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Florence Nightingale

Case Report

Amyloidosis secondary to uncontrolled and untreated ankylosing spondylitis manifested by chronic diarrhea, sacroileitis, and chronic kidney disease

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ABSTRACT

Ankylosing spondylitis (AS) is one of the most common causes of secondary amyloidosis. Amyloidosis is a systemic disease, it may present with different symptoms and signs. The diagnosis of amyloidosis can be made with renal biopsy in patients who have proteinuria and regression in renal functions. Development of symptoms such as chronic diarrhea in patients which suggest gastrointestinal involvement, taking biopsy with endoscopy and colonoscopy imaging can again diagnose amyloidosis. The accumulation of amyloid in the organs may take time, so sometimes suspicious positivity may prolong the process for patients to be diagnosed with amyloidosis. We report the case of a 58-year-old male patient with long-standing AS, presenting with secondary amyloidosis, chronic diarrhea, proteinuria, and renal dysfunction.

Keywords: Amyloidosis, ankylosing spondylitis, chronic kidney disease.

Amyloidosis is characterized by the deposition of extracellular rigid, linear, and nonbranching fibrils in various tissues. In AA (secondary) amyloidosis, the amyloidogenic precursor is serum amyloid A (SAA), an acute phase reactant produced as a result of chronic infection or inflammation.[1] In other words, in AA amyloidosis, the deposited amyloid fibrils are the cleavage products of SAA. Systemic secondary amyloidosis may occur in patients with untreated or poorly controlled chronic inflammatory diseases such as spondyloarthropathies.[1,2] We present a case of secondary amyloidosis in a patient with long-standing untreated ankylosing spondylitis (AS).

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CASE REPORT

A 58-year-old male patient having a history of abdominal operation six years ago for gunshot injury, started complaining of shortness of breath and chronic diarrhea in 2016. Endoscopy and colonoscopy were performed for chronic diarrhea at that time. While macroscopic pathology was not detected in the biopsy of the patient, activity findings were observed in a very limited area in the sigmoid colon biopsy, and polymorphonuclear leukocytes were observed infiltrating only one crypt. In the patient who underwent both abdominal computed tomography and pelvic radiography (AP view), it was reported that bilateral sacroiliac joint distances narrowed and sclerosis increased in the faces adjacent to the joint, suspicious of sacroileitis. The patient, who developed complaints of whole-body pain and swelling in his feet, was examined by Rheumatology. The tests requested by Rheumatology were as follows: anti-cyclic citrullinated peptide immunoglobulin G (anti-CCP IgG) <1 U/mL, C-reactive protein (CRP) 18 mg/dL, rheumatoid factor (RF) 20.2 IU/mL, sedimentation 108 mm/h, Immunoglobulin panel is normal, antinuclear antibody (ANA)

negative. Spot urine protein creatinine ratio 662/125 mg/dL in the patient whose complete urinalysis revealed protein 2+. The patient with proteinuria at the nephrotic level was also evaluated by the Nephrology Department as a consultation. Creatinine 1.6 mg/dL, complement component 3 (C3) 98.4 mg/dL, C4 22.3 mg/dL, Albumin 2.8 g/dL, Globulin 3 g/dL, perinuclear antineutrophil cytoplasmic antibody (p-ANCA) and cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) negative, 24-h urine protein/creatinine 738/126 mg/dL 24-h urine volume was seen as 600 mL. In 2016, a renal biopsy was performed with the recommendation of Nephrology. Congo-red staining of the renal biopsy showed suspicious positivity for amyloidosis in the tubulointerstitial area.

Coronary artery disease and chronic obstructive pulmonary disease were diagnosed in 2019. Bilateral kidney dimensions of the patient, who was evaluated for chronic kidney failure in 2020, were normal in renal ultrasonography, and parenchyma echoes were found to be Grade 2 increased. In 2020, peritoneal dialysis treatment was initiated in the patient whose urea was 193 mg/dL and creatinine was 4.5 mg/dL. The patient, who was hospitalized with a complaint of chronic diarrhea in August 2020, was brought for a re-endoscopy, and a colonoscopy and rectal biopsy was taken. In the sections of the mucosal biopsy samples taken from the rectal, stomach, and colon, thickening of the walls of the vascular structures in the submucosa was observed in the narrow area. In the Congo-red histochemical stain applied to these areas, the presence of staining

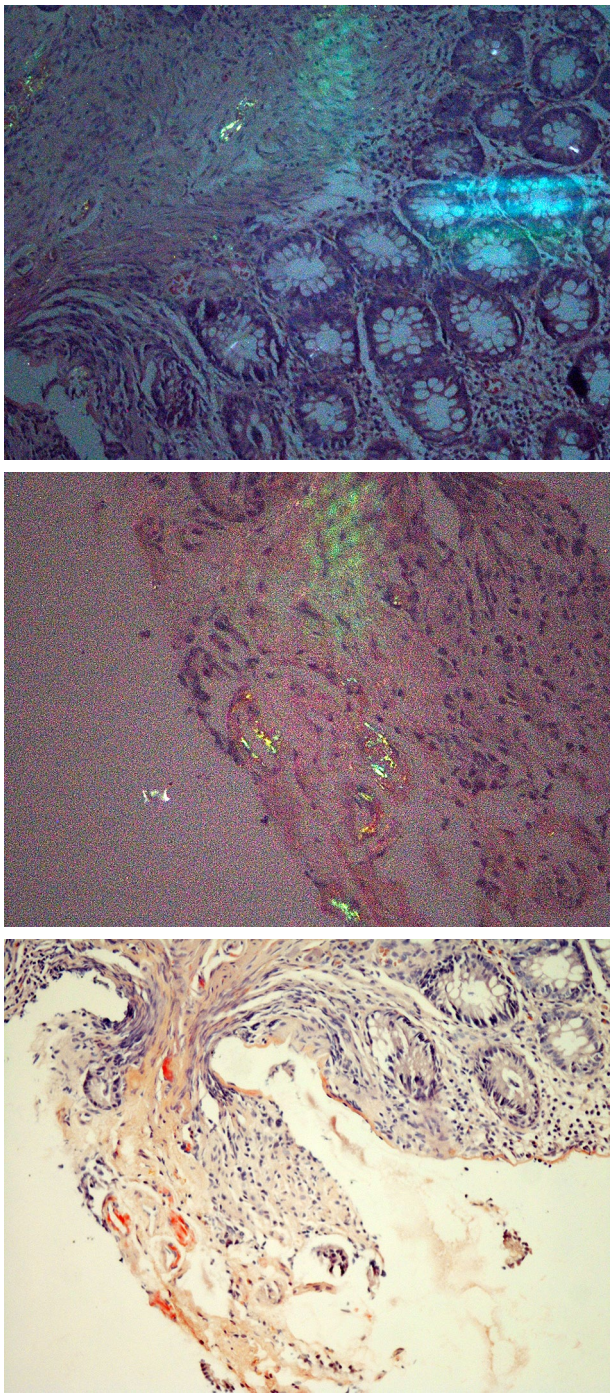

Figure 1. Thickening of the colon submucosal vessel walls, visible in polarized light in this area, apple-green birefringent deposits consistent with amyloid has drawn attention (Congo-red stain, ×400).

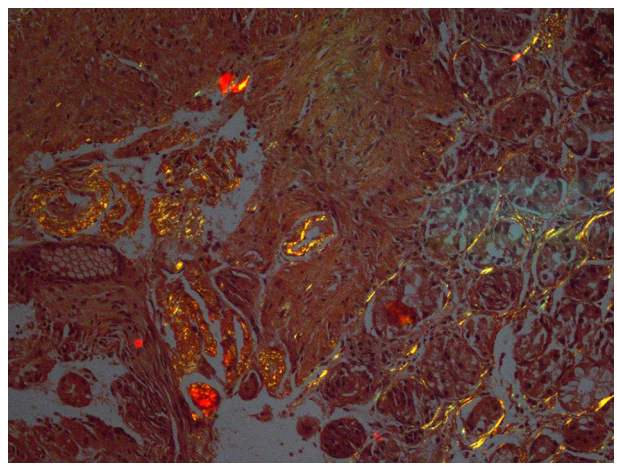

Figure 2. In the stomach oxyntic mucosal area, between glandular structures in the lamina propria and apple-green birefringence in polarized light in submucosal vessels. The presence of accumulation consistent with amyloid was noted (Congo-red stain, ×200).

consistent with amyloid deposition was noted (Figure 1 and 2). The patient was diagnosed with secondary amyloidosis. Cardiology noted that a typical granular form of amyloidosis wasn't detected in his heart. When the patient was evaluated in September 2020 by the Eye Clinic and Rheumatology, respectively, uveitis in the right eye and uncontrolled and untreated AS diagnoses were considered. In March 2021, an aortic valve replacement operation was performed on the patient whose echocardiography revealed left ventricular ejection fraction (LVEF) of 35-40%, apex and apical segments akinetic, second-degree mitral regurgitation, severe aortic regurgitation, and ascending aorta dilatation. A decision was made by Nephrology; peritoneal dialysis was aborted and started hemodialysis. The patient died due to septic shock and had a catheter infection in 2022.

DISCUSSION

Serum Amyloid A, which is an amyloidogenic precursor in secondary amyloidosis, is an acute phase reactant produced as a result of chronic infection or inflammation.[1,2] Persistently elevated SAA levels in the chronic process unless the inflammatory state is kept under control; it is deposited in the form of systemic amyloid fibrils and causes organ dysfunction. Early and timely diagnosis, appropriate medical interventions, and close follow-up to control chronic inflammation are vital to prevent morbidity and mortality due to the development of secondary amyloidosis. Considering the possibility that secondary AA amyloidosis may develop secondary to these conditions in patients with chronic uncontrolled inflammatory conditions is also important in anticipating and preventing undesirable results related to this disease.[2]

We report a case of systemic amyloidosis that presented with chronic diarrhea and shortness of breath in a patient with long-standing AS. In our case, documented extra-articular complications of long-standing AS included amyloid deposition in the gastrointestinal tract and possibly in the kidneys. In an undiagnosed, uncontrolled, and untreated patient with long-term AS, secondary AA amyloidosis should be among our primary differential diagnoses. In this clinical situation, some symptoms suggestive of amyloidosis may be weakness, weight loss, and especially diarrhea. In this case, from the relevant laboratory findings, proteinuria and high serum creatinine level (especially in the absence of nonsteroidal anti-inflammatory drug use) suggest possible renal involvement. Prominent clues for the diagnosis of secondary amyloidosis in our patient were proteinuria, elevated serum creatinine level, and the presence of chronic diarrhea.

As in our patient and previous case reports, the diagnosis often seems to be delayed. In presenting this patient, we would like to emphasize the need for careful clinical and laboratory evaluation, diagnosis, regular follow-up, and tailoring subsequent treatments, as well as being alert to amyloidosis and its impending morbidity and mortality. Overt amyloidosis is often referred to as a late complication of AS, as it has been reported in patients with active and long-standing AS disease.[3] On the other hand, secondary amyloidosis in our patient enabled the diagnosis of AS, which was the primary disease that had not been treated before. Since the clinical presentation in these patients is usually insidious, the diagnosis of secondary amyloidosis depends solely on consideration and suspicion of this diagnosis and performing relevant tissue biopsies.

There are limited reports in the literature of AS patients accompanying gastrointestinal system amyloidosis.[2-7] Amyloidosis leads to perivascular infiltration of the different layers of the intestinal wall, thereby resulting in impaired intestinal innervation or ischemia.[3,4]

Secondary amyloidosis may rarely seriously complicate AS.[2] As in our case, amyloidosis can affect more than one organ in the form of systemic deposition. It is of paramount importance to control the activity of the underlying chronic inflammatory disease. Initiation of therapeutics that block the effects of tumor necrosis factor-alpha in the early period of chronic disease may also change the clinical course of amyloidosis secondary to chronic inflammatory diseases. Tumor necrosis factor inhibitors reduce serum interleukin-6, thus lowering SAA levels and amyloid deposits decrease.[2,8]

In conclusion, chronic diarrhea, arthralgia, and swelling in body parts complaints tell us systemic symptoms of amyloidosis. Depositions

for amyloidosis may take years to show in biopsy. However, patients with systemic findings should be considered multidisciplinary. We must take patients to close follow-ups for taking precautions for amyloidosis complications.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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