Histologic Inflammatory Changes on the Prostatic Gland Due to Immunosuppression for Kidney Transplantation

Affonso Celso Piovesan, Fabio Cesar Miranda Torricelli, Ioannis Michel Antonopoulos, Renato Falci Junior, Hideki Kanashiro, and William Carlos Nahas

OBJECTIVE To determine the incidence of type IV prostatitis in patients with kidney transplantation receiving an immunosuppression regimen and to compare it with that of a nonimmunosuppressed control group.

METHODS We retrospectively reviewed 216 electronic charts of patients who had undergone surgical treatment for benign prostatic hyperplasia from August 2000 to January 2006. Of the 216 patients, 183 did not receive immunosuppressive therapy and were included in the control group (group 1). The other 33 patients had undergone kidney transplantation and were included in the study group (group 2). The patient data were accessed for age at surgery, International Prostate Symptom Score, prostate volume, preoperative serum prostate-specific antigen level, history of acute urinary retention, and surgical approach (open vs transurethral resection of prostate). Histologic findings from the surgical specimens were also recorded.

RESULTS The mean age at surgery, mean serum prostate-specific antigen level, mean prostate volume, and mean International Prostate Symptom Score were not significantly different between both groups. However, histologic evidence of chronic prostatitis was obtained in 145 surgical specimens (78%) from group 1 and in just 3 specimens from group 2 (9%; $P < .001$). Moreover, nonimmunosuppressed patients had a 38.2 times greater risk of presenting with prostatitis than did the immunosuppressed patients.

CONCLUSION Imunnosuppresion therapy in kidney transplantation has a protective factor in the prostatitis incidence. UROLOGY 79: 662–664, 2012. © 2012 Elsevier Inc.

Prostatitis is a histologic inflammation of the tissue of the prostate gland, usually in response to an infection. However, it is not always a previous condition. According to the National Institutes of Health type IV prostatitis includes asymptomatic patients in which diagnosis is performed under biopsy for investigation of an elevated prostate-specific antigen (PSA) level or suspicious digital rectal examination findings, or as a histologic finding in surgical specimens from transurethral or open surgery for benign prostatic hyperplasia (BPH).

The presence of an inflammatory process in the prostatic gland has been implicated as an important etiologic factor for the development of BPH. The enhancement of interleukin concentrations, increasing expression of cyclo-oxygenase-2 receptors, and high levels of C-reactive protein have been documented in patients with an enlarged prostate, suggesting amplification of inflammatory activity on prostatic tissue compared with that of normal glands.[1]

Patients who have undergone kidney transplantation receive immunosuppressive drugs that reduce renal inflammatory reactions. Their action is directed preferentially to the cellular immune response.[2] The immunosuppression action on the prostatic gland is a subject poorly studied, and the few reports of transurethral resection of the prostate (TURP) on patients who had undergone kidney transplantation[3,4] have not discussed the histologic or inflammatory aspects.

The purpose of the present study was to determine the incidence of prostatitis on kidney transplantation patients receiving an immunosuppression regimen and to compare it with a nonimmunosuppressed control group.

From the Renal Transplantation Unit, Division of Urology, University of São Paulo Medical School, São Paulo, São Paulo, Brazil; and Renal Transplantation Unit, Division of Urology, University of São Paulo Medical School, São Paulo, São Paulo, Brazil

Reprint requests: Fábio César Miranda Torricelli, M.D., Av. Vereador Jose Diniz, 3300, Conjunto 208, São Paulo, SP CEP 04604-006 Brazil. E-mail: fabio_torri@yahoo.com.br

Submitted: September 16, 2011, accepted (with revisions): November 7, 2011

0090-4295/12/$36.00
doi:10.1016/j.urology.2011.11.006

Table 1. Preoperative data

Group	Patients (n)	Age (y)	IPSS	Prostate Volume (cm^3)	PSA Level (ng/mL)
1	183	63 ± 4.3	21 ± 6.1	42.4 ± 10.5	5.1 ± 2.5
2	33	61 ± 13.2	18 ± 4.2	35.6 ± 9.3	7.5 ± 4.5

IPSS, International Prostate Symptom Score; PSA, prostate-specific antigen.
Data presented as mean ± standard deviation.

Table 2. Incidence of type IV prostatitis

Prostatitis	Immunosuppressed Patients (Group 2)	Nonimmunosuppressed Patients (Group 1)	Total (n)
No	30	38	68
Yes	3	145	148
Total	33	183	216

Odds ratio (transplanted vs control) 38.2, 95% confidence interval 110-131.8; Fisher's exact test, $P < .001$.

MATERIAL AND METHODS

As is routine in our service, the preoperative evaluation of patients with BPH includes a detailed history with the International Prostate Symptom Score (IPSS) assessment, a complete physical examination, including a digital rectal examination, measurement of the serum PSA level, and suprapubic ultrasonography of the prostate. Antibiotics were given according to a history of acute urinary retention. Patients with a Foley catheter received 1.0 g intravenous ceftriaxone 1 hour before surgery and every 12 hours for 2 days. After discharge, they continued taking ciprofloxacin 1.0 g/d for 5 days, completing 7 days of treatment. The others received cefalotin 2.0 g intravenously 1 hour before the surgical procedure and 4.0 g/d for 2 days or until the Foley catheter was removed.

We retrospectively reviewed 216 electronic charts of patients who had undergone surgical treatment for BPH from August 2000 to January 2006. Of the 216 patients, 183 did not receive immunosuppressive therapy and were included in the control group (group 1). The other 33 patients had undergone kidney transplantation and were included in the study group (group 2). All patients in the present analysis had undergone surgical treatment of BPH because of obstructive or irritative symptoms without a clinical response to conventional drugs.

The patient data were accessed for age at surgery, IPSS, prostate volume, preoperative serum PSA level, a history of acute urinary retention, and surgical approach (open vs TURP). The histologic findings from the surgical specimens were also recorded. All patients had completed the IPSS before and 6 months after surgical intervention.

To determinate the *P* values, we used the Mann-Whitney *U* test or Student *t* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. All statistical analyses were performed, with $P < .05$ considered significant.

RESULTS

The mean patient age was 63 and 61 years old in groups 1 and 2, respectively. In group 1, 40 and 5 patients underwent TURP and 138 underwent suprapubic transvesical prostatectomy. In group 2, all 33 patients underwent TURP. The mean ± standard deviation interval between kidney transplantation and TURP was 59 ± 81 months. Of the patients in group 1, 27 (15%) had urinary retention and presented with a Foley catheter in place compared with 1 patient (3%) in group 2.

The mean age at surgery, mean serum PSA level, mean prostate volume, and mean IPSS were not significantly different between the 2 groups (Table 1). However, histologic evidence of chronic prostatitis was obtained from 145 surgical specimens (78%) from group 1 and just 3 specimens from group 2 (9%; $P < .001$; Table 2). Moreover, nonimmunosuppressed patients had a 38.2 times greater risk of presenting with prostatitis than did the immunosuppressed patients (odds ratio 38.2, 95% confidence interval 11.0-131.8).

COMMENT

The typical histologic signal of prostatitis is invasion of leukocytes into the prostatic ducts and periprostatic tissue, especially polymorphonuclear leukocytes.[1,5] Its clinical presentation varies widely, ranging from asymptomatic patients to those with chronic pelvic pain that can even be incapacitating. The 1995 National Institutes of Health classification divided prostatitis into 4 categories: types I and II are associated with bacterial infection and type III with chronic pelvic pain with (IIIa) and without (IIIb) inflammation of the gland. Type IV prostatitis includes asymptomatic patients in whom the diagnosis is after biopsy for investigation of an elevated PSA level or suspicious digital rectal examination findings or as a histologic finding in surgical specimens from transurethral or open surgery for BPH.

The incidence of type IV prostatitis is unknown, but some previously reported studies have shown that it appears to be very frequent in asymptomatic men. Reviewing the material obtained from 80 patients who had undergone transurethral resection of the prostate, Nickel et al[1] reported inflammation in all specimens. Kohnen and Drach[6] in a similar study found an incidence of 98% in 168 patients. In studies with biopsy sample analysis, the incidence has been more varied, ranging from 17.2% to 47%.[7] In our institution, a previous study found pros-

tatitis in 78% of patients undergoing benign prostatic surgery because of BPH.[8]

The immunosuppressive drugs used after kidney transplantation are directed preferentially to the cellular immune response. Their effect in reducing the inflammation process substantially renal allograft is well-known.[2] Although their action on the prostatic gland has never been studied, it was intuitive to believe it would lead to a considerable reduction in the prostatitis incidence. This impression was strongly enhanced by the results we obtained in the present study. The prostatitis incidence was much greater in the control group than in the immunosuppressed patients. However, the number of patients in group 1 was relatively small, which would have a clear effect in the precision of the odds ratio analysis (wider range in confidence intervals and overestimated value).

The long-term measurement of prostatic growth and the evaluation of lower urinary tract symptoms in kidney transplanted patients versus a control group would seem to be an excellent clinical trial to confirm the investigative data linking the relationship between the inflammatory process and prostatic enlargement. It would be very useful in understanding the role of the inflammatory process in the development of BPH.

CONCLUSIONS

The present study has shown that immunosuppressed patients have a lower incidence of prostatitis than nonimmunosuppressed patients. Imunnosuppresion therapy after kidney transplantation has a protective factor in the incidence of prostatitis.

References

1. Nickel JC, Downey J, Young I, et al. Asymptomatic inflammation and/or infection in benign prostatic hyperplasia. *BJU Int*. 1999;84: 976-981.
2. Metalidis C, Kuypers D. Immunosuppressive therapy after kidney transplantation: current and new strategies. *Minerva Urol Nefrol*. 2011;63:1-19.
3. Védrine N, Nsabimbona B, Soares P, et al. [Transurethral resection or incision of the prostate in the immediate postoperative follow-up of renal transplantation]. *Prog Urol*. 2009;19:845-849.
4. Koziolek MJ, Wolfram M, Müller GA, et al. Benign prostatic hyperplasia (BPH) requiring transurethral resection in freshly transplanted renal allograft recipients. *Clin Nephrol*. 2004;62: 8-13.
5. Jung K, Meyer A, Lein M, et al. Ratio of free-to-total prostate specific antigen in serum cannot distinguish patients with prostate cancer from those with chronic inflammation of the prostate. *J Urol*. 1998;159:1595-1598.
6. Kohnen PW, Drach GW. Patterns of inflammation in prostatic hyperplasia: a histologic and bacteriologic study. *J Urol*. 1979;121: 755-760.
7. Morote Robles J, López López M, Encabo Duro G, et al. [The incidence of lesions associated with prostatic biopsy and its effect on the serum concentration of the prostate-specific antigen]. *Actas Urol Esp*. 1999;23:400-405.
8. Piovesan AC, Freire Gde C, Torricelli FC, et al. Incidence of histological prostatitis and its correlation with PSA density. *Clinics (Sao Paulo)*. 2009;64:1049-1051.