Seropositivity of Rheumatoid Arthritis Specific Tests in a Patient With Nephrotic Syndrome

Successful Treatment With Rituximab

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Presentation of rheumatoid arthritis (RA) with renal complications is very rare without articular symptoms. We here report a case of a 23-year-old woman, presenting with the edema of the extremities, no relevant previous medical history, and the features of acute tubular injury in her percutaneous kidney biopsy. Following the incidental notification of a positive rheumatoid factor test, other immunologic tests including anticyclic citrullinated peptide and antimutated citrullinated vimentin were performed, the positive results of which favored the diagnosis of RA. Administration of rituximab led to the complete remission of the disease. Six weeks later, along with steroid dose reduction, the symptoms of arthralgia was observed, which was managed with methotrexate. Nephrotic syndrome could be rarely the first manifestation of RA, and screening of specific RA autoantibodies might be considered as part of diagnostic evaluations in nephrotic syndrome workup.

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Case Report

INTRODUCTION

Kidney disorders are a frequent cause of death in patients with longstanding rheumatoid arthritis (RA). A study of kidney biopsy specimens indicated that mesangial glomerulonephritis is the predominant histopathologic finding in RA, followed by amyloidosis, membranous nephropathy, focal proliferative glomerulonephritis, minimal change nephropathy, and acute interstitial nephritis.[1] Nevertheless, presentation of RA with renal involvement is very rare without articular symptoms. Here we report a rare case of a young woman initially presented with nephrotic syndrome and was strongly positive for specific autoantibodies, favoring an RA diagnosis, in the absences of any articular symptoms.

CASE REPORT

A 23-year-old woman with no relevant previous medical history was referred to our center, presenting with edema of the extremities and high blood pressure from 12 days earlier. No joint or mucocutaneous symptom was declared by patient. Physical examinations were completely normal except for the presence of leg swelling. The laboratory tests demonstrated normal complete blood count, elevated erythrocyte sedimentation rate (80 mm/h) and serum creatinine (1.6 mg/dL). The 24-hour urine protein test revealed 9 g/d of proteinuria. Urinary sedimentation was blunt. Immunologic tests including rheumatoid factor, anticyclic citrullinated peptide and antimutated citrullinated vimentin were positive. All other laboratory tests were negative.

In percutaneous renal biopsy, the tubules showed features of acute tubular necrosis, which could be responsible for increased serum creatinine level. No crescent, adhesion, or fibrin was seen in the Bowman space. Altogether, the changes favored minimal change nephritic disease.

During admission, her serum creatinine increased to 5 mg/dL that was caused by acute tubular necrosis. Consequently, more aggressive treatment was substituted, using 3 days of methylprednisoslone pulse therapy (1 g/d), followed by 60 mg/d of oral prednisolone and 2 g/d of mycophenolate mofetil. However, mycophenolate mofetil was stopped due to the development of diarrhea, which was considered as its side effect. Subsequently, steroid side effects including Cushingoid appearance, purple striae, acnea, and high blood glucose were observed, along with no improvement in the edema. Serum creatinine did not decrease and proteinuria increased to 11 g/24 h.

Since the patient was nullipar and cyclophsphamid was not a choice, 500 mg/wk of rituximab was started on for 4 weeks, instead. After 3 weeks, serum creatinine dropped to 0.9 mg/dL and 24-hour urine protein dropped to less than 1 g. The patient's blood pressure returned back to normal. The treatment was continued with hydroxycholoroqine sulfate and 15 mg/d of prednisolone. The patient was discharged home with prednisolone tapering. In the follow-up visit, on week 6, along with steroid dose reduction to 10 mg/d, the patient complaint of morning stiffness and arthralgia of the hands and feet's small joints. At this point, considering the normal serum creatinine level of the patient and high titers of anticyclic citrullinated peptide and antimutated citrullinated vimentin, methotrexate was added to the treatment regimen at a dose of 7.5 mg/wk. The arthralgia was completely improved. In the latest follow-up visit, 6 months after the start of methotrexate, the patient was still receiving 7.5 mg/wk of methotrexate and 5 mg/d of prednisolone, and the disease was in complete remission.

DISCUSSION

Initial presentation of RA with extracellular manifestation is very rare. Short and coworkers reported the first and only case of RA presenting as nephritic syndrome in 1988. According to their report, a 62-year-old man with nephrotic syndrome and no past medical history coincidently turned out to have high titers of rheumatoid factor, while some months later, articular manifestation of RA appeared.[2] We also accidently noticed a positive rheumatoid factor test in a 23-year-old woman referred with renal manifestations, including edema of the extremities, proteinuria, and increased serum creatinine. Ruling out other connective tissue disorders, plus further complementary positive tests, including anticyclic citrullinated peptide and antimutated citrullinated vimentin, was highly suggestive of RA in spite of no arthritis and arthralgia.[3] Similar to Short and coworkers' study, our patient developed articular manifestation later in the disease course.[2] This manifestation is probably triggered by the prednisolone tapering.

Arthralgia is also regarded as a rare side effect of rituximab. However, occurrence of joint pain 6 weeks after the administration of rituximab reduces the possibility of rituximab-related arthralgia. Nonetheless, this possibility should be noted in similar cases. Successful management of renal manifestations of RA by rituximab seems promising.[4]

CONFLICT OF INTEREST

None declared.

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