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CASE REPORT

Primary Systemic Amyloidosis of Stomach and Duodenum: A Rare Case Report

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ABSTRACT

Primary amyloidosis is a group of monoclonal plasma cell disorders characterized by the extracellular deposition of immunoglobulin light chain fibrils in multiple organs, leading to progressive multi-organ dysfunction. It is a rare disease that usually occurs in elderly persons and has a poor prognosis.

Primary amyloidosis of the gastrointestinal tract is relatively rare, and symptomatic amyloidosis of the stomach is even more seldom. Monoclonal gammopathy often undervalues nephropathy, a rare condition of renal significance. We present the case of a 28-year-old female who presented with recurrent vomiting, abdominal distension, poor oral intake, and weight loss for two months. Her upper GI endoscopy was done, which showed edematous nodular antral mucosa and superficial ulcers in the third part of the duodenum. Biopsies were taken, which showed features suggestive of primary amyloidosis with kappa light chain restriction. A renal biopsy revealed that she had a lot of damage to her tubes, including an unusual intratubular cast with kappa light chain restriction. People often underestimate monoclonal gammopathy of renal significance (MGRS), a rare condition.

KEYWORDS

• Primary Systemic Amyloidosis • Gastrointestinal tract • MGRS • Cardiac • Light chain

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INTRODUCTION

Amyloidosis, an umbrella term for the accumulation of fibrils made up of tiny pieces of normal serum proteins, refers to some disorders.[1] Clinicopathologically, it falls into two major categories. 1) systemic (generalized amyloidosis) and 2) localized amyloidosis. We further classify systemic amyloidosis into (a) primary (AL) type, (b) secondary (AA) type, (c) hemodialysis-associated, and (d) heredo-familial type. We further classify localized amyloidosis into a) senile cardiac, b) senile cerebral, c) endocrine type, and d) tumor-forming AL type.[2] Primary systemic light chain amyloidosis is still a rare entity with an estimated annual incidence of only about 3000 cases in the United States.[3]

Primary amyloidosis, secondary AA amyloidosis, and dialysis-related (B2 macroglobulin) amyloidosis all exhibit gastrointestinal involvement. Primary amyloidosis of the gastrointestinal tract is not very common. In a group of 769 patients, only 1% had symptoms of amyloidosis in the stomach, and only 8% of patients had amyloidosis in a biopsy from the gastrointestinal tract.[4] If amyloidosis affects the digestive tract, it can lead to problems like changes in movement, bleeding in the gut, or not being able to absorb nutrients. Endoscopically, gastric amyloidosis can look like gastric neoplasia[5,6], hematomas, erosions, ulcerations, or nodular gastritis in the stomach.[7]

The term monoclonal gammopathy of renal significance (MGRS) was coined in 2012.[8] It encompasses a group of renal disorders with a range of renal pathology in the presence of a monoclonal gammopathy. Multiple myeloma is known to be the most common monoclonal gammopathy that damages the kidney. Nevertheless, an increasing number of kidney diseases associated with monoclonal gammopathy do not meet the criteria for multiple myeloma.[9] Patients are often diagnosed with MGUS, although they have a disease that is not of undetermined significance. To further explore this phenomenon, a new term was introduced: monoclonal gammopathy of renal significance.[8]

CASE REPORT

A 28-year-old female presented to AIIMS emergency in May 2021 with complaints of recurrent vomiting, abdominal distension, poor oral intake, and weight loss for two months. On-and-off vomiting was present since 2017. In August 2020 her symptoms worsened with decreased urine output, and she received 6 sessions of hemodialysis. The doctor performed a renal biopsy, which revealed severe tubular injury and an atypical intratubular cast with kappa light chain restriction. The etiology identified her as cast nephropathy with kappa light chain restriction, leading to a diagnosis of CKD stage 3. Bone marrow aspirates from October 2020 showed 8–10% plasma cells. We performed an upper gastrointestinal endoscopy, revealing features indicative of severe gastritis. Non-contrast CT abdomen was within normal limits. Serum protein electrophoresis showed a faint monoclonal band. We started her on cyclophosphamide and tapered her steroids until April 2021.

She was normal till April 2021. She presented to AIIMS for an emergency in May. On examination, her GCS was E4V5M6, pulse rate of 107/min, blood pressure 96/54 mmHg, SpO_2 97%, and RR of 18/min. On systemic examination, the cardiovascular, respiratory, and central nervous systems were normal. Per abdominal examination, the abdomen was distended, soft, and nontender. Despite the absence of an M band in either urine or serum electrophoresis, the serum free light chain ratio was abnormal. The bone marrow biopsy showed 70% cellularity, adequate megakaryocytes, and interstitial plasma cells, but no increase. The biopsies from the upper GI endoscopy revealed edematous nodular antral mucosa and superficial ulcers in the third part of the duodenum. A histopathological examination of the same thing showed signs of primary amyloidosis with kappa light chain restriction. A 2D ECHO revealed grade 2 diastolic dysfunction, moderate systolic dysfunction (EF 40-45%), and myocardial speckling suggestive of cardiac amyloidosis (*Table 1*). Medical oncology registered the patient and advised therapy based on the VCD protocol. Her symptoms resolved with treatment.

Her condition was hemodynamically stable at discharge.

Both the gastric biopsy (A x 100) and the duodenal biopsy (B x 100) show hyaline substance deposits outside of cells (arrows)

in the lamina propria. The deposits show congophilia and apple-green birefringence (arrow) under polarized microscopy (C x 200). The deposits show positivity for the lambda light chain (arrow) with kappa light chain restriction and negativity with serum amyloid-A protein (inset) D x 100 (*Figure 1*).

Table 1: Investigations

24-hour urinary protein	396mg/day
Corrected reticulocyte count	1.3%
Serum M band electrophoresis	No M band seen
Urine M band electrophoresis	No M band seen
Serumfree light chain assay	Serum free kappa/lambda ratio-8.6%
Immunofixation	M band is to be IgG kappa
Bone marrow flow cytometry	Abnormal immunophenotype with kappa light chain restriction suggestive of plasma cell dyscrasia
Serum b2 microglobulin	9.33mg/l
2D ECHO	Grade 2 diastolic dysfunction, moderate LV dysfunction (40-50%), myocardial speckling positive, LV hypertrophy
Histopathology(antral and duodenal biopsy)	Moderately dense mixed inflammation with neutrophilic cryptitis and dense extracellular amyloid deposits. Focal mucosal ulceration is noticed. The amyloid deposits show apple-green birefringence under polarized light and are positive for kappa stain
Low dose whole body CT	No evidence of any lytic lesions in the visualized bones

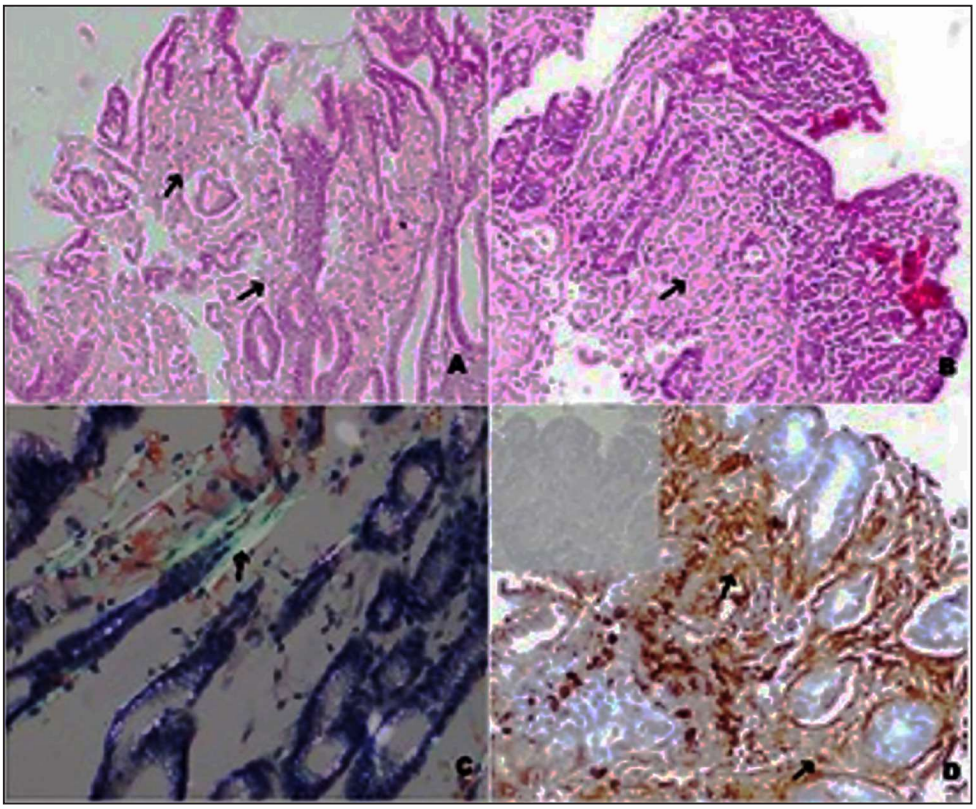

Figure 1: Histopathological findings, **(A)** Gastric biopsy shows extracellular hyaline substance deposits (arrows) in the lamina propria **(B)** Duodenal biopsy shows extracellular hyaline substance deposits (arrows) in the lamina propria **(C)** Congophilia and apple-green birefringence (arrow) under polarized microscopy **(D)** Positivity for Lambda light-chain (arrow) with kappa light-chain restriction and negativity with serum amyloid-A protein

DISCUSSION

Primary amyloidosis is the most common form of systemic amyloidosis, which is a plasma disorder that affects mostly bone marrow but is usually not associated with other diseases.[2] However, it may also occur in association with some form of plasma cell dyscrasia. Systemic amyloidosis can affect virtually any organ, except for the CNS.

Primary systemic amyloidosis affects men slightly more often than women. Primary systemic amyloidosis is a disease of the elderly, and the average age of patients at the time of diagnosis is 65 years; about 10% of patients are less than 50 years old.[10]

Primary systemic amyloidosis affects the kidney, heart, liver, spleen, gastrointestinal tract, peripheral nerves, carpal ligaments, and skin. Kidney involvement is seen in 75% of patients, heart in 50%, macroglossia in 15%, hepatomegaly in 50%, splenomegaly in 10%, and carpal tunnel syndrome in 25%.[10,11]

Our patient had gastrointestinal involvement, biopsy-proven. Also, she had cardiac involvement in the form of restrictive cardiomyopathy and raised cardiac biomarkers. Our patient also had kidney involvement in the form of cast nephropathy, which was light chain restricted, but there was no glomerular involvement, as only moderate proteinuria was present, whereas renal amyloidosis patients usually have massive proteinuria. Since the kidneys were affected in our case, it wasn't because of amyloid buildup, the term for this is monoclonal gammopathy of renal significance. Monoclonal gammopathy is associated with a variety of kidney diseases. [12] Monoclonal gammopathy-related kidney diseases are different in how they start, how they show up in the body, what they find on kidney biopsies, how they get worse, how they end, and how they are treated.[13] This complicated word refers to people whose kidneys are damaged because of monoclonal immunoglobulin released by precancerous or cancerous clones.[13]

For patients who are suspected of having MGRS, it is important to diagnose the type of monoclonal gammopathy, the pathogenic cell clone, and the type of nephropathy.[14] The best way to diagnose the deposits of monoclonal immunoglobulin in the kidney is to perform a kidney biopsy.

To diagnose a case of primary systemic amyloidosis (AL), the following four criteria must be satisfied:[15]

a. Presence of AL amyloid-related systemic syndrome (such as renal, liver, heart, gastrointestinal, or peripheral nerve involvement).
b. Positive amyloid staining by Congo Red in any tissue (fat aspirates, bone marrow, or organ biopsy).
c. Direct examination of the amyloid (immunohistochemical staining, direct sequencing) showed that it is related to light chains.
d. Proof of a disorder that affects the growth of monoclonal plasma cells (serum or urine M protein, an abnormal free light chain ratio, or clonal plasma cells in the bone marrow).

The main goal of treating primary light chain amyloidosis is to get rid of the abnormal plasma cells so that free light chains can circulate. This could lead to the regression of amyloid deposits, improve organ function, and offer survival benefits.[16]

Autologous stem cell transplantation is an effective and rapid way of achieving a clinical response, but less than a quarter of all patients with primary systemic amyloidosis are candidates for this therapy.[17]

To treat MGRS, the toxic monoclonal immunoglobulins should be stopped quickly because they hurt the kidneys.[18]

The therapeutic option should focus on the plasma cell clone with appropriate chemotherapy.

CONCLUSION

The diagnosis of gastric amyloidosis should be considered in patients with plasma cell disease. Upper GI endoscopy rarely finds gastric amyloidosis in people who don't already have a known diagnosis. In fact, only a few endoscopic findings have been published. However, both a general doctor and a gastroenterologist should keep this condition in mind as a possible diagnosis.

The main goal for MGRS patients who are at high risk of getting multiple myeloma or other related diseases is to find early signs of progression to multiple myeloma and stop

complications.

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