Evidence-based rheumatology

edited by M. Matucci Cerinic

Kidney transplantation is a safe therapeutic tool in systemic lupus erythematosus

Authors: P. Grimbert *et al.*
Title: Long-term outcome of kidney transplantation in patients with systemic lupus erythematosus
Source: *Transplantation*, vol. 66, no. 8, October 27 1998, pg. 1000-1003.

Aim: In systemic lupus erythematosus (SLE) patients with end-stage renal disease (ESRD), renal transplantation is generally avoided because of the concern that deposits of immunocomplex might destroy the renal allograft. A retrospective, multicenter study was conducted to evaluate the outcome of renal transplantation in ESRD lupus patients compared to control subjects with non-lupus ESRD.
Methods: A total of 53 patients with ESRD due to lupus nephritis, confirmed by biopsy, received 60 renal transplants between 1971 and 1993. Their medical charts and demographic information, including age, sex, date of transplantation, donor source, degree of HLA matching, duration of SLE before transplantation, duration of pre-transplant hemodialysis, pre-operative serologic SLE activity (based on antinuclear antibodies (ANA), anti-double-stranded DNA titers and hypocomplementemia), maximum panel reactive antibody (PRA) level and post-operative immunosuppression, were retrospectively reviewed. The treatment up to 1984 consisted of azathioprine and prednisone alone (in 9 pts), whereas after 1984 cyclosporine was also introduced (51 pts).
The long-term outcome, including patient and graft survival, post-transplant SLE activity, serum creatinine levels, rejection episodes, cause of graft loss and patient death, was examined. Charts were also reviewed for evidence of recurrent nephritis. The patient and graft survival rates were then compared with those for 106 controls (matched for age, sex, maximum PRA level, date and number of transplants, post-operative immunosuppression) whose ESRD was due to glomerulonephritis, interstitial nephritis, familial nephropathy, hypertension, or unknown causes.
Patient and graft survival estimates were calculated using the Kaplan-Meier product limit estimator. Survival estimates were compared by a log rank test.
Results: The patients were predominantly women (90%), the mean age at the time of transplantation was 33.2 years, 56 transplants (93%) were from cadaveric and 4 (7%) from living, related donors. Forty-six patients (7%) had a primary allograft, while 7 (14%) also received a second allograft. Disease and dialysis duration before transplantation were 93.6 ± 6.2 and 48 ± 6 months, respectively. At the time of transplantation no patient had clinically active SLE.
The one-year graft and patient survival rates were 83% and 98%, while the 5-year graft and patient survival rates were 69% and 96%, respectively. Graft and patient survival rates in SLE patients were not significantly different from those in the matched control group. At least one episode of biopsy-proven acute rejection occurred in 68% of the SLE patients, a rate which was not significantly different from that of the controls (60%). Histologically demonstrated chronic rejection was found in 36 transplanted kidneys in SLE patients and was the major risk factor for graft loss in 15 grafts. After transplantation, lupus nephritis occurred in the graft of one patient, and 4 patients developed extra-renal manifestations (2 with arthralgias, 1 myocarditis, and 1 malar rash).
Conclusion: This study demontrates clearly that SLE renal transplantation has an excellent long-term outcome with a very high graft survival rate and a low rate of recurrent clinical nephritis.

Comment
There are several intriguing facts about renal transplantation in SLE patients who are suffering from end-stage renal failure (E-SRF). Three of them are nicely pointed out in this meritorious French multi-center study.

1. *Graft and patient survival rates are akin to those of matched controls with E-SRF due to various other causes. This is important and should be stressed to avoid having SLE patients placed at the end of the line for the donation of cadaveric kidneys. Indeed, the majority of the grafts in this study were from unrelated donors.*
2. *Lupus nephritis seldom reappears in the graft.*
3. *A minority of SLE patients who undergo renal transplantation develop further extra-renal manifestations of their disease.*

We could tend to attribute these results to previous disease inactivation due to renal failure and/or nephrotic syndrome (1). Indeed, the patient in this study who suffered recurrent lupus nephritis had high pre-operative ANA and anti-DNA titers. However, none of the other patients who had similarly high serological abnormalities suffered recurrent lupus nephritis.
Another explanation could reside in the immunosuppressive treatment administered to prevent graft rejection. Is this form of treatment any better than what the patients had received for the treatment of lupus nephritis, and which did NOT prevent them from developing E-SRF ? Most of the patients received anti-lymphocyte globulines or anti-OKT3, as well as azathioprine, prednisone and cyclosporine post-operatively. Could this form of treatment have prevented E-SRF better than pulse cyclophosphamide did ?
One word of caution should be given regarding kidney transplantation in SLE patients. Antiphospholipid antibodies have

been found to be risk factors for early renal allograft failure (2,3) and so seems to be a history of smoking (3). Whether or not antiphospholipid antibodies (and/or anti-β_2 glycoprotein 1) are present in a patient to be transplanted should also be determined in order to include anti-thrombotic therapy if necessary in their post-operative treatment regimen.

D. ALARCON-SEGOVIA, *MD, MACP*

Department of Immunology and Rheumatology
Instituto Nacional de la Nutrición Salvador Zubiran
14000 Mexico D.F., Mexico.

References

1. HELSAN JM, LAUTIE JP, INTRATOR L, BLANC C, LAGRUE G, SOBEL AT: Impaired IgG synthesis in patients with the nephrotic syndrome. *Clin Nephrol* 1982; 18: 144-7.
2. WAGENKNECHT DR, BECKER DG, LEFOR WM, MCINTYRE JA: Antiphospholipid antibodies are a risk factor for early renal allograft failure. *Transplantation* 1999; 68: 241-6.
3. STONE C, AMEND WJC, CRISWELL LA: Outcome of renal transplantation in 97 cyclosporin-era patients with systemic lupus erythematosus and matched controls. *Arthritis Rheum* 1998; 41: 1438-45.