First report of membranous nephropathy and systemic lupus erythematosus associated with abatacept in rheumatoid arthritis

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Abatacept is a soluble fusion protein that consists of the extracellular domain of human CTLA-4 linked to IgG1, which selectively modulates the CD80/CD86:CD28 costimulatory signal.

Treatment with abatacept is efficacious in patients with rheumatoid arthritis (RA) (1) and overlap syndrome between RA and systemic lupus erythematosus (SLE) (2). Moreover, abatacept has been explored for its efficacy in lupus nephritis and primary glomerulonephritis (3, 4). However, here we described the first case of a patient with RA who developed membranous nephropathy (MN) and SLE after treatment with abatacept.

A 60-year-old Asian woman with an 11-year history of disabling seropositive RA had been previously unsuccessfully treated with bucillamin and sulfasalazine. She also had Sjögren’s syndrome (SS) and primary biliary cirrhosis (PBC), but was on a stable course. Other past history included type 2 diabetes mellitus, bronchiolitis and lumbar canal stenosis. She also had a prior infection with human hepatitis B virus (HBV), but HBV-DNA in sera repeatedly tested negative.

At the age of 59, abatacept was started with informed consent of the patient. At the start of abatacept treatment, ANA titer was 80 IU/ml (normal <50 IU/ml). At month 6, she achieved a moderate response according to EULAR response criteria, nevertheless she still complained of RA symptoms, in which DAS28-ESR was high at 5.31.

After 7 months of abatacept therapy, she exhibited general fatigue and proteinuria. Even after discontinuation of abatacept, she developed significant proteinuria, hypoaalbuminemia, and oedema. She was admitted to our hospital with the diagnosis of nephrotic syndrome.

Laboratory investigations showed the following: ESR of >160 mm/h, lymphopenia, normocytic anemia (Hb 10.6 mg/dl) without autoimmune haemolytic anaemia, elevated CRP (4.44 mg/dl, normal: 0.0-0.3), and low complement levels; urinalysis 4+, hyaline casts, granular casts, waxy casts, no growth; 24 h urine total protein 12.58 g/day for 3 days) with moderate-dose prednisolone (0.5 mg/kg/day) therapy, her proteinuria and other laboratory data, such as low complement levels and lymphopenia improved. The antibodies to dsDNA also disappeared.

She underwent renal biopsy before prednisone treatment, which revealed subepithelial and subendothelial immune deposits on the glomerular basement membrane (GBM) with GBM thickening (Fig. 1A and B). However, immunofluorescence analysis showed only the immune deposits of IgM and IgA, but without IgG, C3c, and C1q. The results were incompatible with lupus nephritis but supported other secondary MN due to comorbidity. Abatacept is generally well tolerated with rare adverse events such as lupus-like syndrome and glomerulonephritis in RA (1). To our knowledge, abatacept might induce mesangial IgA glomerulonephritis in patients with RA (5).

In that case report, abatacept was switched after secondary failure of TNF inhibitors, which might be related with disease progression in IgA glomerulonephritis, whereas our patient is bio-naive RA patient except for abatacept.

Although our patient is characterised by additional complications, such as SS and PBC, which might be associated with secondary MN (6), we found the only efficacy of abatacept in SS (7). According to BCP, the therapeutic effect of CTLA4-Ig was also reported on a murine model (8).

Since a similar case has never been demonstrated before, it is unclear which factor accelerated lupus syndrome and MN in RA. Hence physicians should exercise caution, paying attention to any symptoms associated with SLE and MN during the course of treatment when using abatacept to treat RA patients.

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References