To the Editor: Tumor necrosis factor-α (TNF-α) is a pro-inflammatory cytokine that plays a crucial role in the pathogenesis of rheumatoid arthritis (RA), while the advent of anti-TNF-α agents brings better control and low side effects in RA. The most frequent side effects are infectious disease and drug-induced lupus. Herein, we present a case of Chinese man with a 10-year history of RA developing crescentic immunoglobulin A (IgA) nephritis and multiple autoantibodies during adalimumab treatment.

A 62-year-old Chinese man was admitted for new occurrence of hematuria and proteinuria for 20 days. He had a 10-year history of RA diagnosed according to the American College of Rheumatology Criteria.[1] Thereafter, a low dose of prednisone, oral methotrexate (15 mg/week) and intermittent administration of nonsteroidal anti-inflammatory drugs (NSAIDs) were initiated. Because of tenderness of multiple joints and new occurrence of rheumatoid nodules on the left knee on 16 February 2014, and erythrocyte sedimentation rate (ESR) increased to 70 mm/h and C-reactive protein (CRP) 16.3 mg/L, with a high disease activity score for 28 joints (DAS28) scored 5.44, adalimumab (40 mg subcutaneous every other week) was initiated. Antinuclear antibody (ANA) and antineutrophil cytoplasmic antibody (ANCA) were not detected, and renal parameters were normal before adalimumab treatment. After four doses of adalimumab therapy (2 months later), rheumatoid nodules resolved and ESR decreased to 13 mm/h, CRP was 1.7 mg/L, and DAS28 scored 2.0 suggestive of clinical remission; however, he presented with hematuria, proteinuria and oliguria.

On admission, bilateral pitting edema was found in the lower extremities. His hands showed deformities. Laboratory findings showed elevated white blood cell count, 15.72 × 10⁹/L (normal range: 4.0–10.0 × 10⁹/L); hemoglobin, 90 g/L (120–160); platelets, 232 × 10⁹/L (normal range: 100–300 × 10⁹/L); serum urea nitrogen, 31.84 mmol/L (normal range: 1.07–7.14 mmol/L); serum creatinine (Cr), 249 μmol/L (normal range: 0.7–4.0 g/L); C3 complement fraction, 0.585 g/L (normal range: 0.7–4.0 g/L); IgG, IgM and C4 complement fraction values were normal. Hepatitis B surface antigen, hepatitis C virus antibody, human immunodeficiency virus antibody and anti-streptolysin O test were all negative. Computed tomography scan of chest and abdomen showed no evidence of pulmonary vasculitis and solid tumor. Renal ultrasound showed 10.8 cm of right kidney, 11.7 cm of left kidney. Renal biopsy was performed. The specimen [Figure 1a and b] showed 21 glomeruli, with 9 globally sclerosed glomerulus. It showed proliferation of mesangial cells and matrix and 11 active cellular crescents were observed. There were red blood cell casts and lymphocytic infiltrates in the interstitium. On immunofluorescence (IF) examination [Figure 1c], IgA deposits of strong intensity and C3, κ and λ light chain deposits of weak intensity were detected in the mesangium. IF stainings for IgG, IgM, C4, C1q and fibrinogen were all negative. On electron microscopic examination, electron-dense deposits of high density were detected in the mesangium. Accordingly, crescentic IgA nephritis was diagnosed.

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A previous report\(^1\) showed that renal damage could resolve completely or partially after anti-TNF agent withdrawal and subsequent use of immunosuppressants. Why did our case progress to end-stage renal disease? In our opinion, the co-existence of multiple autoantibodies including ANA, ACL antibody, and ANCA may prompt the immune complex deposition and activate complement unlike the reported cases before. In addition, the infectious complications might contribute to the deterioration of renal function through mechanisms such as molecular mimicry or epitope spreading\(^4\) which could promote autoimmune reactions.

Taken together, we suggest that RA patients especially those with high risk of developing renal disorders be prescribed anti-TNF agents cautiously, and baseline of ANA, anti-dsDNA and ANCA should be screened and renal parameters be monitored closely during anti-TNF agent therapy. Once glomerulonephritis occurs, withdrawal of anti-TNF agents is recommended, and corticosteroid and/or immunosuppressants might be used according to clinical manifestations and kidney biopsy findings.

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Conflicts of interest
There are no conflicts of interest.

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