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SECONDARY AMYLOIDOSIS TREATED WITH TOCILIZUMAB AS A COMPLICATION OF TEMPORAL ARTERITIS

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ABSTRACT

Background: Temporal arteritis is a large-vessel vasculitis mostly seen in the elderly. Amyloidosis may be secondary to a chronic inflammation of body organs. Here, we present the second case report of temporal arteritis complicated by amyloidosis that was successfully treated by tocilizumab.

Case presentation: A 64-year-old female presented complaining of fatigue, fever, and diarrhea accompanied by abdominal pain. One year before presentation, she was diagnosed with temporal arteritis. She was treated with 15 mg/day oral prednisone for the last 6 months, with partial remission, but persistence of the fatigue and an elevated erythrocyte sedimentation rate (ESR, 56 mm/h). Physical examination showed tenderness of both temporal arteries and a soft abdomen. Colon tissue biopsy showed amyloid depositions in the vessels and stroma that were positive for Congo red staining. Tocilizumab was started with 8 mg/kg intravenous, the diarrhea resolved, and the arthralgia improved within 1 month, with a decrease in the ESR to 8 mm/h, and a C-reactive protein (CRP) level of 0.98 mg/dl. Monthly tocilizumab therapy remains efficacious 12 months later and was stopped due to lack of tocilizumab from the hospital. No side effects of tocilizumab were registered.

Conclusion: Chronic inflammation may be complicated by amyloidosis in patients with rheumatic diseases and genetic predisposition. Therefore, it is important to screen for intestinal Amyloid A (AA) amyloidosis in individuals with gastrointestinal disorders complicated by rheumatic disorders. AA amyloidosis may be complicated by temporal arteritis and presented with gastrointestinal symptoms such as diarrhea.

KEYWORDS

Temporal arteritis, amyloidosis, vasculitis, tocilizumab, chronic inflammation

LEARNING POINTS

- Amyloidosis is manifested by the deposition of insoluble protein aggregates in organs.
- Amyloid A (AA) amyloidosis occurs as a complication of chronic inflammation in patients with a genetic predisposition to rheumatic diseases.
- Temporal arteritis complicated with AA amyloidosis is extremely rare.

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INTRODUCTION

Temporal arteritis (TA) is a systemic vasculitis of the large and medium arteries, frequently seen in the elderly[1]. Amyloidosis is manifested by the deposition of insoluble protein aggregates in organs[2]. The extracellular deposition of these aggregates derived from serum amyloid A (SAA) protein are characteristic of secondary (AA) amyloidosis[3]. SAA is an acute-phase reactant that stimulates inflammatory cytokines such as interleukins[2].

Chronic inflammation in people with rheumatic disease and a genetic predisposition may complicate amyloidosis[3,4], primary (AL) amyloidosis may present with different symptoms or signs, including edema, unexplained heart failure, nephrotic proteinuria, and hepatosplenomegaly[1,4], which are mimicked by other disorders. TA complicated with AA amyloidosis is extremely rare[4]. We describe a case of an elderly female with TA, that rapidly complicated with AA amyloidosis.

CASE DESCRIPTION

A 64-year-old female was admitted to the Modern Centre Hospital (Damascus) in January 2023, with fatigue, fever, and recurrent abdominal pain with diarrhea. One year before admission, she was diagnosed with TA, according to the 2022 American College of Rheumatology/European League Against Rheumatology (ACR/EULAR) classification criteria[5] in the presence of age >50, low-grade fever, fatigue, arthralgia with morning stiffness that lasts 2 hours, temporal artery tenderness, elevated erythrocyte sedimentation rate (ESR, 88 mm/h), C- reactive protein (CRP) 10 mg/dl. She was treated with 15 mg/day oral prednisone for the last 6 months, with partial remission, due to the persistence of the fatigue and elevated ESR (56 mm/h).

On admission, she presented with fatigue, morning stiffness, and four to six episodes daily of watery diarrhea. Physical examination showed TA tenderness on both sides and a soft abdomen.

Laboratory data showed a white blood cell count of 8,000/mm, hemoglobin of 9.3 g/dl, CRP of 38 mg/l (reference value <6 mg/l), and ESR of 83 mm/h (reference range <20 mm/h). Laboratory tests of liver function, calcium, thyroid function, uric acid, and renal function were normal. The immune profile of antinuclear antibody, rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibodies, hepatitis B panel, hepatitis C antibody, QuantiFERON-TB Gold test, and angiotensin-converting enzyme was negative. Urinalysis and stool examinations were normal. Blood and stool cultures were negative.

X-rays of the hands, wrists and chest were normal. Ultrasound revealed wall thickening of both TAs. Electrocardiogram and echocardiogram were normal. Brain magnetic resonance imaging (MRI) was normal. Abdominal computed tomography (CT) scan showed segmental wall thickening in the colon, without evidence of malignancy.

On day 7, the oral prednisolone was increased to 40 mg/day (0.5 mg/kg body weight). Fatigue and morning stiffness quickly improved, and inflammatory marker levels decreased. However, the diarrhea persisted. Lower gastrointestinal (GI) endoscopy was performed due to the persistence of diarrhea. Endoscopy showed chronic colitis with ulcers and mucosal atrophy *(Fig. 1)*. Histopathology of the colon tissue confirmed amyloid deposition in the stroma and vessels, shown as a pink amorphous material positive for Congo red staining *(Fig. 2)*, in addition to distorted crypt architecture with chronic colitis, and heavy infiltration of lymph-plasma cells. Circulating levels of SAA were 31.7 mg/dl (normal range: <3 mg/dl).

As prednisolone alone did not improve diarrhea caused by AA amyloidosis, intravenous (IV) tocilizumab was started with 8 mg/kg. The diarrhea resolved, and the arthralgia improved within 1 month, with a decrease in the ESR 18 mm/h, and CRP 0.98 mg/dl. Monthly tocilizumab therapy remains efficacious 12 months later but was stopped due to lack of tocilizumab from the hospital. There were no side effects due to its use.

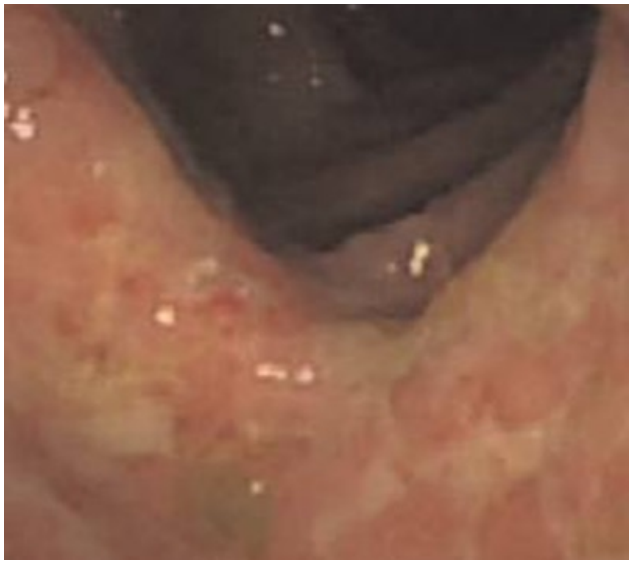

Figure 1. Mucosal atrophy and ulcers.

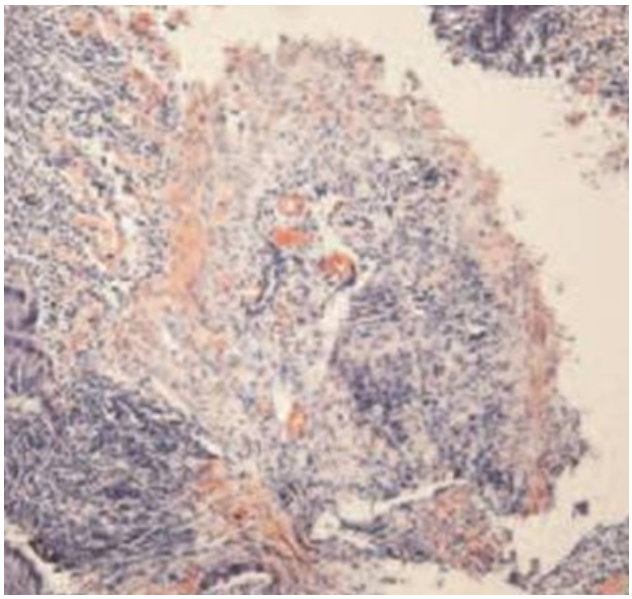

Figure 2. Deposition of amyloid A in colon tissue.

DISCUSSION

Chronic inflammation may be complicated by the occurrence of AA amyloidosis in patients with rheumatic disease and genetic predisposition[3]. In our case of an elderly patient with AA amyloidosis, as a complication of TA the persistence of chronic inflammations due to TA for 6 months was the primary trigger for AA amyloidosis. GI manifestations of amyloid deposition include malabsorption, abdominal pain, bleeding, diarrhea, constipation, steatorrhea, and pseudo-obstruction[6]. Thus, screening the intestinal AA amyloidosis, in individuals with rheumatic disorders, and GI symptoms is important[2].The severity and duration of the rheumatic diseases that are complicated by AA amyloidosis vary[4], but genetic factors may contribute to rapid development of AA amyloidosis[2]. The elderly over 70 years are more predisposed to develop AA amyloidosis after chronic inflammation persists for a few years[8]. Our patient is 64 years old. Controlling the underlying disease is an important treatment for secondary AA amyloidosis. Therefore, biological therapies such as tocilizumab are used to treat AA amyloidosis[9].

Interleukin 6 was reported to play a central role in the pathogenesis of AA amyloidosis[10], because it may result in the improvement of symptoms of AA amyloidosis, and normalize SAA levels in the majority of patients[9]. Glucocorticoid (GC) therapy is the main treatment of TA[10]. However, the percentage of relapses with glucocorticoid alone is high, so it is necessary to have other therapeutic options. Methotrexate can reduces the dose of GC, while tocilizumab is the first biological therapy taking approval for TA treatment, as it increases the remission rate, and the GC sparing effect, and has with a good safety profile[10]. Our patient had no side effects from using tocilizumab.

To the best of our knowledge this is the second case reported of a patient with TA and AA amyloidosis. Yoshida et al described an 80-year-old man with a history of new-onset TA with AA amyloidosis within 3 months, who was treated with tocilizumab and died because of intestinal perforation 1 month after treatment started[2].

CONCLUSION

This case suggests that AA amyloidosis may be complicated by TA, and presented with GI symptoms such as diarrhea, although the underlying mechanisms of this association are still unknown. Large studies are needed to investigate further and determine the best treatment.

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