x10^9$/L. Direct Coombs test was negative, and serum haptoglobulin levels were normal. Plasma bilirubin and serum lactate dehydrogenase levels were markedly elevated. Peripheral blood film showed hypersegmentation of neutrophils (Figure 1A), and bone marrow examination revealed megaloblastic changes and giant metamyelocytes (Figure 1B). The level of serum vitamin B_{12} was low, at 67 pg/ml. An upper gastrointestinal endoscopy showed a gastric mass 5x5x5 mm in size located at the paracardiac region (Figure 2A, 2B) and mucosal changes. Endoscopically visible gastric mucosal changes were mainly in antral localization and were consistent with atrophic gastritis. No mucosal defect was observed. Histopathologic examination of the biopsy specimen showed the deposition of amorphous, homogeneous and

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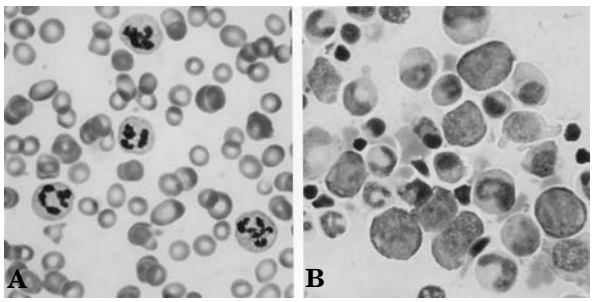

Figure 1. A) Blood film showed hypersegmented neutrophils, and, **B)** bone marrow aspirate revealed megaloblastic changes and giant metamyelocytes (May-Grünwald Giemsa, x1000)

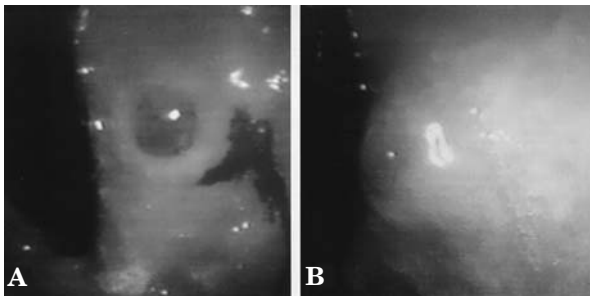

Figure 2. A-B) Endoscopic picture of the gastric mass

acidophilic material in the gastric mucosa (Figure 3A, 3B). Amyloidal protein was further proven by positive Congo red stain (Figure 4A) and it exhibited green birefringence under polarized light. Amyloid deposits gave negative reaction with AA-antibody using peroxidase technique. A more detailed evaluation of the amyloid composition was beyond the capability of our laboratory. The gastric biopsy of the antrum demonstrated a moderately severe chronic atrophic gastritis without *Helicobacter pylori* infection. Similar masses were not detected by endoscopy in other parts of the stomach and gastrointestinal tract, i.e., esophagus and duodenum. Multiple biopsy specimens taken from various parts of the gastrointestinal tract other than the stomach showed no amyloid deposition (Figure 4B).

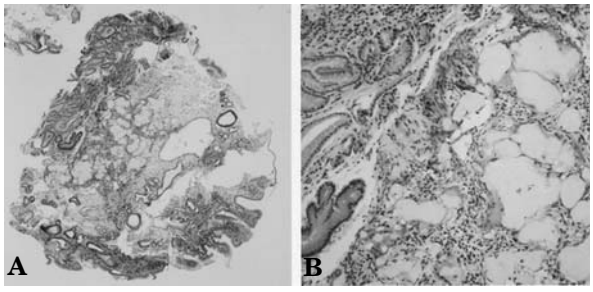

Figure 3. A) Light microscopy showed amorphous, homogeneous, acidophilic amyloidal deposits in gastric mucosa (hematoxylin & eosin, x100). **B)** Amyloid deposits at higher magnification (hematoxylin & eosin, x200)

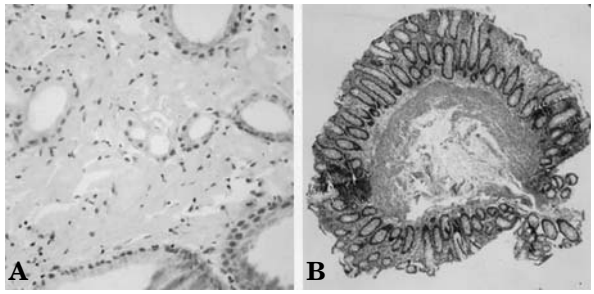

Figure 4. A) Stained with Congo red (x400), **B)** Rectal biopsy was histologically normal (hematoxylin & eosin, x100)

Other laboratory data showed negative results in the detection of urine Bence-Jones protein. Serum immunoglobulin levels were absolutely normal. No abnormal signs were found on the chest and head radiographs. There were no clinical symptoms suggesting amyloidosis, and additional examination revealed no findings characteristic of amyloidosis or any chronic inflammatory disease.

DISCUSSION

Amyloidosis is a disorder characterized by extracellular deposition of a homogeneous, eosinophilic, fibrillar protein in organs and tissues (1). Various subtypes exist, including primary systemic amyloidosis, reactive systemic amyloidosis associated with chronic inflammatory states, and localized forms of aberrant amyloid deposition. Primary amyloidosis refers to the disorder in patients with no preceding or co-existing disease except immunocyte dyscrasias, where the extracellular substance is composed of light chain (AL) protein produced by plasma cells, as typically seen in multiple myeloma. The major forms of systemic amyloidosis also include reactive systemic amyloidosis consisting of a nonimmunoglobulin protein (AA) secreted by the liver in the setting of chronic inflammatory disorders or cancers. Other types of amyloid include Ab2m amyloid, which is associated with hemodialysis, and ATTR amyloid, which is seen in systemic senile and familial amyloidotic neuropathies (1, 7). The localized form of gastrointestinal tract amyloidosis, however, has been shown to consist of a unique form of amyloidosis (6).

The amyloid found in the gastrointestinal system may be localized, or a part of systemic amyloidosis. In systemic amyloidosis, gastrointestinal involvement is common (1); however, local deposition of amyloid in the gastrointestinal system without systemic involvement is an uncommon form (4). As part of systemic amyloidosis, Gilat et al. suggested two patterns of gastrointestinal amyloid deposition. 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 (5). Yamada et al. confirmed these observations in their 21 autopsy cases with amyloidosis (6). Localized gastric amyloidosis is characterized by mucosal or submucosal amyloid deposition in the gastric wall (4).

Subclinical gastrointestinal involvement in amyloidosis is common, occurring in up to 98% of patients (5). 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 (6). 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 (2, 4). Gastric amyloidosis shows association with gastric malignancies, such as carcinoma (8) and stromal tumor (9). Hematologic malignancies including plasma cell dyscrasia and gastrointestinal lymphoma have occasionally been reported in association with amyloidosis (10).

Megaloblastic anemias are hematologic disorders caused by impaired DNA synthesis and characterized by the presence of megaloblastic cells. The most common causes of megaloblastic anemia are folate deficiency and vitamin B_{12} (or cobalamin) deficiency. Cobalamin deficiency is most often a result of defective absorption, most commonly pernicious anemia, a condition in which intrinsic factor production fails (11). Although the detailed mechanism for the deposition of amyloid in a specific organ remains unclear, the accumulation of proteinaceous metabolites might be a possible explanation (12). In this case report, our patient had findings consistent with chronic atrophic gastritis, which might have been a cause of local inflammation, and this inflammation may have lead to localized deposition of amyloidal materials in the gastric mucosa. Amyloid deposits cause pathologic destruction by progressive intercellular accumulation and pressure atrophy of adjacent cells. However, atrophic gastritis is a well-known etiologic agent of megaloblastic anemia (13). It is largely speculative that glandular destruction by amyloidosis impairing gastric secretion of intrinsic factor may have resulted in vitamin B_{12} deficiency and megaloblastic anemia in our case.

Once amyloidosis is diagnosed, an attempt has to be made to detect any underlying chronic disorders such as myeloma or collagen disease. Further investigations in our case showed no particular abnormality in any organs and the patient was free of systemic disease. The findings were consistent with those of localized gastric amyloidosis. In the cases with localized amyloidosis studied in the literature (3, 4), there is always a lack of evidence of systemic involvement, despite extensive searches in many patients for underlying malignancy, inflammatory conditions or myeloma.

We have presented herein a case of localized gastric amyloidosis that was found incidentally. It showed morphological features identical to those previously described and was seen in a case with megaloblastic anemia.

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