



Duodenal Lymphangiectasia with Secondary Amyloidosis in a Patient with Rheumatoid Arthritis

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Abstract

Secondary amyloidosis is known to occur in patients of rheumatoid arthritis. The clinical presentation of cases with gastrointestinal involvement is variable. We report a case of a 62-year-old female known case of rheumatoid arthritis for last 15 years on regular medication who presented with pain abdomen, diarrhea, anemia and weakness. On evaluation was found to have duodenal amyloidosis along with lymphangiectasia. The dilated lymphatics within the lamina propria were filled with aggregates of foam cells. The foam cells were Congo red negative. Association of duodenal amyloidosis with lymphangiectasia is rare with only few cases previously reported in literature. Presence of foam cells in the current case is also a strange finding not reported earlier in amyloidosis. The lymphangiectasia may develop secondary to amyloid deposition making vessel wall more permeable to plasma proteins and can explain protein losing enteropathy noted in these cases.

Keywords: Amyloidosis; Secondary amyloidosis; Lymphangiectasia; Foam cells; Duodenum; Rheumatoid arthritis

Introduction

Gastrointestinal amyloidosis results from the deposition of insoluble extracellular fibrillary protein fragments which are resistant to digestion and thus impair organ function. Gastrointestinal tract can be involved in primary or secondary amyloidosis. Colon is the common site of involvement in GIT. We report a case of secondary amyloidosis of duodenum due to long standing rheumatoid arthritis with associated duodenal lymphangiectasia. The finding of lymphangiectasia in cases of secondary amyloidosis is rare with presence of foam cells within lymphatics as a still rarer phenomenon not yet described previously in literature. Treatment hinges on an adequate suppression of the predisposing inflammatory disorder, or malignancy, followed by supportive therapy for protein losing enteropathy.

Case Presentation

A 62-year-old female presented with complaints of weight loss, anemia, pain abdomen, hyperpigmentation of skin (Figure 1), weakness and altered bowel habits since 8 months to 10 months. Patient was a known case of for rheumatoid arthritis for last 15 years and hypothyroidism for last 11 years on regular medication on tablets Hydroxychloroquine (HCQs - 200 mg OD) and thyronorm (100 and 75 ug/day). Her initial investigations showed Hb of 9.8 g/dl (12 g/dl to 15.0 g/dl), MCV 78.7 (83 fl to 101 fl), MCH 23.4 (27.0 pg to 32.0 pg), MCHC 29.8 (31.5 g/dl to 34.5 g/dl), total bilirubin - 0.35 (up to 1.2 mg/dl), total protein 6.5 (6.4 g/dl to 8.3 g/dl), albumin 3.1 (3.9 g/dl to 4.9 g/dl), globulin 3.4 (2 g/dl to 4 g/dl), A/G ratio 0.9 (1.0 to 2.0), SGOT 17 (0 U/L to 32 U/L), SGPT 12 (0 U/L to 31 U/L), SAP 78 (35 U/L to 105 U/L), GGT 11 (5 U/L to 36 U/L), LDH 239 (135 U/L to 214 U/L) and creatinine 0.84 (0.5 mg/dl to 0.9 mg/dl).

She underwent Gastro-duodenoscopy which showed normal duodenal and gastric mucosa. No ulceration or nodularity seen. Random biopsies were taken from duodenal mucosa in view of anemia. Microscopic examination of duodenal biopsy showed presence of acellular eosinophilic deposits along the submucosal vessels (Figure 2a). The deposits are positive on Congo red staining and showed apple green birefringence on polarizer (Figure 2b and 2c). The deposits are diffusely positive for Serum Amyloid Associated proteins (SAA) on IHC and are negative for Lect 2 (Figure 2d). No light chain restriction noted on Kappa or lambda immunostain. The lamina propria also

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Figure 1: Hyperpigmented skin lesions.

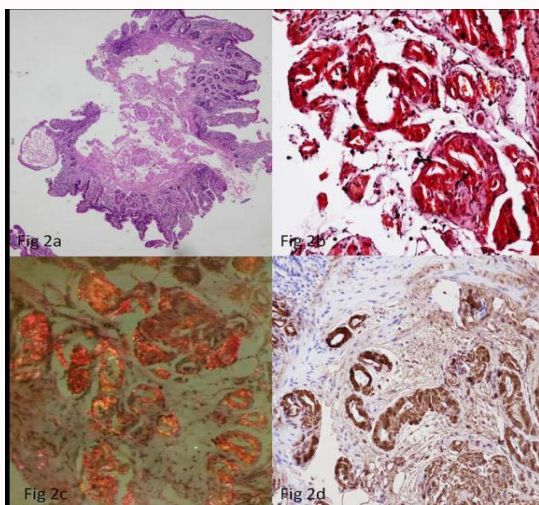


Figure 2: (a) Microscopy showing eosinophilic deposits in vessel wall (H&E x20) (b) Congo red positive deposits (c) Apple green birefringence (d) IHC SAA positive within the deposits.

showed presence of dilated lymphatics filled with foamy histiocytes and proteinaceous fluid. The lymphatic wall was highlighted by D240 Immunostain. Based on histological diagnosis of amyloidosis patient underwent further evaluation for same. Further investigations showed serum cortisol 25.31 (4.3 ug/dl to 22.40 ug/dl), serum calcium 8.6 (8.8 mg/dl to 10.2 mg/dl), B2 microglobulin 5246.0 (609 mg/ml to 2366 mg/ml). Serum free light chains kappa and lambda were 75.10 (3.3 mg/dl to 19.4 mg/dl) and 73.60 (5.71 mg/dl to 26.30 mg/dl). On protein electrophoresis and immunofixation myeloma band was not detected, Spot urine micro albumin 118.6 (2.20 mg/dl), Albumin/creatinine ratio 263.56 mg/g creatinine.

Evaluation for other organs was performed - cardiac evaluation for amyloidosis showed no evidence of restrictive cardiomyopathy. On ultrasonography whole abdomen simple hepatic cyst and small echogenic left kidney was noted. Contrast enhanced computed tomography revealed submucosal edema in pyloric region (Figure 3). Duodenum was normal. Colonoscopy was performed showed normal colonic mucosa.

She improved clinically and symptomatically with Inj. Magnex, Inj. Lesuride, Inj. F. carboxymaltose and other supportive measure. Parenteral iron was supplemented for iron deficiency anemia. She was discharged in stable condition.

Six months later she presented with complaints of fever and cough. Routine investigations showed Hb of 7.7 g/dl (12 g/dl to 15.0

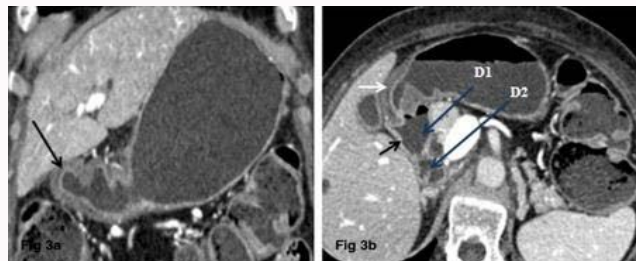


Figure 3: (a) Microscopy showing dilated lymphatics in duodenum (b) Foam cells in dilated lymphatics (c) PAS stain in foam cells (d) D240 stain highlighting vessel wall.

g/dl), TLC 2,400 (4,000 per micro liter to 11,000 per micro liter), platelets 17,600 (15,000 per micro liter to 45,000 per micro liter), PT 12.4 (11-12.5), INR 1.12 (2-3), total bilirubin - 0.51 (up to 1.2 mg/dl), total protein 6.5 (6.4 g/dl to 8.3 g/dl), albumin 2.1 (3.9 g/dl to 4.9 g/dl), globulin 2.5 (2 g/dl to 4 g/dl), A/G ratio 0.8 (1.0 to 2.0), SGOT 41 (0 U/L to 32 U/L), SGPT 25 (0 U/L to 31 U/L), SAP 90 (35 U/L to 105 U/L) and GGT 16 (5 U/L to 36 U/L). Chest X-ray was done which showed non-homogenous opacity in right mid and lower zone. HRCT showed multifocal consolidations in right lung with mild pleural effusion suggesting infective etiology. Bronchoscopy was done which showed hyperemia and congestion of right main and upper lobar bronchus. Bronchoalveolar Lavage (BAL) was done from right upper lobe. Cytology of BAL revealed acute and chronic inflammatory cells. On fungal staining budding yeast cells were detected. Fungal culture was positive. Patient was put on antifungal. Patient condition improved and he was discharged in stable condition. Follow up chest X-ray after one month of follow up showed no residual opacities. Patient is fit and asymptomatic now.

Discussion

Amyloidosis is caused by deposition of extracellular eosinophilic deposits having a fibrillar configuration. These abnormal proteins are rapidly deposited and difficult to break down, resulting in impairment of normal organ function [1]. Amyloidosis is classified into various subtypes based on nature of protein deposited as primary AL amyloidosis, secondary Amyloid A (AA) amyloidosis, familial amyloidosis, and β 2-microglobulin-related Amyloidosis [2]. The most common type of amyloidosis is systemic amyloidosis. Systemic amyloidosis usually develops secondary to long standing chronic disease like tuberculosis, rheumatoid arthritis, Crohn's disease, Ankylosing spondylitis, primary biliary cirrhosis, familial Mediterranean fever, and systemic lupus erythematosus, etc [3,4]. It usually involves gastrointestinal tract, liver, spleen, kidney and adrenals. In gastrointestinal tract colon is the commonest site [5].

Most cases of gastrointestinal amyloidosis pose a diagnostic dilemma as clinical features are nonspecific. Symptoms can range from asymptomatic to life threatening disease. Clinical features include nausea, vomiting, diarrhea, dysphasia, gastro paresis, and gastroesophageal reflux, loss of appetite, constipation or even chronic intestinal pseudo-obstruction. Few cases present as iron deficiency anemia as was also seen in our patient [6].

Presence of foam cells in dilated lymphatics is a strange finding in the current case the significance of which remain uncertain. Lymphangiectasia as a cause of protein losing enteropathy though have been described previously, presence of foam cells within lymphatic channels have not been described in cases of secondary

amyloidosis [7-9]. Their association with secondary amyloidosis is uncertain. Previous authors have postulated leakage of capillary wall secondary to amyloid deposition as a cause for protein losing enteropathy noted in cases of secondary amyloidosis. Presence of foam cells have been described in pediatric lymphangiomas and cystic intra-abdominal hemangioma [10,11] however none of these reports describe foam cells in lymphangiectatic lesions in duodenum.

Endoscopic features of the amyloidosis in the upper gastrointestinal tract are variable, ranging from subtle erosive changes, prepyloric ulcers, mucosal friability and granularity to polypoidal protrusions [12].

Radiological findings of gastrointestinal amyloidosis are rare and nonspecific. There can be diffuse or nodular bowel wall thickening. Very rarely it can present with bowel perforation and bowel hemorrhage [13,14].

Gold standard for diagnosis of amyloidosis is histological evidence of amyloid deposits with rose pink positivity on Congo red and presence of apple green birefringences on a polarized light. Histology can be supplemented with immunostains for kappa, lambda and SAA (Serum Amyloid Associated Protein) to differentiate the type of amyloid.

Treatment of underlying disease is mainstay of therapy for secondary amyloidosis. For protein losing enteropathy somatostatin analogue, high dose steroid, octreotide has been tried by some authors and found useful [7-9].

We thus publish this rare case report of duodenal lymphangiectasia with secondary duodenal amyloidosis in a patient with rheumatoid arthritis presenting as anemia and protein losing enteropathy managed symptomatically.

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