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CASE REPORT

Gastrointestinal Amyloidosis in a Patient with Systemic Sclerosis

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There were more than 90% of systemic sclerosis (SSc) patients developing gastrointestinal tract involvement with affecting esophagus mostly. However, a typical gastrointestinal manifestation may be not the only result of SSc. We described a 70-year-old female with SSc presented poor appetite, intermittent heartburn sensation, nausea, frequent sensation of abdominal fullness, and intermittent dull pain for 2 months. The esophagogastroduodenoscopy showed gastrointestinal as gastroesophageal reflux disease. The biopsy revealed amorphous material deposited in the vascular walls and apple-green birefringence in a polarization examination with Congo red staining which proved amyloidosis. The SSc patient with gastrointestinal involvement suggests to receive esophagogastroduodenoscopy, and a biopsy may be helpful to these patients to examine the possibility of secondary amyloidosis. These patients need more aggressively disease activity control.

Key words: Amyloidosis, gastroesophageal reflux disease, systemic sclerosis

INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune disease characterized by antibody production, small vessel vasculopathy, and increased fibroblast deposition of extracellular matrix. The clinical presentation involves skin thickening and variable internal organ involvement.[1] More than 90% of SSc patients have gastrointestinal tract involvement, which mostly affects the esophagus followed by the small bowel and the anorectal region.[2] The gastrointestinal manifestations from vascular damage, neurogenic impairment, and finally progress to myogenic dysfunction by smooth muscle collagenous fibrosis and atrophy.[3] However, a typical manifestation of gastrointestinal as gastroesophageal reflux disease (GERD) and abdominal discomfort may not the only result of SSc.

CASE REPORT

A 70-year-old female had been diagnosed with SSc 2 years previously. She presented with body weight loss, symmetric tightening, and induration of the skin on her fingers, polyarthralgia, Raynaud's phenomenon, dry eyes, and mouth. Serology showed an antinuclear antibody titer of more than 1:1280 with a centromere pattern and circulating anticentromere level of 304 U/ml but was negative for anti-topoisomerase I (anti-SLC-70), antineutrophil cytoplasmic antibodies (anti-MPO and anti-PR3), anti-Mi-2, anti-RO, anti-LA, anti-Smith, anti-RNP, anti-double-stranded DNA (anti-dsDNA), antihistone antibodies, and anti-ribosomal P protein autoantibodies. She was regularly followed up at our rheumatology clinic and prescription with methylprednisolone 4 mg/day and hydroxychloroquine 200 mg twice per day in November 2014, which was tapered to hydroxychloroquine 200 mg twice per day in February 2015. Due to progressive weakness and stiffness of her fingers, she was prescribed with hydroxychloroquine 200 mg twice per day, azathioprine 50 mg/day, and mycophenolate mofetil 250 mg twice per day in June 2015.

She had a poor appetite, intermittent heartburn sensation, nausea, and frequent abdominal fullness for 2 months. She

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received esophagogastroduodenoscopy which revealed GERD Los Angeles Grade B in September 2015. She then received pantoprazole 40 mg/day and mosapride 5 mg 3 times per day. However, her gastrointestinal upset persisted. For persisted polyarthralgia and gastrointestinal upset, she received rituximab 1000 mg in November 2015 and maintained therapy with hydroxychloroquine 200 mg twice per day, azathioprine 50 mg per day, and mycophenolate mofetil 250 mg twice per day.

The patient came to our emergency department for a poor appetite and vomiting with coffee ground material for 2 days. The esophagogastroduodenoscopy showed GERD Los Angeles Grade B and superficial gastritis in December 2015. A biopsy of the esophagogastric junction was also performed during esophagogastroduodenoscopy. The pathology of her biopsy showed eosinophilic amorphous material deposited in the vascular walls and aggregation of submucosa and focal lymphocytes. The amorphous material showed apple-green birefringence in a polarization examination with Congo red staining [Figure 1].

She was admitted for the evaluation of amyloidosis in January 2016. Serum protein electrophoresis showed albumin 54.5%, alpha-1 globulin 5.2%, alpha-2 globulin 12%, beta globulin 13.2%, and gamma globulin 15.1%. Immunoglobulin (Ig) monoclonality was not noted in her serum, with IgG 1120 mg/dL, IgM 77 mg/dL, IgA 81 mg/dL, IgD <48 U/mL, and IgE <5 IU/dL. Serum-free light chain analysis showed kappa 6.88 mg/L and lambda 10.3 mg/L with a free light chain ratio of 0.67. There was a trace of protein in her urine analysis, and daily protein loss was 96 mg. The 24 h creatinine clearance was 95.56 mL/min. Pathology of an abdominal wall fat pad biopsy revealed a picture of a relatively normal epidermis with focally increased dermal collagen bundles and decreased periadnexal fatty tissue of the skin. She received esophagogastroduodenoscopy and random biopsies of the esophagus, stomach, and duodenum. No vessels were noted on the esophagus and stomach samples. However, the duodenum biopsy showed a picture of amorphous pink material deposition over the perivascular area of the duodenal tissue. This material was focally positive in Congo red and thioflavin-S staining [Figure 2]. The patient reported that her gastrointestinal upset had more partially improved at her follow-up visit in February 2016.

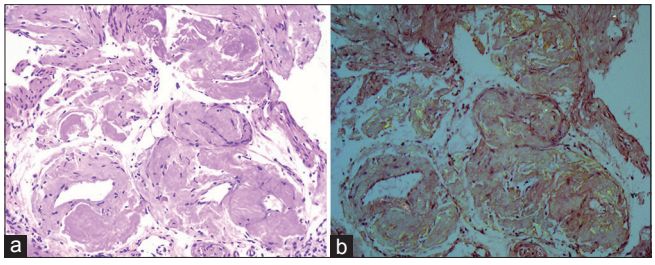

Figure 1: A biopsy of esophageal tissue at the esophagogastric junction. The section showed a picture of eosinophilic amorphous material deposited in the vascular walls and submucosa. (a) The amorphous material showed apple-green birefringence in Congo red staining in a polarization examination (b)

DISCUSSION

There are around 70%–90% of patients with SSc experience involvement of the esophagus, with the distal two-thirds being mostly affected by GERD, esophagitis, stricture, dysmotility, or Barrett's esophagus.[2] The histological lesions are similar to those in other organs affected by SSc, which are fibrotic in nature.[4] Our patient presented with the symptoms of GERD, and she was suspected of having SSc with gastrointestinal involvement initially.

Systemic amyloidosis is a syndrome of amyloid fibril extracellular deposition, which is a combination of more than thirty precursor proteins with a core structure of β strands and various nonfibrillary constituents including glycosaminoglycans and serum amyloid *P* (SAP).[5] The SAP component binds to all types of amyloid fibrils, and this combination of fibrils is resistant to proteolytic and phagocytosis.[6] The gold standard to identify amyloid deposition is Congo red staining with apple-green birefringence under cross-polarized light. Thioflavin T, thioflavin S, and other conformation-specific probes also stain amyloid proteins.[7] Amyloid light chain amyloidosis is a result of plasma cell dyscrasia-related monoclonal Ig light chain deposition and accounts for 68% of cases of amyloidosis, whereas amyloid A (AA) amyloidosis is secondary to inflammatory disorders and accounts for 12% of cases of amyloidosis.[5] The inflammatory properties and expression of cytokines, especially interleukin-6, induce the overproduction of serum AA in the liver.[8] Other types of amyloidosis including hereditary (amyloid transthyretin, fibrinogen A α-chain, apolipoprotein A1 amyloid, lysozyme amyloid, and gelsolin amyloid), long-term dialysis-related β2-microglobulin amyloid, and leukocyte cell-derived chemotaxin 2 amyloid.[5]

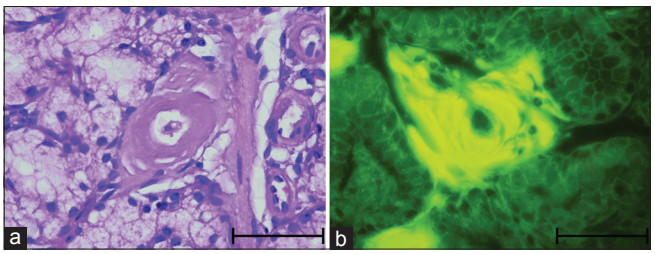

Figure 2: A duodenum biopsy showed amorphous pink material deposited over the perivascular area. (a) When stained with thioflavin S, the material presented with an apple-green color under a fluorescence microscope (b)

Table 1: Published case reports of amyloidosis with systemic sclerosis

Year	Underlying inflammatory disorder	Involved organ with amyloidosis	References (first author)
1985	Systemic sclerosis and lung carcinoma	Unknown	Focan
1989	Rheumatoid arthritis, progressive systemic sclerosis, and polymyositis	Unknown	Kumagai
1990	Systemic sclerosis and Sjogren's syndrome	Digestive canal, thyroid gland, heart muscles, lymph nodes, and small vessel wall of the whole body	Ito
1994	Progressive systemic sclerosis	Skin	Chanoki
1995	Systemic sclerosis	Skin	Azon-Masoliver
1998	Systemic lupus erythematosus and progressive systemic sclerosis	Stomach	Obata
2001	Progressive systemic sclerosis	Kidney	Pamuk
2011	Rheumatoid arthritis and systemic sclerosis	Heart	Wada

According to the disease course, our patient is most likely had AA amyloidosis resulted from chronic inflammation of SSc.

The treatment goal of AA amyloidosis is to control the underlying inflammatory disease. Several clinical trials have focused on SAP or SAA antibodies inducing macrophages to destroy the deposits.[9] Secondary amyloidosis patients require more aggressive treatment of the underlying inflammatory disease to achieve an SAA level of <4 mg/L.[5] We are currently unable to test for SAA, SAP, or perform SAP scintigraphy in our clinic. It is difficult to confirm the relationship between two diseases or is it just coincidence. We reviewed the reports of secondary amyloidosis in a patient with SSc [Table 1]. The SSc patient with gastrointestinal involvement suggests to receive esophagogastroduodenoscopy, and a biopsy may be helpful to these patients to examine the possibility of secondary amyloidosis. These patients need more aggressively disease activity control.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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