Belatacept as Maintenance Immunosuppression in Patients with Thrombotic Microangiopathy and a Kidney Transplant

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Abstract

Two patients with end-stage renal disease secondary to thrombotic microangiopathy received a kidney transplant and were treated with belatacept as maintenance immunosuppression. After 12 and five months, respectively, there was no evidence of recurrence of thrombotic microangiopathy and renal function was normal. **(Trends in Transplant. 2013;7:56-8)**

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Key words

Belatacept. Thrombotic microangiopathy. Renal transplantation.

Introduction

Hemolytic uremic syndrome (HUS) frequently recurs after renal transplantation, and although the risk is lower in patients without mutations in genes encoding complement regulatory proteins and secondary disorders of complement regulation, the most commonly used immunosuppressive drugs, calcineurin inhibitors (tacrolimus or cyclosporine), can be associated with posttransplant thrombotic microangiopathy (TMA)[1]. Cases of HUS after transplantation have also been reported with proliferation signal inhibitors[2].

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Belatacept is a new immunosuppresor that induces costimulation blockade and has shown good results in TMA after kidney transplantation[3,4].

We present two cases of end-stage renal disease (ESRD) secondary to TMA. The patients received a kidney transplant and were treated with belatacept as maintenance immunosuppression.

Materials and methods

Case 1

In August 2008, a 51-year-old woman presented with acute renal failure due to HUS and progressive ESRD despite plasmapheresis and fresh frozen plasma. The patient had factor V Leiden. There were no precipitating clinical factors (or drug treatment) of HUS.

Activity of ADAMTS13 was not assayed. Biochemical and genetic studies discarded genetic susceptibility to TMA, although abnormal regulation of the alternative complement pathway was observed. Forty-two months later she received a kidney transplant from a 59-year-old deceased donor. Pretransplant cytotoxic antibodies were negative. Epstein-Barr virus (EBV) IgG antibodies were positive.

Case 2

A 36-year-old woman was admitted in December 2010 with HUS and urinary tract infection. *Escherichia coli* was cultured in blood and urine (but not strain O157-H7). She was taking oral contraceptives and had a 10-year history of multiple sclerosis, treated with interferon beta. Despite treatment with antibiotics, steroids, plasmapheresis, and fresh frozen plasma she developed ESRD. Oral contraceptives were discontinued. Three months later she presented with decreased consciousness, seizures, and hematologic disorders compatible with HUS. Treatment with plasmapheresis and fresh frozen plasma was commenced. Interferon beta was discontinued and glatiramer acetate started. Molecular genetic study revealed no mutations in genes related with TMA. In September 2012 she received a kidney transplant from a 48-year-old deceased donor. The EBV IgG antibodies were positive.

Both patients received immunosuppression with steroids, mycophenolate mofetil, thymoglobulin 1 mg/kg (seven doses) and belatacept 10 mg/kg (day 8 and weeks 3, 5, and 9) and then 5 mg/kg every four weeks indefinitely. Two sessions of plasma exchange (pretransplant and 24 hours posttransplant) were performed.

Results

Both patients had immediate posttransplant renal function. The follow-up times were 12 and five months, respectively. No episodes of acute rejection were experienced and there was no evidence of recurrence of TMA. Both currently have renal function with serum creatinine 1.04 and 1.24 mg/dl. Proteinuria is negative in Case 1 and 1 gr/24 hours in Case 2. Neither patient has experienced any important adverse effects secondary to the medication.

Discussion

The rate of recurrence of HUS after transplantation varies, but when it happens it is a serious situation both for the patient's life and the survival of the graft. An exhaustive study of complement factors and a genetic study to detect mutations of complement factors is mandatory to discern the risk of recurrence and indication for isolated kidney transplantation or combined liver and kidney transplantation[5,6].

When there is no clear etiological agent, as in our two patients, the risk of HUS is more difficult to predict, but it can be triggered by more than one stimulus as in the case of Patient 2, who presented two episodes, one probably triggered by *E. coli* infection and/or oral contraceptives, and the second associated with interferon beta, as has been described[7]. These patients must therefore avoid anything that might trigger TMA. As both calcineurin inhibitors[1] and proliferation signal inhibitors[2] have been associated with the development of posttransplant TMA, they should be avoided.

Belatacept is an immunosuppressive drug that blocks the interaction between CD80/86 and CD 28 and has not yet been associated with HUS. We decided to use

thymoglobulin induction, given the good preliminary results[8], instead of combined with basiliximab, for which higher acute rejection rates have been described[9]. Two plasma exchange sessions (pretransplant and 24 hours later) were performed, as recommended[6]. The time between renal transplantation and recurrence of HUS varies, but it usually occurs in the first months[10].

We can conclude that in renal transplant recipients, maintenance immunosuppression with belatacept may be appropriate for patients with TMA as a cause of ESRD. The short-term results are excellent and there appears to be good tolerance.

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