Recurrent Crescentic Immunoglobulin A Nephropathy in the Graft Kidney

Recurrence of the original disease is now the third most frequent cause of renal allograft loss at 10 years after transplantation in patients with underlying glomerulonephritis (GN). IgA nephropathy (IgAN) is the most common type of GN and recurs in up to 60% of the patients.[1] Initially considered to be a relatively benign phenomenon, recurrences develop in approximately 33% of patients, ranging between 9% and 61%, among the different series.[2] Clinical recurrence may occur immediately after transplantation, but on an average, the diagnosis is made approximately 3 years after transplantation.[2,3] It is usually suspected by the presence of hematuria and low-grade proteinuria. In the past issue of the Journal, a case of recurrent crescentic IgAN in the renal allograft in two successive kidney transplant surgeries highlighted the limitations of the current day understanding of the aggressive form of this glomerular disease.[4]

The authors have reported two consecutive episodes of rapidly progressive GN in their patient after having received grafts from live as well as deceased donors. Currently, there is no consensus about an approach to reduce the risk or severity of recurrent IgAN. Recurrence tends to occur more frequently in younger patients and those with a rapid progression of the original disease.[1,5,6] It is unclear if recurrence is[7,8] or is not[5,9] more frequent in transplants using related donors. A review of the data collected by the Australia-New Zealand registry reported that biopsy-proven IgAN recurrence was significantly more frequent in zero human leukocyte antigen-mismatched living donor grafts.[10] However, these results should be interpreted with some caution because certain basic details are lacking in the retrospective reviews of this registry data. Most other pretransplant characteristics do not predict recurrence, although some authors have suggested that latent IgA deposits in the donor kidney (in "zero" time biopsies of the transplanted kidney) are highly associated with a recurrence of disease,[11] and underlying crescentic GN with rapid progression to end-stage renal disease may also predict a higher risk for recurrence.[11] There is now, a general agreement that the type and intensity of posttransplant immunosuppression do not influence the risk of IgAN recurrence.[12] However, authors in this issue, have observed that intensifying immunosuppression after recurrence was beneficial in salvaging the renal allograft of their patient.

There is some speculation that the incidence of recurrence of IgAN might be lower in those given anti-thymocyte globulin induction. The induction agent used by the authors was interleukin-2 receptor blocking agent. Berthoux *et al*.[13] have reported that the 10-year cumulative recurrence rate of IgAN was 9% (3 of 29) in patients who received induction with anti-thymocyte globulins versus 41% (21 of 52) in patients who did not receive such induction therapy. The authors hypothesized that the protective effect of anti-thymocyte globulins could be related to an augmented production of regulatory T-cells. Tang *et al*. have reported that ATG has been found to be protective with an 80% reduction in relative risk. However, this needs to be confirmed in a prospective trial.[11] Besides, preference of either one of the two induction agents in preventing recurrence of crescentic GN is debatable due to lack of data.

Recurrent IgAN leads to graft dysfunction or loss in upto 16% of cases.[14-16] Recurrent and *de- novo* crescentic IgAN is a rare entity. This finding is uncommon and is estimated to account for approximately 3–5% (when >50% of glomeruli are involved by crescents) and 32% of cases (if any number of glomeruli are involved).[17] It is clear that IgAN with crescents most often occurs in patients with preexisting IgAN and is an uncommon *de novo* disease in transplanted kidneys.[18] There appears to be a male preponderance and no association with the time since transplantation.[18] It appears that the presence of crescents in a kidney allograft with IgAN, at any time after transplantation, is associated with graft failure significantly earlier than might be predicted as per the natural course of IgAN. None of the factors postulated to be responsible for IgAN recurrence have been implicated for recurrence of crescentic IgAN. The only factor identifiable as a significant risk for the development of IgAN with crescents in an allograft kidney is the presence of IgAN in the native kidneys.[18]

In conclusion, crescentic IgAN in kidney allografts is an uncommon and an aggressive form of disease that can occur at any time during the post transplantation period. It often follows a rapid clinical course and leads to allograft loss within a short period. No single risk factor has been recognized to be responsible for its development. Use of anti-thymocyte globulin as an induction agent may have some protective role in preventing recurrence of this disease. Since, there appears to be no proven prevention strategy, it may be advisable to prefer a deceased donor organ in those who have end-stage renal disease due to crescentic IgAN. Furthermore, both the underlying pathophysiological characteristics and effective treatment for this disease remain elusive and needs further research and evaluation.

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Access this article online	
Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.175982

How to cite this article: Bhargava V. Recurrent crescentic immunoglobulin a nephropathy in the graft kidney. Indian J Nephrol 2017;27:335-6.