Differentiation of Granulomatous Prostatitis from Prostate Carcinoma

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ABSTRACT

Background and Objective: Non-specific granulomatous prostatitis is an uncommon diffuse inflammatory condition of the prostate. It is important because it may be mistaken for prostatic carcinoma. The aim of the study was to determine the prevalence of non-specific granulomatous prostatitis (NSGP) and comparing the results of transrectal ultrasonography, serum prostate specific antigen (PSA) and free prostate specific antigen levels, digital rectal exam (DRE) in NSGP with the prostate carcinoma and benign prostate hyperplasia.

Materials and Methods: During a cross-sectional study, the prostate needle biopsy cases with the granulomatous prostatitis diagnosis that had been referred to one of the largest pathology centers (1 year: 2006) were found and their clinical files were revised from the point of DRE, transrectal ultrasonography (TRUS), fPSA, and PSA. Some clinical and pathology findings such as age, microscopic findings, sonography information and experimental findings that had been necessary for the study were gathered and analyzed using SPSS software.

Results: Out of 783 needle biopsies of prostate, 8 (1.02%) cases were non-specific granulomatous prostatitis. The age range of patients was 55-76 years (with a mean of 66.1 years). Mean of PSA level was 19.45 ng/ml and fPSA level was 0.7 ng/ml. In 2 patients, TRUS showed focal hypoechoic areas and in other 2 of these DRE revealed asymmetry and mild nodularity.

Conclusion: There is no pattern of clinical, biochemical or ultrasound findings that allows a specific diagnosis of granulomatous prostatitis to be made or differentiate it from prostatic carcinoma and the biopsy is still necessary for the certain disease diagnosis.

Key words: Chronic Granulomatous Disease, prostatitis, Carcinoma

Introduction

Non-specific granulomatous prostatitis (NSGP) is an uncommon diffuse inflammatory condition of the prostate which rarely presents clinically in urological practice. It is important because it may be mistaken for prostatic carcinoma both on clinical examination and transrectal ultrasound (TRUS). On TRUS, both NSGP and carcinoma may show focal hypoechoic areas in the peripheral parts of gland (1;2). NSGP is associated with focal necrosis in the absence of acid-fast bacteria or other special microorganisms.
and without relationship to transurethral resection or systemic granulomatous disease. Although NSGP may be clinically indistinguishable from cancer, this entity may also histologically mimic carcinoma. Furthermore, an immunohistochemical panel has been proposed that can reliably distinguish between these two conditions (3).

The aim of this study was to determine the prevalence of NSGP and to compare the results of TRUS, serum prostate specific antigen (PSA), free PSA (fPSA) levels, digital rectal exam (DRE) in NSGP with the prostate carcinoma and BPH.

**Materials and Methods**

During a cross-sectional study, all of the samples that had been sent to one of the largest pathology centers were examined (one year: 2006). From the total number of 9875 samples, 783 cases were prostate needle biopsy. The H&E histological slides were checked by two pathologists and the NSGP cases were determined according to microscopic properties described in reference book (4). Medical file of patients with diagnosed NSGP were evaluated. All patients had been clinically examined with digital rectal examination (DRE) and had serum levels of prostatic specific antigen (PSA) and free PSA estimated prior to imaging and DRE. TRUS was carried out in the axial and sagittal planes using a 7.5 MHz multiplaner transducer. All patients underwent sextant biopsies from the gland including biopsies of any abnormal areas of echogenicity. Biopsies were carried out using an 18G biopsy gun. The clinical finding, serum PSA and fPSA levels, TRUS and pathologic finding of patients with NSGP diagnosis were gathered and analyzed using SPSS software.

**Results**

From a total number of 9875 submitted cases to the laboratory, 783 cases (7.92%) out of them were prostate biopsy cases that were revised and 8 (1.02%) cases were reported as the case of NSGP. Multiple histologic sections showed a mixed inflammatory cells infiltrate containing histiocytes, neutrophils, eosinophiles, lymphocytes, plasma cells and giant cells. The inflammatory cells usually surrounded dilated ducts that contained inspissated secretion with neutrophils and desquamated epithelial cells. Commonly epithelioid histiocytes mixed with multinucleated giant cells effaced the glandular architecture. Some histiocytes had foamy cytoplasms. In the periphery of the granulomatous inflammation, there was prostatic fibrosis (Figs 1-2).

**Fig. 1:** Micrograph showing mixed inflammatory cells (histiocytes, neutrophils, eosinophils, and giant cells). NSGP may histologically mimic carcinoma (H&E ×200)

**Fig. 2:** Micrograph showing mixed inflammatory cells with epithelioid histiocytes. There are dilated and partially effaced ducts or acini (H&E ×400)

The age range of patients was 55-76 years (with a mean of 66.1 years). On the basis of clinical examination, two patients were thought to have possible carcinoma of the prostate and six were considered to have prostatic hyperplasia. The clinical findings for DRE, PSA and fPSA levels, and TRUS are summarized in Table 1.
Table 1: Summary of clinical findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>DRE</th>
<th>PSA (ng/ml)</th>
<th>fPSA (ng/ml)</th>
<th>TRUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>70</td>
<td>BPH</td>
<td>11</td>
<td>0.9</td>
<td>NL</td>
</tr>
<tr>
<td>B</td>
<td>66</td>
<td>BPH</td>
<td>13.4</td>
<td>0.8</td>
<td>NL</td>
</tr>
<tr>
<td>C</td>
<td>68</td>
<td>BPH</td>
<td>25</td>
<td>0.8</td>
<td>NL</td>
</tr>
<tr>
<td>D</td>
<td>63</td>
<td>BPH</td>
<td>0.2</td>
<td>0.1</td>
<td>NL</td>
</tr>
<tr>
<td>E</td>
<td>71</td>
<td>BPH</td>
<td>30</td>
<td>0.1</td>
<td>NL</td>
</tr>
<tr>
<td>F</td>
<td>55</td>
<td>Carcinoma</td>
<td>53</td>
<td>0.9</td>
<td>Focal hypoechoic area</td>
</tr>
<tr>
<td>G</td>
<td>60</td>
<td>Carcinoma</td>
<td>15</td>
<td>1.3</td>
<td>Focal hypoechoic area + calcification</td>
</tr>
<tr>
<td>H</td>
<td>76</td>
<td>BPH</td>
<td>8</td>
<td>1</td>
<td>NL</td>
</tr>
</tbody>
</table>

BPH = Benign prostatic hyperplasia, NL = Normal, TRUS = Transrectal ultrasonography
PSA = Prostate specific antigen, fPSA = free PSA

PSA levels were variable ranging from 0.2-53 ng/ml (with a mean of 19.45), also fPSA levels were variable, ranging from 0.1-1.3 ng/ml (with a mean of 0.7). In 6 patients with NSGP, TRUS was normal (only enlarged prostate) and in 2 patients it was abnormal. In 2 out of these, focal hypoechoic areas were found in the peripheral parts of gland on ultrasound (suggestive of carcinoma). In 6 patients, DRE revealed a prostate enlargement that was firm but symmetry and non-tender and in 2 out of these revealed asymmetric and mild nodularity. All patients were subsequently confirmed to have biopsy-proven granulomatous prostatitis. None were found having cancer histologically at the time of biopsy and none had developed carcinoma of the prostate on 1-year follow up.

Discussion

The exact etiology of granulomatous prostatitis remains unclear and may in many cases be idiopathic, but it can be caused by several specific and non-specific infectious agents, and can also be secondary to prostatic surgery such as transurethral resection and may be a local manifestation of a non-infective systemic granulomatous disease (3;4). It is thought that factors involved in its development include duct obstruction and ectasia with leakage of luminal contents into the glandular stroma, which sets up a foreign body reaction with inflammatory change and fibrosis. Granulomatous prostatitis caused by mycobacterium tuberculosis has been well-described (3). NSGP is the most common form of granulomatous inflammation of the prostate. It is seen in 0.44% of routine prostatectomy specimens, in 0.29% of needle prostatic biopsies, and in 0.77% of the prostatic specimens including simple prostatectomies, transurethral resections, and needle biopsies (3).

In our study, NSGP was observed in 1.02% out of total cases that in comparison with outsider cases it had more prevalence. Male genitourinary coccidioidomycosis is rare but it should be considered in the differential diagnosis of patients with exposure to the endemic area who are presented with prostatitis or epididymitis (5). Most cases of NSGP occur in glands with nodular hyperplasia (BPH) in patients over the age of 50 years (a range from 28 to 80 years; mean: 65 years) (5;6).

In most of our cases, the NSGP was also seen with the BPH. The mean age of our patients was 66.1 years old that was higher than similar studies. PSA levels have also been shown not to be of value in differentiating carcinoma from granulomatous prostatitis, carcinoma producing high levels of PSA, but variable levels being found in patients with granulomatous prostatitis (1). In one study, serum PSA ranged from less than 0. 5 ng/ml to 114 ng/ml (mean = 12.7 ng/ml). This increase of PSA levels is usually transient (3).

In our study, serum PSA level was in the range of 0.2-53 ng/ml with the mean value of 19.45 ng/ml that was higher in comparison with the similar studies. Similar to the carcinoma the high level of PSA can also be observed in some NSGP cases. TRUS is a well-established imaging technique for evaluation of the prostate and for diagnosis of carcinoma when combined with biopsy, but both NSGP and carcinoma can produce similar findings on TRUS. The majority of cancers visible on ultrasound are hypoechoic, but isoechoic and hyper echoic tumors do infrequently occur. Most cancers occur in the peripheral zone of the gland. Whilst areas of abnormal low echogenicity occur in the prostate in NSGP, they do not occur in...
any characteristic pattern to differentiate them from carcinoma. Therefore, whilst TRUS may help in the diagnosis of NSGP, histological confirmation is necessary to obtain a definite diagnosis (6-8).

Grossly, the prostate is commonly enlarged and firm to stony hard. On cross section, the surface shows obliteration of the architecture, with formation of protruding yellow granular nodules (4). Microscopically, a nodular granulomatous infiltrate replaces the components of prostatic lobules. The cellular infiltrate is composed of epithelioid histiocytes, lymphocytes, and plasma cells. Multinucleated histiocytes (giant cells) and noncaseating granulomas may be common. Often in the center of the inflammatory nodules there are dilated and partially effaced ducts or acini (3;4). Using an immunohistologic technique, T lymphocytes are in close association with damaged epithelium, while B lymphocytes occur more peripheral or form follicular structures. Neutrophils and eosinophils are usually a smaller component of the inflammatory infiltrate. However, eosinophils may form a significant proportion of this infiltrate. Furthermore, marked eosinophilia is peripheral blood has been reported in one case. In the absence of any history of allergic disease or fibrinoid necrosis or vasculitis, the presence of eosinophils in non-specific or caused by local hypersensitivity (4). A xanthogranulomatous pattern or prominence of epithelioid histiocytes sometimes bears a resemblance to high-grade carcinoma (9;10). Thus, NSGP may histologically mimic carcinoma (10-12) (figures 1 & 2). Cases mimicking carcinoma including high-grade carcinoma have been reported in up to 20%.

In these cases, a panel of antibodies to cytokeratin, PSA, prostatic acid phosphatase, CD68, and leukocyte common antigen can resolve the differential diagnosis. Epithelial markers must be interpreted with caution because disrupted acini may result in isolated cords and individual positive cells. Misinterpretation has been described even in a telepathology study (3).

Non-specific granulomatous prostatitis is thought to be a reaction to bacterial toxins, cell debris, and secretions spilling into the stroma from blocked ducts. Thus, the lesion is favored with nodular hyperplasia (10). On the other hand, NSGP may coexist with carcinoma. Mbakop et al studied 53 NSGP specimens received over a 12-year period. This lesion was associated with nodular prostatic hyperplasia in 38 cases (71.5%) and with prostatic carcinoma in one case (2%), and occurred alone in 14 cases (26.5%) (3). These authors did not include details or comments on the case combined with the carcinoma, as this association was only mentioned. Gujral and Gillatt reported a 53-year-old case who presented with a short history of lower urinary tract symptoms, dysuria, intermittent frank hematuria, and rigors. Treatment with ciprofloxacin led to the subsidence of the symptoms. Investigations including urine culture, cystoscopy, and intravenous pyelogram were normal apart from his PSA level, which was 12.5 ng/ml. The surgical specimens revealed florid diffuse NSGP and low-grade prostatic adenocarcinoma (Gleason 2+3 = 5). At prostatectomy, the tumor volume was <4 ml. Oppenheimer et al alluded to cases showing the two coincidental lesions in their consultation case, but they did not indicate details of the lesions or document the association. The number of cases showing an intimate admixture of NSGP and prostatic adenocarcinoma was less than three (12% of cases) (3). In this context, it should be mentioned that Osca Garcia et al reported that during the follow-up of 21 cases of NSGP, four patients (19%) develops prostate carcinoma, with an average presentation time of 5.5 years after NSGP diagnosis (3;13).

**Conclusion**

There is no pattern of clinical, biochemical, and ultrasound findings that allows a specific diagnosis of granulomatous prostatitis to be made or its differentiation from prostatic carcinoma. Besides, the diagnostic methods such as TRUS, DRE, and serum PSA and fPSA levels, the biopsy and microscopic findings are still necessary for the certain disease diagnosis and it should be mentioned that may be NSGP during the follow up developed to prostate carcinoma.

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**References**

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