Fellows First

Favorable Outcomes following Kidney Transplant in Patients with AA Amyloidosis

By Rose Mary Attieh

Occurring in patients with chronic inflammatory conditions, AA amyloidosis is a form of systemic amyloidosis characterized by the extracellular deposition of serum amyloid A (SAA) protein fibrils. Renal manifestations are observed in as many as 90% of cases, with up to 10% of patients presenting with kidney failure at the time of diagnosis (1). Due to the prevalent frailty and multi-organ involvement in individuals with kidney failure secondary to AA amyloidosis, these patients have frequently faced exclusion from kidney transplant. This exclusion is also driven by concerns about the heightened risk of disease recurrence in the allograft, observed in up to 25% of cases (2).

Novel biotherapies such as interleukin (IL)-1, IL-6, and tumor necrosis factor-α inhibitors have demonstrated efficacy in halting SAA synthesis and, consequently, amyloid deposition. Therefore, Schwarz and colleagues (3) hypothesized that the increase in use of these biotherapies, coupled with advancements in post-transplant care, may improve outcomes of kidney transplant recipients (KTRs) with AA amyloidosis. The investigators conducted a retrospective cohort study analyzing outcomes in 86 patients who underwent kidney transplant between 2008 and 2018 across 26 centers in France. Patients were eligible for inclusion if they were 18 years or older at the time of transplant and only if the diagnosis of renal AA amyloidosis was established through either kidney biopsy or the presence of AA amyloid deposition in another tissue. The mean KTR age was 49.4 years. Familial Mediterranean fever was the cause of amyloidosis in 43% of cases.

Although the study was unable to assess the association of biotherapy use with post-transplant outcomes due to the low percentage (18.6%) of KTRs receiving these drugs, it did yield interesting observations. Patient survival rates were not inferior to the general kidney transplant population in France (4), reaching 94.0% at 1 year and 85.5% at 5 years post-transplant. Allograft survival also aligned with national data, with a 10.5% cumulative incidence of graft loss at 1 year and 13.0% at 5 years post-transplant. Recurrence of AA amyloidosis was documented in only 5.8% of cases. Notably, there was a high rate of infection requiring hospitalization, involving 55.8% of cases, despite the use of per-protocol antimicrobial prophylaxis in each center. Infection therefore emerged as the leading cause of post-transplant death. In addition, there was an increased incidence of acute allograft rejection of 27.9%. Interestingly, the use of biotherapy post-transplant showed no correlation with either acute rejection or infection. Furthermore, multivariable analysis revealed that the C-reactive protein level at the time of transplant was associated with both patient survival (hazard ratio [HR], 1.01; 95% confidence interval [CI], 1.00–1.02; p = 0.01) and allograft survival (HR, 1.68; 95% CI, 1.10–2.57; p = 0.02), highlighting the importance of adequate control of the underlying inflammatory process to attain good outcomes post-transplant.

In sharp contrast to earlier reports, this study is the first, to our knowledge, to demonstrate favorable outcomes in KTRs with AA amyloidosis, arguing that these patients should not be denied transplant. Although these results are certainly encouraging, some limitations of the study must be considered. For instance, the study lacked a matched control group. Consequently, the observed similarities in outcomes with the general kidney transplant population in France may have been partly attributed to the younger age and lower comorbidity burden in the study's cohort with AA amyloidosis (3). Furthermore, it is challenging to ascertain whether the low recurrence rate was associated with the biotherapies or under-reporting, given that only 51.2% of the cohort underwent at least one kidney biopsy with Congo red staining analysis.

Although more research is required to examine the impact of biotherapies on post-transplant outcomes, future studies should also strive to find effective treatments that can mitigate infection-related morbidity and mortality in KTRs with AA amyloidosis. ■

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METHODS

- Retrospective cohort
- France
- Patients with renal AA amyloidosis who underwent kidney transplant
- 2008–2018

RESULTS

- N = 86
- Median age, 49.4 y (IQR, 39.7-61.1 y)
- Cause of amyloidosis: Familial Mediterranean fever (n = 37; 43%)
- Amyloidosis recurrence: n = 5 (5.8%)

Patient Survival	Allograft Loss
1 Year: 94.0% (95% CI, 89.1%–99.2%)	1 Year: 10.5% (95% CI, 4.0%–17.0%)
5 Years: 85.5% (95% CI, 77.8%–94.0%)	5 Years: 13.0% (95% CI, 5.8%–20.1%)

Conclusion: Patients who received a kidney transplant for AA amyloidosis experienced favorable rates of survival and lower recurrence rates than previously reported. IQR, interquartile range.

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Visual Graphic by Jia H Ng, MD, MSCE