

Secondary Renal

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Submission date: 07-Apr-2023 07:16PM (UTC+0700)

Submission ID: 2058337981

File name: Secondary_Renal.pdf (612.93K)

Word count: 2415

Character count: 13684

Secondary Renal Amyloidosis in Rheumatoid Arthritis Patient

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is one of systemic chronic progressive inflammatory disorders based on immunological disharmonies. Poorly controlled systemic inflammation in RA often leads to renal diseases such as secondary amyloidosis.

Case presentation: A 30-year-old man complained of swelling and tenderness of multiple joints gradually worsened the past 7 years. His laboratory examination showed anemia, positive rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA). C-reactive protein (CRP) was 48.7 mg/L (Normal value is <5 mg/L), increase in serum creatinine and protein was +3 in urine. His estimated glomerular filtration rate (e-GFR) was 58.3 mL/min/1.73 m². Radiologic examinations of joints revealed features that support the diagnosis of rheumatoid arthritis. Renal biopsy was done revealed amyloid deposit. He was diagnosed with rheumatoid arthritis and secondary renal amyloidosis.

Conclusion: Early proper diagnosis of RA is important and immunosuppressive drugs might slow disease progression by controlling the inflammatory process. We discussed the importance of early diagnosis and the use of better treatment in managing RA to prevent renal amyloidosis.

Keywords: rheumatoid arthritis, renal amyloidosis, early diagnosis

INTRODUCTION

Rheumatoid arthritis (RA) is a representative of collagen vascular diseases, a group of systemic chronic progressive inflammatory disorders based on immunological disharmonies. About 60% of all renal disease in RA was found to be subclinical and is detected only on laboratory investigations.¹ Previous study presented that elevated serum creatinine were found in 19% of RA patients (20% were in stage 2 and 15% were in stage 3 of CKD). Proteinuria, hematuria and leucocyturia were observed in 16%, 17% and 20% of the patients, respectively.^{2,3}

Despite many potential renal involvements in RA patients, data on the prevalence of renal disorders in RA are scanty. An autopsy data showed some causes of renal disease in RA are glomerulonephritis, amyloidosis, tubulointerstitial nephritis, and drug toxicity. Poorly controlled systemic inflammation in RA often leads to renal diseases such as mesangial proliferative glomerulonephritis (GN) or secondary amyloidosis.⁴ Some studies proposed immunosuppressive drugs might slow disease progression by controlling the inflammatory process, which underlined the importance of early proper diagnosis.⁵⁻⁷

Herein, we report a case of renal amyloidosis as an early systemic complication in seven years late-diagnosed RA patient.

CASE REPORT

A 30-year-old man complained of swelling and tenderness of multiple joints that gradually worsened the past seven years. He noticed morning stiffness lasting for about 60 minutes. In addition, he had episodes of low-grade fever, decrease in body weight and appetite. He had twice sought consult and was treated with non-steroidal anti inflammation drugs (NSAID) and steroid. He also tried herbal medications to relieve the joint pain however, he developed melena

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Figure 1. Clinical features: swollen and tenderness of bilateral knees, elbows, 1st-5th PIPs and MTPs joints.



Figure 2. Anteroposterior and lateral view of the radiology of bilateral knees showed narrowing the joints and erosion of sub-articular of epicondyle of both knees.

after taking those medications. The condition progressed and his mobility was limited to sitting up and confined in bed in the past three months prior. There was no similar illness known in his family. Physical examination revealed bilateral erythematous, tender and swollen elbows joints, wrist joints, 1st to 5th proximal interphalangeal (PIP) joints, knee joints, and 1st to 5th metatarsophalangeal (MTP) joints. His laboratory examination showed anemia, positive rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA). C-reactive protein (CRP) was 48.7 mg/L (Normal value is < 5 mg/L), serum creatinine was 1.57 mg/dL and protein were +3 in urine. His estimated glomerular filtration rate (e-GFR) was 58.3 mL/min/1.73 m².⁸ Laboratory in previous hospital was normal for CD4 and non-reactive for hepatitis B and hepatitis C. Chest X-ray showed no tuberculosis. Radiologic examination of the knees showed narrowing of the joints and erosion of sub-articular epicondyle in both knees which supported the diagnosis of rheumatoid arthritis. Renal biopsy was done, and histopathology revealed hyaline deposit in glomerular basement membrane tissue. He also underwent upper endoscopy which showed erosive gastropathy,

scarring ulcer at antrum, and pyloric deformity. He was diagnosed with rheumatoid arthritis and secondary renal amyloidosis. He got methylprednisolone 8 mg once daily, chloroquine 250 mg OD. Methotrexate was not available in our center at that time; therefore, tocilizumab was planned to be given. However, due to financial constraint, the patient got sulfasalazine 500 mg three times daily. Other medication were folic acid, paracetamol, omeprazole, and sucralfate syrup. After a year of follow up, our patient showed no increase of proteinuria, reduced swelling and tenderness of both knees and elbows.

DISCUSSION

Several chronic inflammatory disorders induce reactive systemic amyloidosis as one of the serious complications. Organ and tissue damage results from the extracellular aggregation of proteolytic fragments from serum amyloid A protein (SAA) as insoluble AA amyloid fibrils. AA amyloidosis occurs in association with chronic inflammatory disorders, chronic local or systemic microbial infections, and occasionally malignant neoplasia.⁹ In developing country, rheumatoid arthritis was also found to be the second most prevalent causes of renal amyloidosis after tuberculosis infection.¹⁰⁻¹² As reported in our case, we excluded tuberculosis as possible etiology.

Amyloidosis is a rare disorder with a variable clinical presentation. Early clinical manifestation, proteinuria (24-hour protein more than 0.5 g per day) with or without nephrotic syndrome was found to be the most common clinical finding of renal amyloidosis.¹³ Karstila *et al* assessed the frequency of abnormal clinical renal findings in a population of 103 RA patients. In those patients, 9% had isolated hematuria, 5% had isolated proteinuria, 1% had combined hematuria and

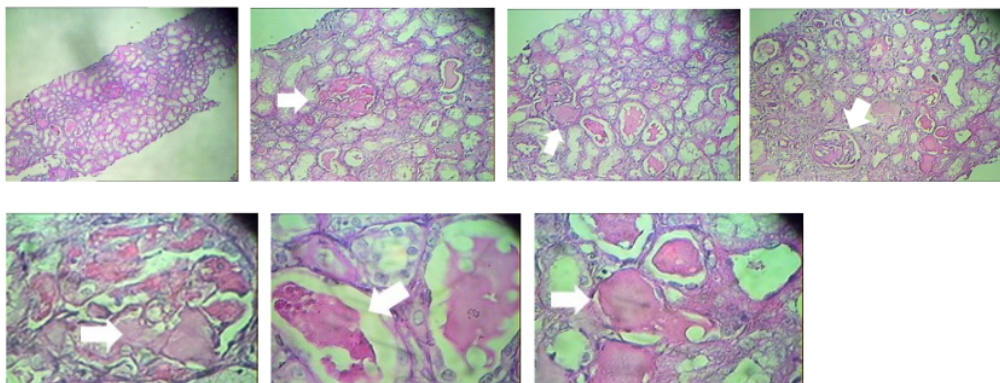


Figure 3. Photomicrograph of a kidney biopsy using hematoxylin-eosin staining demonstrating deposit of amyloid (arrow)
Approximate magnification: upper 100x, lower 400x.

proteinuria and 3% had isolated renal insufficiency [defined as a $\geq 100 \mu\text{mol/l}$ in women and $\geq 115 \mu\text{mol/l}$ in men]. Thus, heterogeneous renal lesions may complicate advanced RA even if they are not clinically apparent.¹⁴

Principal management in treating RA patients with AA amyloidosis is to suppress the underlying inflammatory process and therefore reducing the SAA production. Early diagnosis and the use of better treatment may reduce the incidence of renal amyloidosis.^{15,16} Previous study presented longer median time from the onset of RA until the detection of clinical amyloidosis by 16 to 19 years in the 1990s.¹⁷ Another study showed, clinical amyloidosis was detected after median time of 17 years of chronic inflammatory disease.¹⁸ In our case, the patient was diagnosis with RA after having the symptoms for seven years. Uncontrolled inflammation might play role in the faster development of renal amyloidosis. Unfortunately, no treatment modality has successfully demonstrated their ability in completely reducing amyloid deposits. Corticosteroids, one of the drugs in our patient, are thought to reduce acute phase reaction including synthesis of CRP and SAA. Some studies suggested treating secondary amyloidosis in RA patients using combination of disease-modifying anti-rheumatic drugs (DMARDs) and low dose corticosteroid control of inflammatory reactions.^{6,16,19,20} It is suggested that the use of immunosuppressive agents can improve prognosis.²¹ However, it should be noted that some DMARDs, such as cyclosporine, gold, and D-penicillamine might have serious renal side effects especially in the concomitant use with NSAID.¹¹ Methotrexate has pleiotropic therapeutic effects on various immune cells and mediators, resulting in an overall dampening of the inflammatory response. However, due to unavailability of MTX in the case, our patient received sulfasalazine 500 mg three times daily as RA management.²² Biologic agents, as reported in some studies, might be a more beneficial treatment modality, but it was not available yet in our national health insurance program at that time.^{16,23,24}

A previous study reported that the median survival of secondary amyloidosis patients was about 63 months

and 5 years survival rates were 50 to 80.7%. Higher serum creatinine and massive proteinuria were several predictors of mortality.²⁵ Our patient had unquantified proteinuria and close monitoring should be done in order to prevent progression to end stage renal disease or the need for dialysis in order to give our patient better prognosis and quality of life.

CONCLUSION

Uncontrolled chronic inflammation showed faster onset of secondary amyloidosis. Both proper RA diagnosis in patient having multiple joints inflammation and early detection of renal amyloidosis complication is needed in order to prevent the progression of end stage renal disease and the future need of renal dialysis.

Disclosure

The authors did not receive any funding and have no conflicts of interest in conducting this study.

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