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Research

Renal Transplantation in Patients with Alport Syndrome

Alport Sendromlu Hastalarda Böbrek Nakli

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ABSTRACT

Objective: Alport syndrome is an inherited disease that occurs in 1/50,000 and is characterized by hematuria, kidney failure, deafness and ocular anomalies. Alport syndrome, which is inherited as X-linked recessive with a rate of 85%, may be inherited also as autosomal dominant or autosomal recessive. Defective type-4 collagen participating in the structure of glomerular basement membrane causes a progressive decline in kidney functions. This research investigates the results of end-stage renal failure in patients with Alport syndrome following kidney transplantation.

Methods: In our Hospital Organ Transplant Center 11 kidney transplantations were performed in 10 patients with Alport syndrome between October 2010 and December 2020. The recipients were analyzed retrospectively for acute rejection, complication rate, graft and patient survival.

Results: Eleven (0.88%) of 1,251 kidney transplants were performed in patients with Alport syndrome. Acute rejection did not occur in any patient after kidney transplantation and no medical or surgical complications were observed in the early postoperative period. One patient died 19 months after surgery because of pneumonia and sepsis while his graft was functional. Graft loss was observed in two patients. In one of these patients, graft loss developed due to drug incompatibility in the 11th month after kidney transplantation. In the other patient, graft loss was observed due to chronic allograft nephropathy in the 63rd month postoperatively. This patient underwent a second kidney transplant surgery from a living donor.

Conclusion: Alport syndrome is a rare cause of chronic kidney failure. Kidney transplantation is an effective and successful treatment method for end-stage renal disease patients with Alport syndrome.

Keywords: Renal transplantation, Alport syndrome, graft survival

ÖZ

Amaç: Alport sendromu 1/50.000'de ortaya çıkan, hematüri, böbrek yetmezliği, işitme kaybı ve oküler anomalilerle karakterize kalıtsal bir hastalıktır. %85 oranında X'e bağlı resesif olarak kalıtılan Alport sendromu, otozomal dominant veya otozomal resesif olarak da kalıtılabilir. Glomerüler bazal membranın yapısına katılan arızalı tip-4 kollajen böbrek fonksiyonlarında ilerleyici bir düşüşe neden olur. Bu araştırma, böbrek nakli sonrası Alport sendromlu son dönem böbrek yetmezliği hastalarının sonuçlarını araştırmaktadır.

Gereç ve Yöntem: Hastanemiz Organ Nakli Merkezi'nde Ekim 2010 ile Aralık 2020 tarihleri arasında Alport sendromlu 10 hastaya 11 böbrek nakli yapıldı. Alıcılar retrospektif olarak akut rejeksiyon, komplikasyon oranı, greft ve hasta sağkalımı açısından incelendi.

Bulgular: Bin iki yüz elli bir böbrek naklinin 11'i (%0,88) Alport sendromlu hasta idi. Böbrek nakli sonrası hiçbir hastada akut rejeksiyon olmadı ve ameliyat sonrası erken dönemde herhangi bir tıbbi veya cerrahi komplikasyon görülmedi. Bir hasta ameliyattan 19 ay sonra greft fonksiyonel iken pnömoni ve sepsis nedeniyle öldü. İki hastada greft kaybı gözlendi. Bu hastalardan birinde böbrek nakli sonrası 11. ayda ilaç uyumsuzluğuna bağlı greft kaybı gelişti. Diğer hastada postoperatif 63. ayda kronik allogreft nefropatisine bağlı greft kaybı gözlendi. Bu hastaya canlı bir donörden ikinci bir böbrek nakli ameliyatı yapıldı.

Sonuç: Alport sendromu, kronik böbrek yetmezliğinin nadir bir nedenidir. Böbrek nakli, Alport sendromlu son dönem böbrek yetmezliği hastalarında etkili ve başarılı bir tedavi yöntemidir.

Anahtar Kelimeler: Böbrek nakli, Alport sendromu, greft sağkalımı

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INTRODUCTION

Alport syndrome (AS) is a rare hereditary disorder that is first described in 1927 and characterized by progressive renal function loss, hematuria, sensorineural deafness and typical ocular anomalies (1,2). Mutations in the *COL4A5* or *COL4A3/COL4A4* genes cause abnormal production of collagen type-IV, which causes lamination in the glomerular basement membrane (GBM) (3). 85% of cases appear X-linked inheritance with the mutations in COL4A5. It can also be seen in autosomal recessive and rarely autosomal dominant resulting from mutations in both gene copies of *COL4A3* and *COL4A4* (4,5). Patients with AS present most commonly hematuria in the first decade and a history of familial renal failure and deafness is diagnostic for AS (5,6). Renal failure before the age of 30 is the most important cause of mortality in AS and renal replacement therapy is the initial type of treatment modality in such patients. Kidney transplant outcomes of patients with AS have been discussed in many studies. Göbel et al. (7) compared survival of kidney transplant patients with AS and patients who are not AS. One- and five-year patient survival was 100 and 91% in AS and 89 and 78% in controls ($p>0.05$, respectively) (7). In another study, Byrne et al. (8) evaluated 41 kidney transplant patients with AS and they revealed that 1-, 5-, and 10-year patient and graft survival rates were 95.1%, 90.2%, and 80.5% and 86.8%, 66%, and 45.3%, respectively.

This study reveals the clinical outcomes of renal transplantation (RTx) in patients with AS.

METHODS

Eleven of 1,251 kidney transplantation was performed in patients with end-stage renal disease (ESRD) due to the AS between October 2010 and December 2020 in our hospital Organ Transplant Center. The data were retrospectively collected from hospital records and expressed as frequencies and percentages. The main outcomes that were assessed in this study were the presence of anti-GBM disease or acute rejection, intraoperative complication rate, renal allograft and patient survival. The study protocol was approved by the Ethic Committee of Acibadem University in December 2021 with the approval number 2021-25/14.

Statistical Analysis

The results were analyzed using the Statistical Package for the Social Sciences, version 22 (SPSS, Chicago, Ill, United States).

RESULTS

A total of 1251 kidney transplants were performed in our hospital Organ Transplant Center between October 2010 and December 2020. Eleven (0.88%) of these transplants were performed in 10 patients with ESRD caused by AS. While only one transplant was carried out from cadavers, 6 of the remaining 10 transplants were performed from 1. degree relatives, 2 from 2. degree relatives and 2 from unrelated donors. 8 of 10 living donor nephrectomies were performed transperitoneal and the remaining 2 with a transvaginal laparoscopic approach. The mean age and follow-up duration of recipients were 25±9.1 years and 46.7 months, respectively. All patients were male in gender. Overall patient survival is 90.9%, only one patient died 19 months after the operation because of pneumonia and sepsis while his graft was functional. The survival of renal allografts in patients with ESRD due to the AS was 81.8%. Two recipients have lost their grafts during the follow-up period; first patient lost his graft 11 months after the kidney transplantation because of the drug incompetence In the second patient graft loss was developed in the 63rd month due to the chronic allograft nephropathy (Chronic active T-cell-mediated rejection) and in this patient the second RTx was performed from the living donor (Table 1). No patient developed the anti-GBM disease, acute rejection, or intra- and postoperative complication.

DISCUSSION

AS is a rare inheritable disorder characterized by renal failure in early ages, hematuria, deafness and ocular anomalies. AS made up quite a low prevalence (0.5-1.6%) in all RTx patients in the literature (2,3). Genetic mutations in collagen type IV result in involvement and dysfunction of multiple organs and the most common cause of mortality in patients with AS are ESRD before 30 years of age (9). This retrospective analysis reports the transplant-related outcomes of 10 patients with AS at our center.

Because of younger age at RTx and fewer episodes of acute rejection have the patients with AS a high twenty-year patient survival rate (70.2%) in compared to RTx patients due to the other renal diseases (44.8%). However, there was no statistically significant difference found in the national case series of Kelly et al. (3) in terms of median graft survival between and non-AS patients with AS.

Yilmaz et al. (10) found no significant difference between 25 AS and 50 non-AS patients in terms of graft and

patient survival at years 1, 3, 5 and 10, requirement for postoperative dialysis, BK virus-associated nephropathy and cytomegalovirus infection. Only lower rates of acute rejection and higher rates of chronic allograft dysfunction were observed in patients with AS compared to the non-AS patient group (10).

The most catastrophic complication in RTx patients with AS is anti-GBM nephritis, which causes rapid allograft loss after the transplantation (3,10). Despite the study by Gumber et al. (9) in 2012, which reported anti-GBM nephritis-related graft loss with an incidence of 12%, the literature manifests lower incidence such as 3-4% of anti-GBM nephritis in RTx with patients with AS (7,11). The more current studies mention the incidence of anti-GBM nephritis 0-0.3%, which can be attributed to the modern and effective usage of immunosuppressive therapy (2,3,10). Also in our study, no allograft rejection was detected due to the anti-GBM nephritis.

Study Limitations

The limitations of this study are the small sample size and lack of long-term follow-up.

Table 1. Main baseline characteristics

	Kidney transplant patients with AS (n=10) Kidney transplantation (11 kidney transplantation to 10 patients)
Recipient gender; n (%)	
Female	0
Male	10 (100%)
Age (years)	25±9.1
Type of transplantation; n (%)	
Cadaveric	1
Living	10
Degree of relationship; n (%)	
1st degree	6
2nd degree	2
Unrelated	2
Overall patient survival (%)	90.9
Overall patient survival (%)	81.8
Cause of graft loss	Drug incompliance Chronic active T-cell-mediated rejection

AS: Alport syndrome

CONCLUSION

This study reveals that RTx is an effective treatment modality in patients with ESRD with AS and shows comparable results with RTx due to the other renal diseases.

ETHICS

Ethics Committee Approval: The study protocol was approved by the Ethic Committee of Acibadem University in December 2021 with the approval number 2021-25/14.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: A.H.K., E.Ö., İ.B. Concept: A.H.K., G.Y., Ü.Ç., İ.B., Design: A.H.K., G.Y., Ü.Ç., İ.B., Data Collection or Processing: U.C., E.Ö., Analysis or Interpretation: E.Ö., M.Y., Literature Search: G.Y., M.Y., Writing: A.H.K., G.Y.

Conflict of Interest: The authors declare that they have no conflict of interest.

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