Fine Needle Aspiration Cytology and Detection of Lymphocyte Subsets in Kidney Transplant Patients Receiving Induction with Basiliximab or Thymoglobulin: Impact on Kidney Function

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Abstract

Monitoring the expression of the receptor CCR4 by cytometry in the conventional CD4 T-cell and T-regulatory cell subsets may be useful to study the course of the immune response in transplant patients with delayed graft function or worsening graft function. **(Trends in Transplant. 2013;7:74-5)**

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Key words

Kidney transplantation. CD4. T-cells. Immunosuppression.

Introduction

Induction therapy with basiliximab or thymoglobulin after kidney transplantation modifies the expression of lymphocyte subsets, including T-regulatory (T_{reg}) cells (CD127lowCD25high)[1,2,3], which may influence renal graft function. Monitoring subpopulations using blood samples allows control of these modifications. However, this has scarcely been studied using fine needle aspiration cytology (FNAC). We monitored the lymphocyte populations, using FNAC, in renal transplant recipients with delayed renal function or renal dysfunction as measured by creatinine levels. We detected the high expression of the guiding CCR4 chemokine receptor in T lymphocytes and $CD4^+$ T_{reg} conventional cells as lymphocytes with these characteristics can be responsible for the alloresponse[4].

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Material and methods

This cross-sectional study involved 27 patients of both sexes that received a kidney transplant at Carlos Haya Hospital in 2012. We used a blood sample and FNAC of the graft obtained six months posttransplantation. We studied by flow cytometry the expression of the receptor CCR4 in $CD127^{high}CD25^{low}$ and T_{reg} cells.

Statistical analysis

Results of quantitative variables are expressed as mean ± standard deviation and qualitative variables as relative percentages. We used the T test and Fisher exact probability test for quantitative and qualitative variables, respectively. A value of $p < 0.05$ was considered significant.

Results

The mean age of the 19 men and eight women was 53.5 ± 15 years; none had acute rejection. Overall, the patients who received basiliximab (as compared with thymoglobulin) had a greater percentage of CD4 T-cells (31.4 ± 10.3 vs. 19.5 ± 12.3%; $p = 0.033$) and a lower proportion of CD8 T-cells (22.7 ± 12.5 vs. 43.1 ± 23.7%; $p = 0.020$) in the FNAC. The CD4/CD8 ratio was significantly higher in the basiliximab group (2.36 ± 3.11 vs. 0.33 ± 0.15; $p = 0.0001$).

Thymoglobulin was associated with an increased percentage of T_{reg} cells as compared with basiliximab in blood samples (13.2 ± 10.7 vs. 9.5 ± 6.0%), although this trend was not seen in the FNAC samples (9.1 ± 6.7 vs. 9.5 ± 7.0%). The patients with posttransplant delayed graft function had increased CD8 T-cells (39.5 ± 21.0 vs. 19.6 ± 14.5%; $p = 0.029$) and expression of the receptor CCR4 on the T_{reg} cells (14.0 ± 22.4 vs. 9.6 ± 17.0%) as compared with those who had immediate graft function. Likewise, a worse renal function (Crs ≥ 2 mg/dl) at six months was associated with a similar result (CD8: 44.6 ± 14.6 vs. 24.5 ± 20.0; $p = 0.06$ and CCR4: 24.0 ± 27.0 vs. 7.6 ± 14.7%; $p = 0.09$).

Discussion

The main finding was that the CD4/CD8 ratio in patients receiving basiliximab as induction therapy remains at normal levels (> 2). However, this ratio was < 1 in the thymoglobulin group. In addition, the T_{reg} cell populations were similar at the sixth month regardless of the induction therapy. In a previous report, thymoglobulin induced a prolonged decline of the CD4/CD8 ratio up to five years after treatment, which could be a consequence of $CD4^+$ T-cell depletion and an increased regeneration of $CD8^+$ T-cells[1].

The second finding was that the results showed a trend toward an increasing percentage of CD8 and CCR4 T_{reg} cells in patients with delayed renal function. The same trend was observed in patients with Crs ≥ 2 at the sixth month posttransplantation. In the absence of confirmation by biopsy, these data could allow us to detect subclinical rejection[5].

In summary, our data suggest that it is feasible to use basiliximab as induction therapy since the determination of cell markers detected by flow cytometry and FNAC showed normal lymphocyte populations. Further longitudinal studies are needed to confirm these findings.

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