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The Long-Term Prognosis of Renal Transplant in Patients With Systemic Vasculitis

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Little information is available about the long-term outcome of renal transplantation in patients with systemic vasculitis (SV). We compared the outcomes of 19 renal transplant recipients with SV with those of 38 controls matched for time of transplantation, age, gender and source of donor. The mean post-transplant follow-up was 58 ± 57 months for vasculitic patients and 61 ± 49 months for controls. The actuarial 10-year patient survival was 87% in vasculitic patients and 90% in controls, death-censored graft survival were 84% and 100%, respectively. The risks of acute and chronic rejection, and arterial hypertension were not significantly different between the two groups. Infection was significantly more frequent in vasculitic patients (74% vs. 34%; p = 0.01). Seven patients (36.8%) had a recurrence of vasculitis in mean 45 months after renal transplant (0.076/patients/year). After recurrence, one patient had an irreversible humoral rejection, another died from hemophagocytosis and another restarted dialysis 1 year later. Long-term patient and renal allograft survival in vasculitic patients was good. Although graft function recovered in most relapsers after reinforcement of immunosuppression, one patient died and two lost graft function.

Key words: Necrotizing glomerulonephritis, renal transplant, systemic vasculitis

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Introduction

A number of case reports or small-sized studies have reported the outcome (1–10) and only a few studies the long-term outcome (3,11,12) of renal transplant recipients with systemic vasculitis (SV). The UNOS registry reported a 3-year graft survival rate of 78% for deceased donor transplants and 84% for living donor transplants in 114 renal transplant recipients with Wegener granulomatosis (13). These data are similar to the 70% graft survival at 3 years reported by the ERA-EDTA registry on 115 patients (14). The Collaborative Transplant Study (15) reported in the form of an abstract a 10-year patient survival of 80% and a graft survival of 65% for renal transplant recipients with Wegener granulomatosis. However, these registries did not provide any information about the complications, the rate of relapses of the original disease and the causes of death or graft failure. Only few data are available on post-transplant polyangiitis (6,11).

The aims of this single-center analysis were (i) to compare the long-term patient and renal allograft survival of patients transplanted because of SV with those of well-matched controls, (ii) to compare the long-term complications in these two groups of patients and (iii) to assess the rate and the outcome of recurrence in renal transplant recipients with SV.

Methods

Patients

Adults (>18 years) with SV who received a kidney transplantation at Ospedale Maggiore of Milan between December 1987, when the first renal transplant in a patient with SV was performed, and January 2006 were admitted to the study. The diagnosis of SV had to match the 'Chapel Hill Consensus Conference' on SV (16). The diagnosis of SV was based on clinical and serological criteria as well as on renal biopsy. All SV patients were Caucasian.

Renal allograft recipients transplanted immediately before and after SV patients, matched for age (±5 years), gender and source of the donor (deceased or living) were considered as controls. None of the 38 control patients showed any clinical or lab signs of SV. Seven patients were carriers of autosomal dominant polycystic kidney disease, 6 had congenital urinary tract abnormalities, 15 had biopsy-proven glomerulonephritis (IgA nephropathy 13 patients, membranoproliferative glomerulonephritis 1, lupus nephritis 1), 2 had hypertensive nephrosclerosis, 2 had chronic pyelonephritis, 1 post-partum bilateral cortical necrosis and 4 patients had renal failure of unknown origin. All controls were Caucasian.

Definitions

Acute rejection was diagnosed on the basis of a double-checked increase of 20% or more in plasma creatinine over the baseline, not explained by causes other than rejection and confirmed by the response to anti-rejection

therapy. Proteinuria of more than 0.5 g/day, and/or persistent hematuria or cellular casts at the urinary sediment gave weight to the diagnosis. In 75% of the cases, rejecting patients received a graft biopsy that confirmed the diagnosis. Renal biopsies were evaluated by light microscopy and immunofluorescence. Electron microscopy was performed in doubtful cases. For the aims of this study the severity of rejection and the classification of chronic histological lesions were scored retrospectively according to the recently revised Banff classification (17). Unspecific sclerosing lesions were defined by the presence of interstitial fibrosis with tubular atrophy, glomerular and arteriolar sclerosis, without evidence of any specific etiology. Chronic rejection was defined by the presence of chronic allograft artheriopathy and/or chronic transplant glomerulopathy.

Acute cellular rejections were treated with intravenous methylprednisolone pulse therapy; acute vascular rejections were treated with anti-thymocyte globulins.

Anti-neuthrophil cytoplasmic antibodies (ANCA) were detected by enzyme-linked immunoassays (ELISA) for antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3).

Immunosuppression

Fifteen out of 19 (79%) grafts in SV group and 30 out of 38 (79%) in the control group were initially treated with a triple therapy (cyclosporine or tacrolimus plus azathioprine or mycophenolate mofetil plus steroids). No vasculitic patients were treated with cyclosporine plus steroids alone but three (8%) controls were. Two (5%) controls but no SV patients were treated with tacrolimus and steroids. Four SV patients and three controls (16% vs. 8%) were treated with sirolimus plus cyclosporine and steroids.

Statistical analysis

The statistical package S-Plus was used to analyze sample data. Means ± SDs were used for descriptive analysis. The *t*-test and the nonparametric Wilcoxon-test were used to investigate differences between the two groups of patients. Cross-tabulated data were analyzed by chi-square test, or by Fisher's test when the expected cell count was less than five. Survival curves were drawn using the Kaplan–Meier estimate and compared using the log-rank test.

Results

Of the 1225 renal transplants performed in our Hospital between December 1987 and January 2006, 19 first transplants (1.5%) were performed in patients with SV. Of them, 15 (79%) had been submitted to renal biopsy before transplantation. In the other 4 patients, the diagnosis of SV was based on clinical symptoms and signs as well as biochemical and urine analysis. On the basis of clinical signs and symptoms as well as on ANCA PR3 or MPO patterns, Wegener granulomatosis was diagnosed in 10 patients and microscopic polyangiitis (MPA) in 9 patients. SV was diagnosed 97.2 ± 44.1 months (range 55–234) before transplant. The diagnosis of nephritis was made 92.2 ± 38.2 months (range 55–178) before transplantation; in 9 patients the duration of renal disease before entering dialysis was less than 1 year.

During dialysis, SV activity quenched in 12 patients, while extra-renal activity persisted or relapsed in 7 patients requiring new courses of steroids. At the time of renal transplantation, all SV patients showed clinical quiescence for at least 6 months.

The demographic characteristics of SV patients as well as the number of HLA mismatches and the levels of panel-reactive antibodies (PRA) revealed no differences from those of the 38 controls. (Table 1). In both groups, 26% of patients received a kidney from living related donors.

Patient and renal graft survival

The mean follow-up after renal transplantation was comparable in vasculitic patients and in controls (58 ± 57 and 61 ± 49 months, respectively). The actuarial 10-year patient survival was 87% in SV patients and 90% in controls

Table 1: Demographic and laboratory characteristics of systemic vasculitis and controls recipients at renal transplantation

	Systemic vasculitis (19 patients)	Controls (38 patients)	p
Age (years) at transplant (mean ± SD)	46.6 ± 12.7	47.7 ± 6.7	ns
Sex (male/female)	13/6	26/12	ns
Living/deceased donors	14/5	28/10	ns
Months between diagnosis of renal disease and ESRD (mean ± SD)	41.8 ± 71.7	126 ± 105	0.002
Length of dialysis, months (mean ± SD)	64 ± 37	51.5 ± 43.5	ns
CAPD/HD	2/17	11/27	ns
HCV positive/negative	2/17	5/31	ns
Follow-up post-transplant months (mean ± SD)	58 ± 57	61 ± 49	ns
HLA mismatches (number)	2.7 ± 1.25	3.7 ± 0.5	ns
Panel reactive antibodies (N°positive)	2	4	ns

CAPD = continuous ambulatory peritoneal dialysis; HD = hemodialysis; ESRD = end stage renal disease.

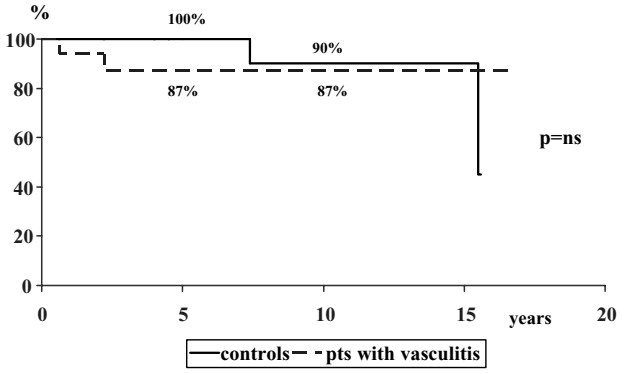

Figure 1: Kaplan–Meier estimates of patient survival in renal transplanted patients with systemic vasculitis (dashed line) and in controls (solid line).

(p = ns) (Figure 1). Two out of 19 vasculitic patients (10%) died, from lung cancer and hemophagocytic syndrome, 26 and 8 months, respectively, after renal transplant. In the control group 2 patients died (5%), from myocardial infarction and cerebral hemorrhage, 86 and 186 months, respectively, after renal transplant.

Two patients with SV lost their graft because of acute vascular rejection and chronic rejection 6 and 52 months, respectively, after renal transplant. Three graft failures occurred in the control group 131, 148 and 154 months, respectively, after renal transplant, all due to chronic rejection.

The actuarial 10-year graft survival rate censored by death was 84% in vasculitic patients versus 100% in the control group (p = ns) (Figure 2). After 10 years of follow-up, the graft survival rate maintained unchanged in SV patients, while in controls it progressively decreased to 40% at 154 months, but at that time the number of patients at risk was

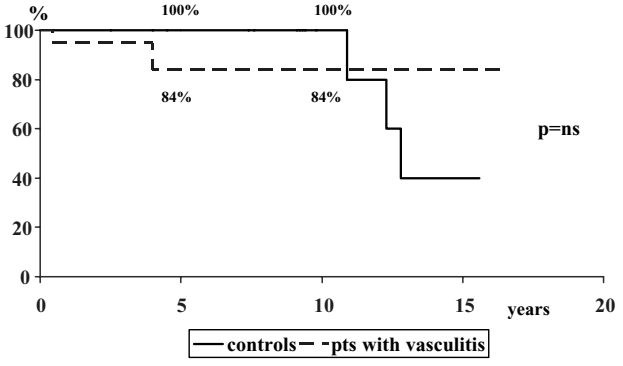

Figure 2: Kaplan–Meier estimates of renal survival probability censored for death in renal transplanted patients with systemic vasculitis (dashed line) and in controls (solid line).

Table 2: Main complications after kidney transplantation

	Vasculitic patients	Control patients	p
Delayed graft function ≥3 days	1	4	ns
Acute rejections	5 (26%)	11 (29%)	ns
-Vascular rejections	1	1	
- Cellular rejections	3	7	
- Clinical acute rejections	1	3	
Chronic rejection	2	2	ns
Unspecific sclerosing lesions	4	7	ns
Arterial hypertension	19 (100%)	37 (97%)	ns
Infections n° of patients	14 (74%)	13 (34%)	0.01

very low. However, no significant difference between the two curves was found.

Post-transplant complications (Table 2)

Delayed graft function occurred in one vasculitic patient and in four controls.

Acute rejection was diagnosed in 5 out of 19 grafts in SV patients (26%). Graft biopsy was performed in four patients and showed one vascular rejection (Banff IIB) and three cellular rejections (Banff IA: two patients, IB one patient). Another rejection was diagnosed on clinical grounds. The vascular rejection was irreversible; the cellular rejections completely recovered after therapy. Eleven acute rejections occurred in the control group (29%). Graft biopsy was performed in eight cases and showed one vascular rejection (Banff IIA) and seven cellular rejections (Banff IA five patients, IB two patients). In three patients the diagnosis was made on clinical grounds. The vascular rejection and a cellular rejection IB were partially reversible, while all the other rejections completely recovered after therapy.

During the follow-up, two patients with SV and two controls developed a biopsy-proven chronic rejection. Unspecific sclerosing lesions were documented at graft biopsy in four SV patients and in seven controls.

Looking only at patients with functioning graft at the end of the follow-up (15 of 19), the mean levels of serum creatinine and proteinuria were 1.7 ± 1.7 mg/dL and 0.35 ± 0.08 mg/dL, respectively, in patients with SV.

A higher number of SV patients developed severe infections requiring hospitalization in comparison to controls (14/19 vs. 13/ 38; p = 0.01). The types of infection are reported in Table 3.

Outcome of SV during renal transplantation (Table 4)

Seven patients (36.8%) showed a recurrence of vasculitis (MPA five patients, Wegener granulomatosis two patients) in mean 45 months after renal transplantation (range 0.5–192) with a relapse rate of 0.076/patient/year. The relapse was clinically characterized by proteinuria with microscopic

Table 3: Severe infections requiring hospitalization in transplanted patients with systemic vasculitis and in the control group

	Systemic vasculitis patients (19) Number of infections	Control patients (38) Number of infections
Pneumonia	3	1
Herpes zoster	1	5
CMV infections	2	4
Urinary infections	6	4
EBV infections	1	0
Other infections	4*	2**
Total	14 patients (17 episodes)	13 patients (16 episodes)

*Acute gastroenteritis = two patients; cutaneous abscess = one patient; BK virus infection = one patient.
**Cutaneous abscess = two patients.

hematuria in all cases and by an increase in serum creatinine in six out of seven patients. Lung hemorrhage developed in two patients, associated with cutaneous vascultis in one of the two patients. Histologically, all patients showed a pauci-immune necrotizing glomerulonephritis. At the time of recurrence, all but two patients had positive ANCA.

Four out of the 7 recurrent patients (numbers 1–4) developed recurrence of vasculitis 0.5–3 months after renal transplantation and all of them developed an acute rejection during the first year after renal transplant. Three of them (patients 1,2,4) had had a rapidly progressive renal insufficiency leading to dialysis.

The other three patients developed a recurrence of necrotizing glomerulonephritis 3 to 16 years after renal transplantation. The recurrence was characterized in all cases by an increase of serum creatinine, proteinuria and hematuria

There was no significant difference between the seven patients with recurrence and the other 12 SV patients as far as sex, age, duration of renal disease before dialysis, duration of dialysis, episodes of recurrence during dialysis, type of ANCA, source of kidney (deceased, living) or type of post-transplant immunosuppression. The only significant difference was a higher number of acute rejections in patients with recurrence than in nonrecurrent patients ($p = 0.04$) (Table 5).

All the seven patients with recurrence were treated with three methylprednisolone (MP) pulses (500 mg/day each) followed by oral prednisone 0.5 mg/kg/day associated with oral cyclophosphamide 2 mg/kg/day for 2–12 months in five of them. During cyclophosphamide therapy all the other anti-rejection immunosuppression therapies were withdrawn in three patients (numbers 1,3,6). In the other two patients, mycophenolate mofetil (patient 5) and azathioprine (patient 7) were withdrawn, while tacrolimus (patient 5) and cyclosporine (patient 7) were continued unchanged.

Patient 4 had a second relapse of vasculitis 5 years later with an increase in serum creatinine and proteinuria. Mycophenolate mofetil was stopped and replaced by cyclophosphamide for 6 months while tacrolimus and steroids were continued.

In three patients (1,4,6) serum creatinine returned to the pre-recurrence levels. At last observation, 43, 66 and 95 months, respectively, after renal transplant all these three patients had stable renal function with normal urinalysis in patients 1 and 6 and mild proteinuria in patient 4. In patient 5, the episode of recurrence was well controlled with MP pulses and cyclophosphamide, but 1 year later serum creatinine progressively increased without any clinical or laboratory signs of recurrence of vasculitis. Renal biopsy allowed the diagnosis of chronic rejection without any sign of vasculitis. The patient had to restart dialysis 52 months after renal transplant. Patient 7 was treated with a course of MP pulses and cyclophosphamide. Serum creatinine and proteinuria improved. Six months later, when a control renal biopsy demonstrated interstitial fibrosis without signs of vasculitis, cyclophosphamide was withdrawn. At the last observation, 1 year after SV recurrence, serum creatinine

Table 4: Patients with recurrence of systemic vasculitis

					At recurrence			Outcome after therapy					At last observation	
Pts	Sex	Age	Time of recurrence	ANCA at flare	S.creat from-to mg/dL	U.prot g/24h	Ery hpf	Therapy	S.creat mg/dL	U.prot g/24h	Ery hpf	Follow-up after Tx	S.creat mg/dL	U.prot g/24h
1	M	59	1 month	Neg	3.3 → 6	4	3+	MP 3 Cyclop	1.8	0.2	0	43	1.8	0.2
2	M	31	0.5 month	PR3 pos	2 → 3.5	0.7	3+	MP 3	1.5	0.24	1+	8	2	0.5
3	M	48	3 months	Neg	1.8 → 1.8	3.1	3+	MP3 Cyclop	1.5	5.7	1+	6	6 ESRD	5.9
4 I°	M	51	2 months	MPO pos	1.6 → 2.5	1.3	3+	MP 3	1.4	0.14	0			
4 II°	M	57	65 months	MPO pos	1.8 → 2.6	2.8	2+	Cyclop	1.79	1.5	1+	66	1.8	0.9
5	F	54	37 months	MPO pos	1.7 → 5.4	3.9	3+	MP 3 Cyclop	2.1	1.3	2+	52	5.9 ESRD	1.45
6	M	40	78 months	MPO pos	1 → 1.5	1.4	3+	MP 3 Cyclop	1	0.06	0	95	1.0	0.09
7	F	48	192 months	PR3 pos	2 → 3.4	1.9	2+	MP 3 Cyclop	2.7	0.9	0	200	2.7	0.9

Pts = patients; ANCA = anti-neuthrophil cytoplasmic antibodies; s.crea = serum creatinine; U.prot = proteinuria; Ery = Erythrocyte; hpf = high power field; MP = methylprednisolone pulses; Tx = transplant; MPO= myeloperoxidase; PR3 = proteinase 3; neg = negative; pos = positive.

Table 5: Demographic, clinical and laboratory characteristics of patients with systemic vasculitis who relapsed and whose who did not

	Patients with recurrent renal vasculitis: 7	Nonrecurrent patients 12	p
Age at tx (years) mean ± SD	53 ± 10.3	55.3 ± 11.8	ns
Sex (male/female)	5/2	8/4	ns
Months between diagnosis of vasculitis and ESRD mean ± SD	70.6 + 108.2	25 + 34.6	ns
Duration of dialysis (months) mean ± SD	49.8 ± 21.4	72.3 ± 42.1	ns
Patients with recurrence of vasculitis during dialysis N° (%)	1 (14%)	6 (50%)	ns
Type of dialysis HD/CAPD	5/1	11/1	ns
Follow-up post-tx (months) mean ± SD	66.6 ± 67	52.4 ± 52.1	ns
Deceased/living donors	6/1	8/4	ns
HCV positivity (yes/no)	2/5	0/12	ns
Immunosuppressive therapy 1/2/3/4	1/4/2/0	2/6/0/4	ns
HLA mismatches (number)	2.4 ± 1.14	2.7 ± 1.5	ns
Panel reactive antibodies (N° positive)	1	1	ns
Arterial hypertension yes/no	7/0	11/1	ns
Acute rejection yes/no	4/3	1/11	0.04
Chronic rejection number	1	1	ns
Unspecific sclerosing lesions number	1	3	ns
N° patients with infections yes/no	6/1	8/4	ns
Final serum creat. (mg/dL) mean ± SD	2.3 ± 0.9	1.4 ± 0.4	0.02
Final proteinuria (g/24 h) mean ± SD	1.47 ± 2	0.26 ± 0.26	0.02
N° of deaths	1	1	ns
N° of lost kidney	2	0	ns

Immunosuppressive therapy 1 = steroids + cyclosporine + azathioprine; 2 = steroids + tacrolimus + mycophenolate; 3 = steroids + cyclosporine + mycophenolate; 4 = steroids + sirolimus + cyclosporine.

was 2.7 mg/dL with mild proteinuria (0.9 g/24 h). Of the remaining two patients, patient 2 died from hemophagocytic syndrome and patient 3 lost the allograft because of humoral rejection, 8 and 6 months, respectively, after renal transplantation. If we look at the results at the last follow-up visit, the patients who had recurrence showed significantly higher mean levels of serum creatinine and proteinuria (Table 5).

Discussion

In this study we have reported our single-center experience with renal transplantation in 19 SV patients followed in mean for 58 months, one of the longest follow-ups reported up until now. All patients were Caucasian and all were treated with calcineurin inhibitors after transplantation. We used as controls those patients who were transplanted immediately before and after those with SV and matched with them for many of the variables, which might influence the outcome of renal transplant recipients. The actuarial 10-year patient and pure graft survival were, 87% and 84%, respectively, in SV patients, and 90% and 100% in the control group. A limitation of this study is represented by the small number of patients. Our data seem to suggest that good results can be obtained, even in the long-term, with renal transplantation in SV patients, although a lower survival rate has been observed at 5 and 10 years for vasculitic patients when compared to controls.

The number of rejections, the risk of developing late allograft failure as well as the prevalence of arterial hypertension were not different between SV patients and controls. In contrast vasculitic patients had a significantly higher number of infections requiring hospitalization than controls. There is only one other paper reporting the frequency of these complications in 20 transplant patients with vasculitis (4). In that paper no difference in the rates of rejection and infection was found between vasculitic patients and the total population transplanted in the same institution. No other data are available regarding these complications in the published studies.

The risk of recurrence of SV after renal transplantation is a controversial issue. The relapse rate after renal transplant is lower than that observed before and during dialysis (12,18). However, the rate of post-transplant vasculitic recurrences and the impact on patient and graft survival are not clearly defined. Nachman et al. (5), in 28 patients (7%) followed for 56 months, reported two recurrences, with graft failure in one of them. The same investigators reported the results of a pooled analysis on 127 renal transplant recipients with SV; recurrence occurred in 22 patients (17%) with renal involvement in 12 of them. Of the 16 patients for whom information about the outcome was available, 11 went into stable remission after therapy, 2 relapses led to graft loss, 1 patient lost the graft in spite of the remission of the vasculitic flare and 1 patient died as a consequence of the relapse. Nyberg et al. (3) reported 6 renal recurrences in 17 patients submitted to 22 renal transplants (27%), in 2 cases the graft was lost due to renal relapse. Also the number of relapses per patient per year varied significantly being 0.02 patient/year (12), 0.06 patient/year (19) and 0.10 patient/year (4), respectively, in three different studies.

Seven out of 19 patients followed in our Unit for a mean period of 5 years after renal transplantation developed a recurrence of vasculitis, which means an incidence of relapses of 0.076/patient/year. In all cases, the recurrences were characterized by biopsy proven pauci-immune necrotizing glomerulonephritis associated in two cases with lung involvement. Microscopic hematuria and proteinuria were the heralding signs for all the renal recurrences.

We could not find any significant difference between patients who relapsed and those who did not in terms of duration of dialysis, episodes of recurrence during dialysis, type of ANCA, deceased or living transplant or type of immunosuppressive therapy after renal transplant. The only significant difference between the two groups was a higher incidence of acute rejection during the first year after transplant in those patients who had a relapse. Although the relapses occurred in mean 45 months after renal transplantation, in 4 out of the 7 patients the recurrence occurred within 3 months after transplantation.

After MP pulses and cyclophosphamide, all our patients recovered renal function, but one patient died of hemophagocytosis. The pathogenesis of this syndrome is still unclear. However, the strict link between systemic inflammation and hemophagocytosis, coupled with peripheral T-cell expansion and deficient natural killer activity often found in patients with this syndrome (20) supports the hypothesis of a dysregulation in the inflammatory and immune response. It is possible to speculate that the combination of inflammation during recurrence with the immune dysregulation caused by treatment may have contributed to the development of this rare syndrome in our patient.

Two other patients lost their graft function because of acute vascular and chronic rejection, respectively, and another patient showed a progressive increase in serum creatinine. At the last follow-up, the mean levels of serum creatinine and proteinuria were more elevated in patients with recurrence than in the other vasculitic patients. Thus, in spite of a good early response to therapy it appears that recurrence of vasculitis eventually may have an unfavorable impact on renal allograft function in at least half of the patients. Whether recurrence should be considered as a marker or a trigger of a high immunological response is still a matter of speculation.

In conclusion, our results, although based on a small sample size, underline that transplanted vasculitic subjects may have good patient and graft survival rates at 10 years, although infections were more frequent in vasculitic patients than in controls. Therefore, patients with SV may be considered as suitable candidates for kidney transplantation. However, the risk of recurrence is not infrequent and can have severe consequences, implying the need of continuous and careful surveillance to promptly diagnose and treat such complication. We suggest checking for ANCA every 6–12 months, bearing in mind that negative results do not rule out completely the possibility of SV relapse. As an increase in urine protein/creatinine ratio and/or the onset of hematuria and cylindruria in the urine sediment may suggest a relapse of SV, we suggest to monitor urinalysis every month during the first year after transplantation and every 3 months during the follow-up. The final diagnosis may require graft biopsy.

Conflict of Interest

Ponticelli C is an external consultant of Novartis, Italy.

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References

1. Lyons GW, Linsday WG. Renal transplantation in a patient with Wegener granulomatosis. Am J Surg 1972; 124: 107.
2. Kuross S, Davin T, Kjellstrand CM. Wegener's granulomatosis with severe renal failure: Clinical course and results of dialysis and transplantation. Clin Nephrol 1981; 16: 172–180.
3. Nyberg G, Akesson P, Norden G, Wieslander J. Systemic vasculitis in a kidney transplant population. Transplantation 1997; 63: 1273–1277.
4. Schmitt WH, Haubitz M, Mistry N, Brunkhorst R, Erbsloh-Moller B, Gross WL. Renal transplantation in Wegener's granulomatosis. Lancet 1993; 342: 860.
5. Nachman PH, Segelmark M, Westman K et al. Recurrent ANCA-associated small vessel vasculitis after transplantation: A pooled analysis. Kidney Int 1999; 56: 1544–1550.
6. Rostaing L, Modesto A, Oksman F, Cisterne JM, Leao G, Durand D. Outcome of patients with antineutrophil cytoplasmic autoantibody-associated vasculitis following ceased kidney transplantation. Am J Kidney Dis 1997; 29: 96–102.
7. Wrenger E, Pirsch JD, Cangro CB et al. Single-center experience with renal transplantation in patients with Wegener's granulomatosis. Transpl Int 1997; 10: 152–156.
8. Elmedhem A, Adu D, Savage CO. Relapse rate and outcome of ANCA-associated small vessel vasculitis after transplantation. Nephrol Dial Transplant 2003; 18: 1001–1004.
9. Lowance DC, Vosatka K, Whelchel J et al. Recurrent Wegener's granulomatosis. Am J Med 1992; 92: 573–575.
10. Reaich D, Cooper N, Main J. Rapid catastrophic onset of Wegener's granulomatosis in a renal transplant. Nephron 1994; 67: 354–357.
11. Gera M, Griffin MD, Specks U, Leung N, Stegal MD, Fervenza FC. Recurrence of ANCA-associated vasculitis following renal transplantation in the modern era of immunosuppression. Kidney Int 2007; 71: 1296–1301.
12. Allen A, Pusey C, Gaskin G. Outcome of renal replacement therapy in antineutrophil cytoplasmic antibody-associated systemic vasculitis. J Am Soc Nephrol 1998; 9: 1258–1266.
13. Cecka JM, Terasaki PI. The UNOS Scientific Renal Transplant Registry. In: Cecka JM, Terasaki PI (eds). Clinical transplants. Los Angeles, CA: UCLA Tissue Typing Laboratory; 1995: 1–18.
14. Douglas Briggs J, E. Jones on behalf of the Scientific Advisory Board of the ERA-EDTA Registry Renal transplantation for uncommon disease. Renal transplantation for uncommon diseases. NDT 1999; 14: 570–575.

15. Schimtt WH, Opelz G, Ven Der Woude FJ. Renal transplantation is safe and successful in Wegener granulomatosis: Data from the Collaborative Transplant Study (abstract). J Am Soc Nephrol 2002; 13: 564A–565A.
16. Jennette JC, Falk R, Andrassy K et al. Nomenclature of systemic vasculitis. Proposal of an international consensus conference. Arthritis Rheum 1994; 37: 187–192.
17. Solez K, Colvin RB, Racusen LC et al. Banff'05 Meeting Report: Differential diagnosis of chronic allograft injury and elimination of chronic allograft nephropathy ('CAN'). Am J Transplant 2007; 7: 518–528.
18. Westman KW, Bygren PG, Olsson H, Ranstam J, Wieslander J. Relapse rate, renal survival, and cancer morbidity in patients with Wegener's granulomatosis or microscopic polyangiitis with renal involvement. J Am Soc Nephrol 1998; 9: 842–852.
19. Haubitz M, Kliem V, Koch KM et al. Renal transplantation for patients with autoimmune disease: Single center experience with 42 patients. Transplantation 1997; 15: 1251–1257.
20. Schmid JM, Junge SA, Hossle JP et al. Transient hemophagocytosis with deficient cellular cytotoxicity, monoclonal immunoglobulin M gammopathy, increased T cell numbers and hypomorphic NEMO mutation. Pediatrics 2006; 117: 1049–1056.