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Website: www.ijhonline.org

DOI: 10.4103/ijh.ijh_15_23

A case of primary systemic amyloidosis with amyloid deposits in the duodenum and bone marrow aspirate: A rare finding

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Abstract:

Amyloidosis is a group of diseases characterized by extracellular abnormal proteinaceous material (amyloid) deposition in various organs. As amyloid fibrils accumulate, tissues and organs may fail to function properly. Evidence of amyloid deposition in duodenal biopsies and bone marrow (BM) aspirates is uncommon and often overlooked. Here, we present a patient diagnosed with primary systemic amyloidosis who complained of pain in the abdomen, vomiting, loose stools, and generalized weakness. Histological examination of an endoscopic duodenal biopsy revealed amyloid deposits. BM aspiration cytology revealed amyloid deposition with BM plasmacytosis. She was eventually diagnosed with plasma cell dyscrasia based on a series of biochemical tests. To the best of our knowledge, reports of simultaneous amyloid deposition in the duodenum and BM aspirate smears are very rare and unpublished. This case serves to highlight the significance of careful microscopic histo-cytology and the utility of special stains for prompt diagnosis and treatment outcomes in a disease of poor prognosis.

Keywords:

Amyloidosis, bone marrow cytology, duodenum histology, plasma cell dyscrasia

Introduction

Amyloidosis is a protein disease. In this disease, proteins change shape (misfolding) and then bind together to form amyloid fibrils that deposit in organs. Deposition of amyloid can be local or systemic. Plasma cell dyscrasia has been linked to primary systemic amyloidosis. The duodenum is the most common location for gastrointestinal (GI) amyloid deposits, followed by the stomach, colon, rectum, and esophagus.[1] Amyloid deposition is more visible in bone marrow (BM) biopsy specimens than in aspirate smears.[2] We report a case of amyloid light chain (AL) amyloidosis with GI symptoms and amyloid deposits in the duodenum and BM aspirates associated with plasma cell dyscrasia.

Case Report

A 37-year-old woman presented to the gastroenterology outpatient department with a 3-week history of abdominal pain and generalized weakness. She reported vomiting and loose stools for 3 days. The patient was hemodynamically stable at the time of presentation. A slight pallor of the conjunctiva was noted during the general examination. Cardiovascular, respiratory, and neurological examinations were normal. Abdominal examination excluded hepatosplenomegaly, tenderness, or shifting dullness. Upper GI endoscopy

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Submission: 10-02-2023
Revised: 07-03-2023
Accepted: 11-03-2023
Published: 28-04-2023

How to cite this article: Momin MA, Ingle A, Reddy R, Reddy GV. A case of primary systemic amyloidosis with amyloid deposits in the duodenum and bone marrow aspirate: A rare finding. Iraqi J Hematol 2023;12:111-4.

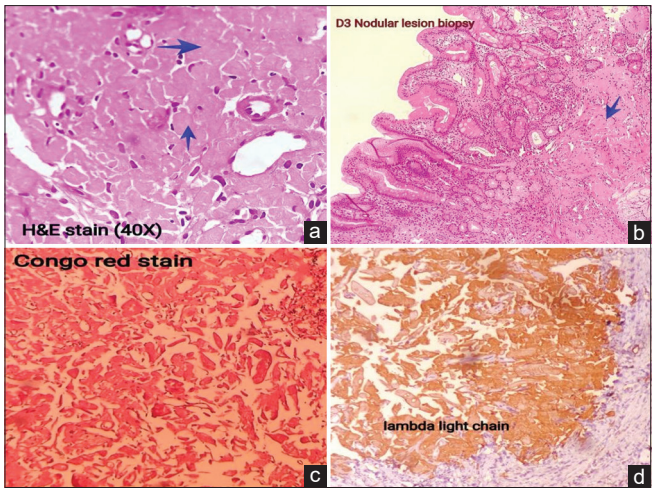

Figure 1: (a and b) Duodenum (D1 and D3) biopsy histological examination (H and E stain) showed amyloid deposit (blue arrow), (c) Congo red stain, (d) IHC with positive lambda chain. IHC = Immunohistochemistry

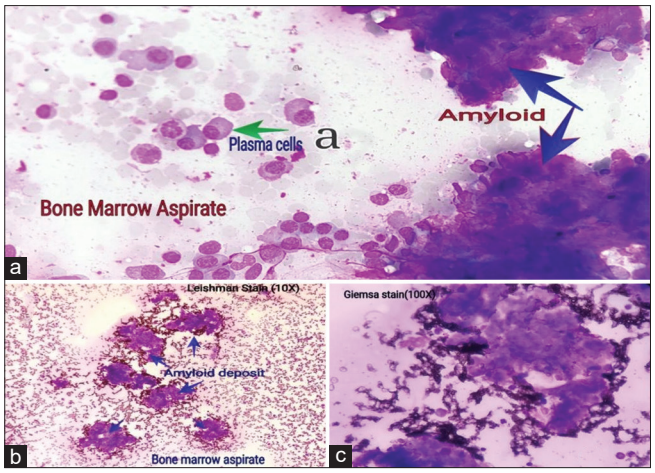

Figure 2: BM aspirate examination showed amyloid deposit (blue arrow) and plasma cells (green arrow). BM = Bone marrow

was planned and routine laboratory investigations were performed. Laboratory results revealed hemoglobin levels of 8.9 g/dl, total leukocyte count of 9200/cumm, and platelet count of 3.2 lakhs/cumm. Erythrocyte sedimentation rate was 80 mm at the end of 1 h. The results of the blood coagulation study, including prothrombin time, activated partial thromboplastin time, and fibrinogen, were normal. Serological tests for hepatitis B virus, hepatitis C virus, HIV, and syphilis were negative. A complete urine examination showed proteinuria (3+, 500 mg/dl). Biochemical parameters showed normal random plasma glucose, liver function test, renal function test, and normal serum electrolytes. The C-reactive protein was <5 mg/L. The chest X-ray showed the normal study. A computed tomography scan of the chest and abdomen reveals minimal bilateral pleural effusion and mild ascites, respectively. Esophagogastroduodenoscopy revealed edematous mucosa with nodular lesions in the first (d1) and third (d3) parts of the duodenum. A biopsy was performed from the same. Histological examination showed deposition of homogeneous, eosinophilic, hyaline acellular material with mixed inflammatory infiltrates that are favoring amyloidosis [Figure 1a and 1b]. Under polarized microscopy, special stain (Congo red) revealed red-colored amyloid accumulation [Figure 1c] with apple-green birefringence. The acellular material stained positive for lambda light chains [Figure 1d] but negative for kappa light chains on immunohistochemistry, further supporting AL amyloidosis.

In the meantime, a BM aspiration was performed based on histomorphological suspicion of amyloidosis, which revealed cellular aspirate with marrow plasmacytosis (14%) Figure 2a green arrow. An amorphous purple-blue deposit was observed among hematopoietic cells, which could be an amyloid deposit Figure 2a (blue arrow) and Figure 2b (blue arrow) & Figure 2c. Congo red staining revealed red-colored amyloid deposition.

The serum protein electrophoresis (SPE) showed the presence of M band with peak in beta 2 as well as gamma region [Figure 3].

Serum immunofixation report concludes IgA lambda monoclonal gammopathy [Table 1].

Finally, the patient was diagnosed with duodenal and BM amyloidosis secondary to plasma cell dyscrasia. She was given standard AL amyloidosis treatment, which included cyclophosphamide, bortezomib, and dexamethasone. The patient's symptoms improved and she was eventually discharged from the hospital. The patient is doing well and is being closely monitored.

Discussion

Amyloidosis is the term first described by Rokitansky in 1842, the substance was subsequently named by Virchow as amyloid under the mistaken belief that the material was starch-like. The amyloid having a common morphological appearance, staining properties, and physical structures with variable protein composition. The nomenclature of different forms of amyloid is done by putting the alphabet A for amyloid, followed by the suffix derived from the name of specific protein constituting that type, for example, AL.[3] The AL type is associated with disorders of immunoglobulin synthesis such as multiple myeloma, B-cell lymphoma, or other plasma cell dyscrasia. In this, there is excessive production of intact immunoglobulins or light chains (kappa/lambda) or rarely heavy chains. These light chains are pieces of antibodies made by plasma cells, which misfold and

Table 1: Serum electrophoresis, electrophoretic zone and serum immunofixation with light chain assay quantitative data

Test report status	Results	Biological reference interval
Myeloma M band	Detected	Not detected
Electrophoretic zone		
IgG band	Not detected	Not detected
IgM band	Not detected	Not detected
IgA band	Present	Not detected
Kappa band	Not detected	Not detected
Lambda band	Present	Not detected
IF-quantitative (mg/dL)		
Total IgA	1301	70–400
Total IgG	466	700–1600
Total IgM	58	40–230
Serum light chains (kappa and lambda) (mg/dL)		
Kappa light chain	14.1	0.30–19.40
Lambda light chain	91.7	5.71–26.30
Kappa lambda ratio	0.15	0.26–1.65
B2-microglobulin	2.96	0.81–2.19

IgA=Immunoglobulin A, IgG=Immunoglobulin G, IgM=Immunoglobulin M, IF=Immunofixation

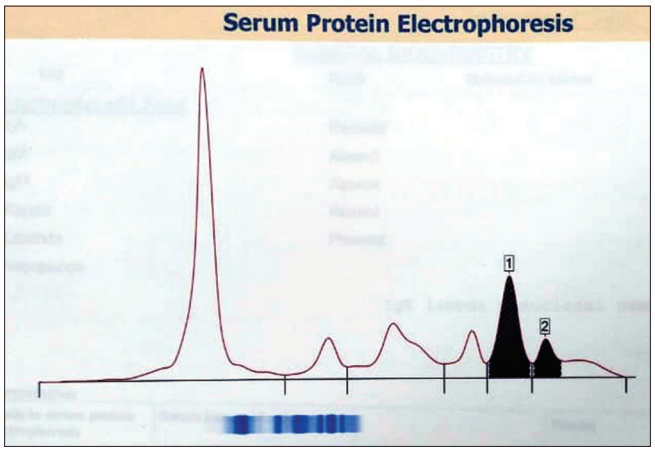

Figure 3: Serum protein electrophoresis showed presence of M band with double peak in beta 2(1)and gamma region(2)

bind together to form amyloid fibrils. The fibrils are then deposited in the organ. The organ affected is the heart kidneys, stomach, duodenum, large intestine, liver, nerves, skin, and tongue.[4] In our case, duodenum and BM were involved which is an extremely rare findings.

Abdominal pain, heartburn, weight loss, malabsorption, GI bleeds, reflux, diarrhea, and vomiting are the most common clinical manifestations of GI amyloidosis. In 25%–45% of patients, GI hemorrhage is the presenting complaint. Primary systemic amyloidosis is associated with AL type amyloid deposition in muscularis mucosa, submucosa and muscularis propria of bowel wall, which which can result in polypoidal protrusions and thickenings, causing the patient to encounter mechanical obstruction and constipation. Secondary amyloidosis is characterized by the deposition of AA-type amyloid protein in the mucosa alone, resulting in mucosal friability and a fine granular appearance on endoscopy as well as diarrhea or malabsorption as symptoms. However, it is difficult to confirm the diagnosis of GI amyloidosis by endoscopy alone, as several studies have not shown a clear correlation between endoscopic features and disease.[5]

An endoscopic tissue biopsy must be histologically examined to diagnose amyloidosis. Amyloid appears extracellular, homogeneous, structureless, and eosinophilic hyaline material under light microscopy with hematoxylin and eosin staining, which is positive with Congo red staining and it shows apple-green birefringence under polarizing microscopy. When amyloid is found, IHC should be used to determine the type of protein. Primary amyloidosis is indicated by positive kappa or lambda light chain staining.[6] In our case, careful histological examination of the duodenal biopsies raised strong suspicions of amyloidosis, which was confirmed by Congo red staining. The subsequent IHC examination revealed that the lambda light chain was positive and the kappa light chain was negative.

It is important to rule out the type of amyloidosis, as treatment strategies vary depending on the source of the precursor protein. This can be done by BM aspiration and biopsy along with extensive biochemical studies. BM aspiration facilitates quantification of plasma cells, plasma cell clones by flow cytometry, and evidence of amyloid deposition in the BM. Although BM biopsy is considered the standard for diagnosing amyloidosis, evidence of amyloid deposition in BM provides early clues for therapeutic intervention.[4] The biochemical studies include SPE and serum immunofixation (IF) with serum light chain assay. When all three serum tests were combined, the sensitivity for detecting monoclonal proteins increased to 94% and when urine IF was added,

the sensitivity increased to 98%.[7] In the present case, BM cytology showed 14% plasma cells with extensive amyloid deposition. SPE showed the presence of M band and IF study revealed IgA lambda light chain monoclonal gammopathy.

The goal of treatment is to lower the precursor protein by reducing the proliferation of plasma cells, using cytotoxic agents, and immunosuppressants. The prognosis of AL-amyloidosis with GI involvement is poor. The presence of myeloma in primary systemic amyloidosis has been shown to have poor prognosis than in multiple myeloma, even when asymptomatic at diagnosis. Other predictors of adverse outcomes include clinically significant cardiac involvement and high levels of free light chains.[8]

Conclusion

The coexistence of amyloid deposits in the duodenum and BM aspirate cytology is an extremely rare finding that has received little attention in the literature. Careful histological and cytological examination, use of special stainings such as Congo red staining and biochemical tests such as protein electrophoresis (PE) and serum immunofixation (SIF) are required for early diagnosis and therapeutic intervention in a disease like amyloidosis, which has nonspecific symptoms and nonspecific endoscopic findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Acknowledgment

We would like to thank Dr. Milap shah and technical histopathology team for special staining and phase contrast microscopy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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