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LETTER TO THE EDITORS

Belatacept in recurrent focal segmental glomerulosclerosis after kidney transplantation

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Dear Sir,

Recurrence of primary focal segmental glomerulosclerosis (FSGS) occurs in approximately 40% of patients after kidney transplantation and no efficient treatment exists as yet [1]. Recently, Yu *et al.* [2] have shown that five patients with recurrent FSGS after kidney transplantation were successfully treated with only one or two doses of abatacept, a B7-1 blocker. Herein, we report the outcome of five kidney transplant patients who were given long-term treatment with belatacept, a B7-1 blocker that binds approximately fourfold more avidly to CD86 and approximately twofold more avidly to CD80 than abatacept, for the recurrence of FSGS.

Five kidney transplant patients experienced recurrence of FSGS within the first week after transplantation. Two were undergoing a second transplant and had lost their first kidney allograft from FSGS recurrence. At transplantation, all patients had received a prophylactic protocol for FSGS recurrence that included plasmapheresis or immunoadsorption before transplantation, rituximab (375 mg/m^2 before transplantation and at 1 week later), and intravenous cyclosporine A was started at least 12 h before transplantation if it was a deceased donor and 1 week before transplantation in cases of living donation. Cyclosporine A therapy was continued for 10 days after transplantation (target circulating level 250–300 ng/ml) for all patients (Table 1).

After FSGS had recurred, four were treated by plasmapheresis or immunoadsorption, three with rituximab, four with galactose, and all received full-dose angiotensin-converting enzyme inhibitors (ACEi). Because of persistent heavy proteinuria, these therapies (except for ACEi) were stopped and belatacept was started. In the fifth patient, recurrence of FSGS was mild and belatacept was immediately started without using any of the other therapies. As has been previously reported [3], belatacept was given at the dose of 5 mg/kg on days 0, 15, and 30, and then monthly. All patients were also given mycophenolic acid (1 g/day) and steroids (5 mg/day). In addition, three patients, who were highly sensitized, were given low-dose tacrolimus (target trough level 3–5 ng/ml). None of these patients presented with antibody-mediated rejection (AMR) before the initiation of belatacept.

Kidney biopsies that were performed before the initiation of belatacept showed features of FSGS in four patients without any signs of AMR. B7-1 immunostaining was found to be negative in all patients.

After a median follow-up of 11 (6–12) months, the urinary albumin-to-creatinine ratio was slightly decreased in two patients. It remained stable in another patient. Kidney function declined in the two other patients and both had to restart dialysis at 6 and 12 months after having started belatacept. No adverse events or acute rejection episodes were observed during belatacept therapy.

In contrast to the study by Yu *et al.* [2], but similar to the report by Alachkar *et al.* [4] who treated five kidney transplant patients with FSGS recurrence with B7-1 blockers as well as a recent pediatric case series [5], we found that treating kidney transplant patients with FSGS recurrence with belatacept was unsuccessful: mainly in those patients with heavy proteinuria that already had severe histological injuries. Further studies are required to assess the efficacy to B7-1 blockers in the setting of post-transplant FSGS recurrence.

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Conflict of interest

No conflicts of interest exist.

Table 1. Description of kidney transplant patients treated with belatacept for recurrent focal segmental glomerulosclerosis.

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	63	51	50	39	24
Gender	Male	Woman	Male	Male	Male
Donor	Deceased	Living related	Deceased	Deceased	Living related
Rank of transplantation	1	1	2	1	2
DSA at transplantation	No	Yes	Yes	No	Yes
Prophylactic treatment	PP/R/IV CsA/RATG	PP/IA*/R/IV CsA/RATG	PP/R/IV CsA/RATG	R/IVCsA/RATG	IA*/R/IV CsA/RATG/ IVIg
Maintenance immunosuppression	Tac/MPA/S	Tac/AZA/S	Tac/MPA/S	Tac/MPA/S	Tac/MPA/S
Treatment of recurrence FSGS	PP/R/Galactose	IA/R/ Galactose	PP/Galactose	–	PP/R/Galactose
Time between transplantation and belatacept initiation (months)	9	18	8	4	40
Time between belatacept initiation and last follow-up (months)	9	12	12	11	6
Histological findings before starting belatacept	FSGS (mild histological lesions) Negative C4d staining Negative B7-1 staining†	FSGS (severe histological lesions) Negative C4d staining Negative B7-1 staining†	FSGS (mild histological lesions) Negative C4d staining Negative B7-1 staining†	Normal biopsy‡ Negative C4d staining Negative B7-1 staining†	FSGS (severe histological lesions) Negative C4d staining Negative B7-1 staining†
Anti-proteinuric agents at belatacept initiation/last follow-up	Ramipril (7.5 mg/ day)/Irbesartan (150 mg/day)	Irbesartan (150 mg/ day)/–	Irbesartan (300 mg/ day)/Irbesartan (300 mg/day)	Perindopril (5 mg/ day)/Perindopril (10 mg/day)	Irbesartan (300 mg/ day) + Perindopril (10 mg/day)/–
GFR§ at belatacept initiation/last follow-up (mL min/1.73 m^2)	32/32	15/Dialysis	48/47	67/69	24/Dialysis
Urinary albumin to creatinine ratio at belatacept initiation/last follow-up (mg/g)	4453/2000	6230/5300¶	2246/1400	1056/813	7068/5000§
Outcome	Partial responder	Non responder	Partial responder	Stable	Non responder

PP, plasmapheresis; R, rituximab; IV CsA, intravenous cyclosporine A; RATG, rabbit anti-thymoglobulins; IVIg, intravenous immunoglobulins; Tac, tacrolimus; MPA, mycophenolic acid; AZA, azathioprine; S, steroids; GFR, glomerular-filtration rate.
*Patients 2 and 5 had undergone 10 immunoadsorption sessions before transplantation because they were included in a desensitization protocol.
†B7- 1 staining was done using the Mouse B7-1/CD80 Affinity Purified Polyclonal Ab, Goat IgG AF740, R&D Systems Europe, Lille, France.
‡No histological features of focal segmental glomerulosclerosis (FSGS) by light microscopy. However, no electronic microscopy was performed.
§GFR was determined using the MDRD equation.
¶At the initiation of dialysis.

References

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