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Incidence and Risk Factors for Posttransplant Subcapsular Cataract: A Long-Term Retrospective Cohort Study

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ABSTRACT

Background. The occurrence and risk factors for posterior subcapsular cataract (PSC) after renal transplantation have received little attention.

Objectives. To analyze the cumulative incidence of PSC after renal transplantation and identify risk factors for the development of PSC.

Methods. Retrospective review of the records of the patients who underwent kidney transplantation between May 1986 and December 2008.

Results. We included 94 renal transplant recipients who showed PSC incidence at 5, 10, and 15 years of 3.5%, 40.5%, and 50.1%, respectively. Cumulative incidence of PSC during the follow-up was 37.2%. On multivariate analysis, age, body mass index (BMI) and cumulative corticosteroid dose were significantly associated with PSC. Recipient age above 50 years (hazard ratio [HR] = 2.88, 95% confidence interval [CI]: 1.42–5.83; $P = .003$), BMI above 25 kg/m^2 (HR = 2.28, CI: 1.09–4.78; $P = .029$), and prednisolone dose above 3 mg/kg/mo (HR = 7.79, CI: 3.34–18.99; $P < .001$) were independent risk factors for PSC. Diabetes, renal diagnosis, duration, and type of dialysis and posttransplant immunosuppressive regimen did not influence the occurrence of PSC.

Conclusion. The risk of PSC was low during the first years after transplantation reaching a plateau at 15 years posttransplantation. Among the risk factors for PSC, cumulative corticosteroid dose and body weight were the only modifiable risk factors.

ONE ADVERSE EVENT of corticosteroids, posterior subcapsular cataract (PSC), is the most common ocular complication following renal transplantation.[1] Yet, there is a lack of data on the long-term development of PSC in renal allograft recipients under modern immunosuppression using lower steroid doses. This retrospective study assessed the long-term development of transplant-related cataracts to identify risk factors in the era of modern immunosuppression.

METHODS

Subjects

We retrospectively studied living patients ($n = 150$) transplanted between May 1986 and 31 December 2008 with a follow-up of at least 1 year after consent of the local Ethics Committee. Reasons for exclusion were (1) steroid treatment ($n = 6$) or cataract surgery ($n = 2$) before transplantation; (2) loss to follow-up ($n = 9$) or graft loss within 1 year ($n = 2$); (3) ophthalmologic examination not available ($n = 30$) or (4) type of cataract not specified ($n = 7$).

Data Collection and Analysis

The following recipient variables were recorded at the time of transplantation: age, gender, renal diagnosis, duration of dialysis, type of dialysis, diabetes mellitus (DM), immunosuppressive drugs and human leukocyte antigen (HLA) CW3 haplotype. To calculate the body mass index (BMI), we calculated the mean body weight every 6 months from transplantation to the last follow-up. Because of the risk of a more aggressive PSC in cases of DM, we also recorded posttransplant DM.

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0041-1345/–see front matter
doi:10.1016/j.transproceed.2011.10.007

We analyzed the results of annual opthalmologic examinations performed in our department or in private practice. The moment a PSC was diagnosed was considered to be the start of PSC.

Among the patients who developed PSC, we calculated the months from transplantation to diagnosis, and the cumulative dose of corticosteroids during this period. For patients without PSC, we also estimated the months from transplantation to the last follow-up as well as the corresponding cumulative dose of corticosteroids, which was converted into prednisolone equivalents. The number of steroid pulses for treatment of acute rejection episodes was included in the cumulative corticosteroid dose.

We followed both eyes of 94 patients; for two other patients, only one eye was included because the other eye had been operated during follow-up without knowledge of the underlying reason.

Immunosuppression

All patients were initially treated with corticoids, a calcineurin inhibitor, and azathioprine or mycophenolate mofetil (MMF). Prior to 1996, all kidney transplant recipients received cyclosporine (CsA) as the calcineurin inhibitor associated with azathioprine and corticoids. From 1996 onward, the immunosuppression consisted of CsA or tacrolimus in combination with MMF plus corticoids.

Acute rejection episodes were treated with high-dose intravenous steroid pulses (methylprednisolone 1 g for 3 days).

Statistics

The initial analyses of our data were descriptive with baseline characteristics presented as the number of patients and percentages for categorical data, and as mean values with standard deviations for continuous data. The cumulative incidence of developing PSC after renal transplantation was calculated by Kaplan-Meier estimates. Results are presented graphically with cumulative incidences and associated 95% confidence intervals (CI). Univariate analysis of potential risk factors were performed for gender; age; BMI; duration dialysis; type of dialysis; renal pathology; HLA CW3+; diabetes pre- and posttransplantation, doses of prednisolone (>3 mg/kg/mo), MMF, CsA, tacrolimus, azathioprine, and steroid pulses as well as rejection episodes. The univariate relationship between the risk of developing PSC and the above-mentioned factors was evaluated by the log-rank test.

Multivariate analysis of potential risk factors was performed by the Cox stepwise proportional hazards method. All of the above-mentioned factors were included in the Cox proportional hazards model. Results are expressed with hazard ratios and associated 95% CIs. All analyses were performed employing the PASW software package (PASW version 17.0, SPSS Inc, Chicago, Ill, USA).

Our initial plan was to use the generalization of the Cox proportional hazards model to correlate time-to-event data. This method allows us to analyze data for outcome events that can occur in more than one body part in the same person, and to adjust for correlations between body parts (eyes) in the same person. We observed that the vast majority of patients with incident PSC developed the outcome event in both eyes at the same time, thus we considered only counting one PSC episode (outcome event) per patient in our analyses, and, thus, did not use the generalization of the Cox proportional hazards model.

RESULTS

Patient Demographics at Transplantation

The 94 patients including 55 males and 39 females had an overall mean patient age at renal transplantation of 49.4 ± 12.1 years with 44.1% at least 50 years old. The mean BMI was 25.8 ± 4.5 kg/m^2 with more than 50% showing a BMI of at least 25 kg/m^2. Their mean duration of dialysis prior to transplantation was 25.6 ± 22.5 months. Sixty-seven patients (72%) had received hemodialysis. Their renal diagnoses were: glomerulonephritis (30.1%), interstitial nephropathy (22.6%), nephroangiosclerosis (21.5%), congenital nephropathy (18.3%), and unknown etiology (7.5%). Eight patients had DM before transplantation (8.5%) and 19 after transplantation (20.2%).

The immunosuppressive protocols consisted of CsA (85.1%) or tacrolimus (12.8%) in combination with MMF (62.4%) or azathioprine (37.2%) plus corticosteroids. The mean prednisolone dose was 3.45 + 1.73 mg/kg/mo with a median of 3 mg/kg/mo. Seventy-two patients (76.6%) were free of rejection while 22 (23.4%) had been treated with steroid pulses.

Incidence of PSC

Thirty-five (37.2%) of 94 renal recipients developed PSCs during the observation period. The diagnosis of PSC was made between 12 and 159 months after transplantation (mean = 50.3). Thirty patients had bilateral PSC (85.7%); only five patients showed unilateral PSC (14.3%). Table 1 presents the cumulative incidence estimates of PSC after renal transplantation.

Risk Factors for Developing a PSC

Upon univariate analysis, only age and corticosteroid dose had impact on the development of PSC. When divided according to mean age, recipients aged at or above 50 years showed a significantly higher risk to develop PSC than those younger than 50 years (log-rank test, $P = .036$). The cumulative incidence of PSC for aged versus younger patients is shown in Fig 1.

When divided according to median corticosteroid dose, recipients treated with prednisolone > 3 mg/kg/mo displayed a significantly higher risk to develop PSC than those who received less than 3 mg/kg/mo (log-rank test, $P < .001$). The cumulative incidence of PSC for patients receiving

Table 1. Cumulative Incidence Estimates for PSC Among Renal Transplantation Recipients (n = 94)

	Posterior subcapsular cataract	
Years after renal transplantation	Cumulative incidence (%)	95% confidence limits
5	3.5	0–13.1
10	40.5	29.1–51.9
15	50.1	36.1–64.1
20	50.1	36.1–64.1

PSC, posterior subscapsular cataract.