Inflammatory lesions associated with BPH – impact on post TURP symptoms

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Abstract

Introduction: Association between BPH and prostatic inflammation has been well recognized. The ways that inflammation influences prostatic growth and symptoms progression are still under investigation and generated both interest and controversies. The aim of this study was to assess the impact of prostatic inflammation on early post TURP symptoms.

Material and methods: We analyzed 100 consecutive patients who underwent TURP for symptomatic BPH in our clinical department between January and July 2012. The patients with other possible causes of LUTS or with a history of prostatitis within 1 year prior to surgery were excluded. On the basis of the histopathological reports we divided the patients in 4 groups: patients without inflammatory lesions associated to BPH were included in group 1. Group 2, 3 and 4 included patients with mild, moderate and severe inflammation, respectively. All tissue samples were analyzed by the same pathologist. The correlation between the presence and the degree of inflammation and different pre, intra and postoperative parameters were assessed. The patients were evaluated at 6 weeks and 6 months.

Results: The comparative evaluation of preoperative parameters of patients from the 4 groups demonstrate higher IPSS, PSA, prostate volume and urinary retention rate values in patients with inflammation on histopathological exam. No significant differences were described concerning the operative time, catheterization and hospital stay period or intra- and postoperative complications. The evaluations at 6 weeks and 6 months demonstrate differences only in symptoms, Qmax and residual volume being relatively similar in the 4 groups. During the follow-up period re-catheterisation was necessary in one patient from group 2 and 2 patients from group 4.

Conclusions: The presence and the degree of inflammation on histopathological exam correlate with higher IPSS, PSA and prostatic volume values and increased risk of urinary retention. Postoperative, significant differences exist only for symptoms.

Key words: BPH, inflammation, TURP, symptoms, postoperative

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Introduction

Frequent association of benign prostatic hyperplasia (BPH) and inflammation has generated much interest in the recent decades. The precise mechanisms that inflammation influences the growth of prostate and the development of symptoms in patients with BPH are still under investigation.

The incidence of inflammation (acute but especially chronic) on prostate biopsy specimens or in tissue obtained by transurethral resection of the prostate (TURP) varies between 43 % and 98 % [1, 2]. In the literature has been published many studies and data on various histological and clinical correlations of this association. Most of them were focused on the type of inflammation associated with BPH, predominance of specific inflammatory cells, inflammation influence on PSA and prostate volume, symptom progression and the risk of complications and surgery [3]. The current concern is, however, to evaluate possible drug treatments for inflammation that probably trigger for the histological and clinical progression of BPH. For this reason there are several recent studies in the literature related to the medical treatment of patients with BPH and inflammation, but only limited data regarding the impact of associated inflammation on postoperative evolution in patients undergoing surgery for BPH. For this reason, the aim of this study was to assess the influence of associated inflammation with the development of postoperative patients who underwent TURP.

Material and methods

The study was conducted on a group of 100 patients operated in the Urology Clinic of Emergency Hospital “St. John” between January 2012 and July 2012. Patients with other causes of lower urinary tract symptoms (urethral strictures, neurological disorders, bladder stones, etc.) and those with a history of prostatitis in the last 12 months prior to surgery were excluded from the study. All patients had sterile urine cultures and normal number of leukocytes in preoperative urinalysis. We considered that a high number of leukocytes in urinalysis may signify the presence of inflammation induced by infection in adjacent tissues, including the prostate.

Assessment protocol included preoperative patient history to calculate IPSS score, digital rectal exam, abdominal ultrasound to determine prostate volume and residual volume, PSA and Qmax. Based on histopathological reports, patients were divided into four groups according to the scale proposed by Irani [4]: patients without associated inflammatory lesions were included in group 1, patients with BPH and mild inflammation in group 2 (fig. 1), those with moderate inflammation in group 3 (fig. 2) and those with severe inflammation associated in group 4 (fig. 3). All tissue samples were analyzed by the same pathologist.

Based on these data, we evaluated the correlations between the presence and degree of inflammation and different pre-operative parameters: prostate volume, IPSS score, residual urine volume, presence of urine retention (AUR).

We also studied the immediate postoperative aspects such as intra- and postoperative complications rate, duration of catheterization, length of hospital stay and re-catheterization rate for all groups.

The patients were re-evaluated at 6 weeks after surgery and then at every 6 months. Control at 6 weeks included clinical and rectal examination, abdominal
ultrasound to determine the residual urine volume and Qmax. Assessment at 6 months included the determination of PSA.

**Results**

After histopathological evaluation of resected tissue, patients were included in 4 groups as follows (Table 1):

- Group 1 (without associated inflammation) - 34 patients
- Group 2 (with mild inflammation) - 28 patients
- Group 3 (with moderate inflammation) - 24 patients
- Group 4 (with severe inflammation) - 14 patients.

The average preoperative IPSS score was 23.1. In the group of patients without inflammation was 22.5 compared to 23.4 in those with inflammatory issues highlighted histopathological. The differences were significant, especially in patients with severe inflammation (26.2).

PSA has values which ranged from 1.7 ng/ml in group 1 to 3.7 ng/ml in patients in group 4.

And in terms of the average prostate volume, there were differences depending on the presence of inflammation, this being 48.5 cc in patients with non-inflammatory aspects and 54.2 cc in those with inflammation. Similar, the differences in the case of PSA were more important in patients with severe inflammation (62.3 cc).

In all seven patients who presented preoperative urinary retention, inflammatory factors were detected on histopathological examination.

<table>
<thead>
<tr>
<th>Table 1. Preoperative characteristics of the patients in the study group</th>
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<tbody>
<tr>
<td><strong>Number of cases</strong></td>
</tr>
<tr>
<td>Group 1</td>
</tr>
<tr>
<td>Group 2</td>
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<tr>
<td>Group 3</td>
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<tr>
<td>Group 4</td>
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There were no significant differences in the duration of surgery, the rate of intra or immediate postoperative complications (Table 2).

<table>
<thead>
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<th>Table 2. Perioperative issues in the 4 groups</th>
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<td><strong>Duration of surgery</strong></td>
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<td>Group 1</td>
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<td>Group 2</td>
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<td>Group 3</td>
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<td>Group 4</td>
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The patients evaluation at 6 weeks (Table 3) showed difference regarding symptomatology, this being significantly improved in patients without inflammation, while the residual urine volume and Qmax and were very similar in the four groups.

<table>
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<th>Table 3. Results at 6 weeks</th>
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<tr>
<td><strong>IPSS</strong></td>
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<td>Group 1</td>
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<tr>
<td>Group 2</td>
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<td>Group 3</td>
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<td>Group 4</td>
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In addition, assessment at 6 months (Table 4) showed no difference in the Qmax, residual urine volume or PSA values, but the differences being main-
tained regarding to symptoms. During follow-up, re-
catheterization was necessary for a patient in group 2
and for 2 patients in group 4.

Table 4. Results at 6 months

<table>
<thead>
<tr>
<th></th>
<th>IPSS</th>
<th>Qmax</th>
<th>Residual volume</th>
<th>PSA</th>
</tr>
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<tbody>
<tr>
<td>Group 1</td>
<td>5,2</td>
<td>22,4 ml/s</td>
<td>22 ml</td>
<td>0,82 ng/ml</td>
</tr>
<tr>
<td>Group 2</td>
<td>5,4</td>
<td>23,5 ml/s</td>
<td>34 ml</td>
<td>0,76 ng/ml</td>
</tr>
<tr>
<td>Group 3</td>
<td>7,2</td>
<td>22,5 ml/s</td>
<td>25 ml</td>
<td>0,92 ng/ml</td>
</tr>
<tr>
<td>Group 4</td>
<td>7,6</td>
<td>23,2 ml/s</td>
<td>37 ml</td>
<td>1,2 ng/ml</td>
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</table>

Discussions

Benign prostatic hyperplasia (BPH), the most com-
mon urological disease of elderly men, is defined his-
tologically by epithelial and stromal cells hyperplasia
of the transition zone and periurethral area of the pros-
tate. It is a progressive disease, histological incidence
of BPH is over 70% in men 61 to 70 years and over 90% of
those over 70 years of age [5]. Enlargement of the pros-
tate leads to bladder neck obstruction and clinically
to the development of lower urinary tract symp-
toms, the risk of acute urinary retention and the need
for surgery [3, 6]. The literature data has shown that
there is not a close correlation between histological
BPH and symptoms, meaning that the presence of his-
tologic BPH does not necessarily imply the occurrence
of clinical symptoms.

Although highly studied, BPH pathogenesis re-
mains unclear. It was clearly demonstrated that andro-
gens play a key role in pathogenesis, but at the same
time, there are multiple theories regarding other fac-
tors involved in the development and progression of
this disease.

More recent data suggest that inflammation is an
important factor that affects the growth of the prostate
and progression of the symptoms. Both acute inflam-
mation, but especially the chronic inflammation was
frequently detected in fragments of tissue obtained by
prostate biopsy or after TURP with an incidence rang-
ning between 43% and 98% [1] . In our study, inflamma-
tion was detected in 66% of cases.

The association of histological BPH - inflammation
aroused much interest and, therefore, there are nu-
umerous published data in the literature on the fre-
quency of this association. These include MTOPS (Me-
dical Therapies of Prostatic Symptoms) and REDUCE
(Reduction by Dutasteride of prostate Cancer Events),
regarded as two of the largest randomized clinical tri-
als conducted, both in terms of number of patients
enrolled and the duration of the deployment period.
Thus, based on the data provided by REDUCE study,
Nickel et al reported the identification of association of
chronic inflammation in 77.6% of patients enrolled,
while acute inflammation was present in only 16.5% of
cases [7].

In another study, the same author prospectively
examined the tissue specimens obtained after TURP in
80 patients with BPH and no history or symptoms of
prostatitis and incidence of inflammation was 100% [8].

Analysis of prostatic biopsy specimens collected at
the enrollment in MTOPS study identified the presence
of acute prostatic inflammation in 2.6% of patients while
chronic inflammation had an incidence of 43% [9].

An increased incidence of association BPH - chronic
inflammation, ranging between 43% and 98% is con-
firmed by Kohnen and Drach after the analysis of post
TURP tissue samples from patients with no symptoms
of prostatitis [10].

Once demonstrated the frequent association of
inflammation in patients with BPH there were also
studied and its implications on prostate volume, lower
urinary tract symptoms progression and risk of acute
urinary retention. Thus, the 2.6% of patients enrolled in
the MTOPS study on which it was identified the pre-

dence of acute inflammation, the prostate volume were
significantly higher compared with patients without
associated inflammation, respectively 41.1 ml vs. 36.8
ml [9]. Di Silverio et al found, after analysis of tissue
specimens obtained by TURP, that the incidence of
chronic inflammation founded parallel increases with
prostate volume from 8.9% in prostates volume of 30-
39 ml at 61.4% in prostates of 80-89 ml [11]. In our
study group there were also significant differences,
prostate volume being 48.5 cc in those without inflam-
atory aspects comparing with 54.2 cc in those with
inflammation.

Several authors have suggested that the presence of
histologic inflammation is a predictor of clinical pro-
gression of BPH. The impact of BPH associated inflam-
mation on LUTS and risk of urinary retention was prob-
ably the most intensively studied by Roehrborn who
has published several articles on this subject, the most
important being that result from the analysis of data
generated by MTOPS study . Follow-up of the patients
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TURP, that the incidence of chronic inflammation founded parallel increases with prostate volume from 8.9% in prostates volume of 30-39 ml at 61.4% in prostates of 80-89 ml [11]. In our study group there were also significant differences, prostate volume being 48.5 cc in those without inflammatory aspects comparing with 54.2 cc in those with inflammation.

Several authors have suggested that the presence of histologic inflammation is a predictor of clinical progression of BPH. The impact of BPH associated inflammation on LUTS and risk of urinary retention was probably the most intensively studied by Roehrborn who has published several articles on this subject, the most important being that result from the analysis of data generated by MTOPS study. Follow-up of the patients enrolled in this study demonstrated that regardless of the treatment arm they were included, the progression of symptoms and the risk of urinary retention or surgery was higher in patients with associated inflamma-
tion. The progression of symptoms was described in 13.2% of patients without inflammation, need for surgery in 3.9%, and no patients in this category did not develop acute urinary retention. Comparison, in patients with chronic inflammation, the progression of symptoms occurred in 21% of them, need for surgery in 7.3% and urinary retention in 5.6% [12]. In our study, all patients who had urinary retention have had inflammatory elements detected on histopathological examination.

Several studies suggest a strong correlation between the presence of prostatic inflammation and the risk of urinary retention. Roehrborn in the same MTOPS data analysis shows that patients with acute inflammation associated have a higher risk of urinary retention (2.4%) than in patients without inflammation (0.6%) [12]. Kefi et al concluded that chronic prostatic inflammation is a predictive factor for acute urinary retention more important than age, prostate volume or PSA value [13].

With the demonstration of frequent association inflammation - BPH and its close correlations with clinical progression and complications such as urinary retention appeared natural assumption that the treatment of associated inflammation may represent a new target for the treatment of BPH. A proponent of this theory is Nickel that stresses the importance of additional treatment (anti-inflammatory) in patients with BPH and inflammation [3]. Some of the usual treatments of BPH (alpha blockers, 5-alpha reductase inhibitors) besides the main mechanism of action presents and anti-inflammatory effects by inducing or increasing prostate apoptosis [14, 15]. However, most published studies relate to effects of using NSAIDs in combination with usual medication to treat inflammation associated with BPH. A study by Di Silverio however shows that there are no significant differences in IPSS score improvement between patients treated with finasteride and rofecoxib (COX-2) and those treated with finasteride only [16]. More recent data published by Minnery and Getzenberg however shows that it can achieve significant improvement in IPSS score using anti-inflammatory - alpha blocker association comparing to alpha blocker monotherapy [17].

In the past decade, herbal medicine treatment has been widely increasingly used for BPH, and one of the main effects attributed to these products is anti-inflammatory. A study published by Navarrete show a reduction of inflammatory infiltrates in prostatic resection tissue in patients who have received treatment with extract of Serenoa repens [18]. Other authors have found that use of NSAIDs decreases twice the risk of prostate volume growth, reducing lower urinary tract symptoms and the risk of urinary retention [19].

Using different types of medication to treat inflammation associated with BPH is still under investigation, and obtaining data to reduce inflammation and clinical response is hampered by the low rate of confirmation of inflammation before treatment [6].

In literature there are few data on the influence of inflammation on the results of surgical treatment of prostate adenoma. A study published in 2011 by Yalcinkaya [20] assessed the impact of asymptomatic prostatitis (NIH IV) association in patients with BPH. Studying the data of 247 patients, the authors observed a significantly higher rate of re-catheterisation in patients with associated inflammation. Also, symptoms assessed at 90 days after surgery by IPSS and QoL was significantly improved in the group with BPH without histological evidence of prostatitis. From the point of view of Qmax, no differences were found between the two groups.

Another recently published study on 144 cases [21] points out that the severity of lower urinary tract symptoms is increased both preoperatively and after TURP in the presence of inflammatory lesions, which are correlated with the degree of inflammation.

Data from our study showed a correlation between the symptomatic postoperative score and the presence of inflammation in resection specimens, without Qmax and residual volume to be influenced. Also, re-catheterisation was necessary only in patients with associated inflammation.

Conclusions

The presence and degree of histopathological evidenced inflammation is associated with significantly higher values of IPSS score, prostate volume, PSA and incidence of urinary retention. Intraoperative and immediate postoperative issues are not influenced by the presence of these lesions. After the surgery, there are significant only in respect of the symptoms and the rate of recatheterisation. Further studies are needed to confirm these data and to determine any additional remedial measures to improve the results of surgical treatment in these patients.
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