



Evaluation of tonsillectomy before kidney transplantation in patients with IgA nephropathy



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ABSTRACT

The effectiveness of a tonsillectomy before kidney transplantation (KTx) in suppressing the recurrence of IgA nephropathy (IgAN) has never been studied. The aim of this study was to analyze the effectiveness of a preoperative tonsillectomy for preventing IgAN recurrence and to identify predictive risk factors for IgAN recurrence. Of the 462 recipients who underwent a KTx between 2006 and 2011, a total of 78 patients had biopsy-proven IgAN as their primary disease. Among these 78 patients, 28 patients (group 1) underwent a tonsillectomy and 50 patients (group 2) did not undergo a tonsillectomy before KTx. The time to recurrence was 15.5 ± 8.7 months, in group 1 and 20.2 ± 18.6 months in group 2. No significant difference was observed between the two groups ($P = 0.63$). Using a multivariate Cox regression analysis, ABO incompatible KTx and acute rejection were associated with a lower incidence of recurrence ($P = 0.02$ and 0.002 respectively). These results suggested that a preoperative tonsillectomy might not affect the recurrence of IgAN during a short-term follow-up period, whereas preoperative desensitization and the use of a higher steroid dose were effective for suppressing the recurrence of IgAN.

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1. Introduction

IgA nephropathy (IgAN) is the most common form of glomerular nephritis worldwide. Despite therapeutic approaches for the treatment of IgAN, 20%–30% of patients develop kidney failure [1,2]. Kidney transplantation (KTx) is a successful treatment for patients with end-stage renal disease caused by IgAN. However, the recurrence of IgAN after KTx has increased in importance and can ultimately lead to graft loss. Since the pathogenesis of IgAN is not completely understood, many approaches to the treatment of IgAN in the native kidney have been proposed. A tonsillectomy is one such approach. Bene et al. [3] reported that the urinary protein level and microhematuria of 34 IgAN patients had decreased significantly at 6 months after a tonsillectomy, with no significant change in the serum creatinine (s-Cr) level. Although the use of a tonsillectomy for the treatment of progressive IgAN remains controversial, a tonsillectomy is regarded as one of the most effective approaches for the treatment of IgAN recurrences after KTx.

Although Kennnoki et al. [4] reported that a tonsillectomy alone reduced proteinuria in patients with IgAN recurring after KTx, the

efficacy of a tonsillectomy before transplantation for preventing the recurrence of IgAN has never been studied. The aim of the present study was to determine the incidence of IgAN recurrence as assessed using protocol and/or episodic biopsies and to examine the recurrence rate so as to verify whether a tonsillectomy before transplantation is effective for preventing recurrence and/or reducing the time to recurrence. The time until the appearance of hematuria, the time until the appearance of proteinuria, the degree of mesangial proliferation, and the MSET score according to the Oxford classification [5] at the time of recurrence were also analyzed to determine the effect of a tonsillectomy before transplantation on IgAN recurrence among patients with or without tonsillectomy before KTx who subsequently exhibited the recurrence of IgAN. Moreover, we also aimed to identify the predictive risk factors for IgAN recurrence after transplantation using a multivariate Cox regression analysis.

2. Materials and methods

2.1. Kidney transplant recipients

Between 2006 and 2010, KTx was performed in 462 patients at our department. Among these 462 kidney recipients, as shown in Fig. 1, 78 recipients whose primary disease was biopsy-proven IgAN were enrolled in this study. Of these 78 recipients, 75 patients had received a transplant from a living donor and 3 patients had received a transplant from a deceased donor; 4 patients had a previous history of renal transplantation.

Abbreviations: ABO-i, ABO-incompatible transplantation; AR, acute rejection; DSA, donor-specific antibody; eGFR, estimated glomerular filtration rate; IgAN, IgA nephropathy; KTx, kidney transplantation; MP, methylprednisolone; MMF, mycophenolate mofetil; rit, rituximab; s-Cr, serum creatinine level; FK506, tac, tacrolimus.

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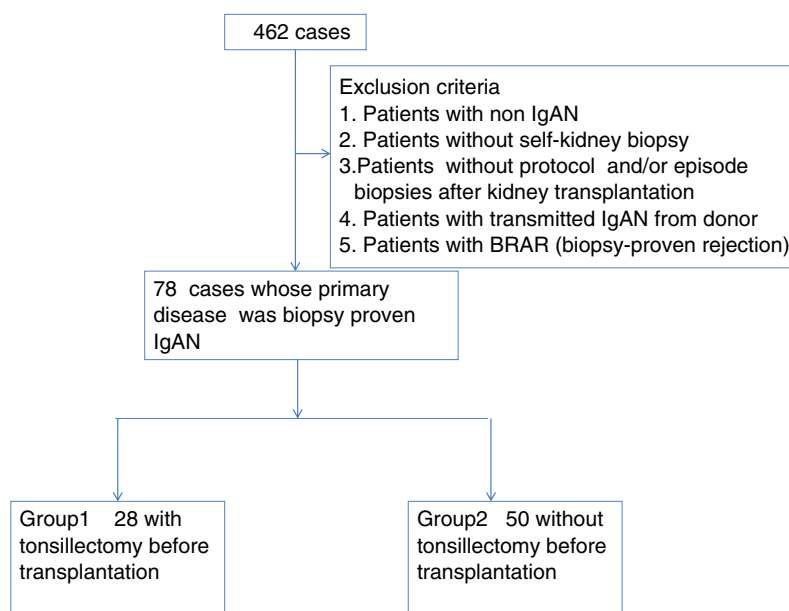


Fig. 1. Subject flow chart for this study. Between 2006 and 2011, KTx was performed in 462 patients at our department. Of these 462 patients, patients without a self-kidney biopsy, patients without protocol and/or episodic biopsies after KTx, patients with transmitted IgAN from the donor, and patients with biopsy-proven rejection were excluded from this study. We performed KTx in a total of 78 patients in whom the underlying renal disease before the surgery was biopsy-proven IgA nephropathy (IgAN). Of these 78 patients, 28 patients (group 1) had undergone and 50 patients (group 2) had not undergone a tonsillectomy before the KTx.

Of the 78 patients, 28 patients (group 1) had undergone a tonsillectomy before KTx and 50 patients (group 2) had not undergone a tonsillectomy before KTx. The graft survival rate and time to recurrence were analyzed respectively in both groups (Table 1-1, Fig. 2).

The time until the appearance of hematuria, the time until the appearance of proteinuria, and the degree of mesangial proliferation were also analyzed among the patients with IgAN recurrence (Table 1-2); biopsies for recurrences were evaluated according to the Oxford classification (Table 2). Finally, we analyzed the predictive factors associated with the recurrence of IgAN using a multivariate Cox regression analysis (Table 3).

This study was performed in accordance with the Declaration of Helsinki.

2.2. Baseline immunosuppressive therapy protocol and antihypertensive medications

All 78 patients received immunosuppressive therapy consisting of tacrolimus (FK506, tac), mycophenolate mofetil (MMF) and methylprednisolone (MP) during both the induction period and the maintenance period. No changes in the immunosuppressive regimen were made in either group during the study period.

2.3. Evaluation using light microscopy and immunohistochemistry

In our department, in addition to an episode biopsy, a protocol biopsy is generally conducted at 0 h, 1 month, 12 months, and 2 years after KTx. The zero-hour biopsy was performed using a wedge tissue resection during the operation to exclude the possibility of IgA-transmitted nephropathy from the donor.

Biopsies were performed using 16-Gauge needles. The tissue specimens were fixed using a routine method, followed by immunostaining. The sections were then stained with hematoxylin and eosin, periodic acid-Schiff (PAS), Masson trichrome, and periodic acid methenamine silver (PAM) stains for examination using light microscopy. The primary antibodies used were rabbit polyclonal antibodies against IgG, IgA and C3, and IgM (Hoechst, Behringwerke, AG, Marburg, Germany).

Recurrent IgAN was diagnosed histologically based on IgA deposition and the Oxford classification. These criteria were almost the same as those used for the diagnosis of primary IgAN.

2.4. Diagnosis of acute rejection

Acute rejection (AR) was diagnosed based on an increase in serum creatinine over the baseline value that could not be explained by any other cause. Rejection occurring within three months after transplantation was regarded as AR. The type of rejection was classified by two pathologists according to the Banff '07 criteria.

2.5. Evaluation of clinical data

Clinical data collected from our department included donor and recipient demographics, human leucocyte antigen (HLA) antibodies, HLA mismatches, and the type and number of transplantations. The data also included the occurrence of acute rejection (AR), the length of the follow-up period, and the use of immunosuppressive therapy. AR was considered as a non-time-dependent variable in the analysis. The occurrence of hematuria and proteinuria were also noted during the observation period.

2.6. Tonsillectomy

A tonsillectomy was performed for the treatment of original IgAN at a younger age (before the induction of dialysis) in 7 patients in group 1, while a tonsillectomy was performed in preparation for transplantation within 2 years before the actual transplantation in the remaining patients in group 1.

Unfortunately, no standard criteria have been established for performing tonsillectomy prior to transplantation. Even in the case of original disease of IgAN, tonsillectomy is controversial. However, the fact remains that no clearly effective treatments have been established for either the initial presentation of IgAN or recurrent IgAN. Tonsillectomy is one of the possible treatments for recurrent IgAN. However,

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