Inflammatory Atrophy of the Prostate
Prevalence and Significance

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Context.—Recently, prostatic atrophy associated with chronic inflammation has been linked to carcinoma either directly or indirectly by first developing into high-grade prostatic intraepithelial neoplasia.

Objective.—The purpose of our study was to test this hypothesis in autopsies.

Design.—A step section method was used to cut the posterior lobe in coronal planes at intervals of 0.3 to 0.5 cm in 100 consecutive autopsies of men older than 40 years. Prostatic atrophy was classified as simple, hyperplastic (or postatrophic hyperplasia), and sclerotic and was analyzed for the presence of chronic inflammation. Prostatic atrophy without (group A) and with inflammation (group B) was correlated with the following variables: age, race, histologic (incidental) carcinoma, high-grade prostatic intraepithelial neoplasia, and extent of both these lesions.

Results.—Of the 100 prostates examined, 12%, 22%, and 66%, respectively, had no atrophy, atrophy without inflammation (group A), and atrophy with inflammation (group B). There was no statistically significant difference between groups A and B for age (P = .55), race (P = .89), presence of histologic (incidental) carcinoma (P = .89), extensive carcinoma (P = .43), presence of high-grade prostatic intraepithelial neoplasia (P = .65), extensive high-grade intraepithelial neoplasia (P = .30), or subtypes of prostatic atrophy. Neither a topographical relation nor a morphologic transition was seen between prostatic atrophy and histologic carcinoma or high-grade intraepithelial neoplasia. Sclerotic atrophy either alone or combined with other subtypes was more frequent in the group with inflammation. A striking morphologic finding was a topographical relation of focal inflammation with sclerotic atrophy in areas with erosion of the epithelium.

Conclusions.—Inflammatory prostatic atrophy does not appear to be associated with histologic (incidental) carcinoma or high-grade intraepithelial neoplasia. One possible cause of inflammatory infiltrate associated with prostatic atrophy may be the extravasated prostatic secretions, which were noted in areas of eroded epithelium, a common finding in the sclerotic type of prostatic atrophy.

(March Pathol Lab Med. 2003;127:840–844)

Materials and Methods

The material for this retrospective study was obtained from 100 consecutive autopsies of men older than 40 years who died of diseases other than carcinoma of the prostate. Autopsies were conducted at the University Hospital, a general hospital and the main teaching hospital of the School of Medicine, State University of Campinas (UNICAMP), Campinas, Brazil. Race of the patients was considered to be either white or African Brazilian. In Brazil, the African Brazilian population comprises blacks and mulattos (persons of mixed white and black ancestry).

The prostates were dissected free from the surrounding tissue and fixed uncut in 10% formalin for 5 days or longer. The glands were cut in 2 parts through a sagittal section passing through the middle of the organ. The ejaculatory ducts were easily visualized on each section plane because of the presence of yellow-brown pigment. The prostate was sectioned through the plane indicated by the presence of the ejaculatory duct. The posterior lobe was considered to be that portion of the gland lying posterior to a plane passing the ejaculatory ducts, according to Moore, Kahler, and Strahan, and corresponds to the largest part of the peripheral zone, according to McNeals's classification.

The glands were step-sectioned at intervals of 3 to 5 mm. Only the posterior lobe was examined microscopically. Blocks were embedded in paraffin, cut at 6 μm, and 1 section from each block was stained with hematoxylin and eosin.

The microscopic study looked for the following features:

1. Presence of prostatic atrophy. Prostatic atrophy was histologically subtyped into simple atrophy, hyperplastic atrophy (or...
postatrophic hyperplasia), and sclerotic atrophy. Simple atrophy (Figure 1) usually involves an entire lobule, although isolated acini may be affected. The acini are small and show a decrease in the height of the epithelial cells, and the surrounding stroma may or may not show fibrosis. Hyperplastic atrophy (Figure 2) shows small acini packed closely together and lined by atrophic epithelium. Fibrosis may or may not be present in the stroma. When present, the proliferation is irregular and can result in distortion of the acinar lumen. Sclerotic atrophy (Figure 3) shows simultaneous atrophy of the epithelium and proliferation of the fibroblasts about the acini, which progressively dilate. Elastosis of the stroma was a useful microscopic feature for the identification of prostatic atrophy of any subtype.

2. Presence of atrophy with inflammation (or inflammatory atrophy) (Figures 1 through 3). This lesion was considered when chronic inflammation (as judged mostly by the presence of lymphocytes) was seen in areas of prostatic atrophy of any kind (simple, hyperplastic, or sclerotic).

3. Presence of histologic (incidental) carcinoma (HC). Histologic carcinoma was diagnosed according to the criteria of Mostofi and Price. The diagnosis was based on invasion or architectural disturbance.

4. Presence of HGPIN. Four common patterns of HGPIN were identified, all with nucleomegaly and prominent nucleoli. The patterns were described as tufting, micropapillary, cribriform, and flat, according to Bostwick et al.

5. Evaluation of extent of lesions. Extent was evaluated according to the percentage of sections that showed the lesion of interest. When more than 50% of the sections per prostate showed the lesion, it was considered extensive. A total of 1384 sections were examined (average of 14 sections per prostate).

The data were statistically analyzed by the chi-squared test and Fisher exact test for differences between proportions. P ≤ .05 was considered statistically significant. The comparison of age between groups was done using the Mann-Whitney nonparametric statistical test.

RESULTS

Of the 100 prostates examined, 12%, 22%, and 66%, respectively, had no atrophy, atrophy without inflammation, and atrophy with inflammation.
rophy with either HGPIN or HC. Morphologic transitions from HGPIN (84.2) to extensive HC (84.2) were noted in 2 (2.56%) of the total of 78 patients examined, including 3 (25%) of the 12 cases without inflammation (Table 1).

Table 1. Comparison Between 22 Prostates Without Inflammation (Group A) and 66 Prostates With Inflammation (or Inflammatory Atrophy) (Group B) for Race, Histologic (Incidental) Carcinoma (HC), Extent of HC, High-Grade Prostatic Intraepithelial Neoplasia (HGPIN), and Extent of HGPIN

<table>
<thead>
<tr>
<th>Race</th>
<th>Group A, No. (%)</th>
<th>Group B, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>16/22 (72.72)</td>
<td>49/66 (74.24)</td>
<td>.89</td>
</tr>
<tr>
<td>African-Brazilian</td>
<td>6/22 (27.27)</td>
<td>17/66 (25.75)</td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>5/22 (22.72)</td>
<td>16/66 (24.24)</td>
<td>.89</td>
</tr>
<tr>
<td>Not extensive</td>
<td>4/5 (80)</td>
<td>15/16 (93.75)</td>
<td>.43</td>
</tr>
<tr>
<td>Extensive</td>
<td>1/5 (20)</td>
<td>1/16 (6.25)</td>
<td></td>
</tr>
<tr>
<td>HGPIN</td>
<td>16/22 (72.72)</td>
<td>53/66 (80.30)</td>
<td>.65</td>
</tr>
<tr>
<td>Not extensive</td>
<td>10/16 (62.5)</td>
<td>42/53 (79.24)</td>
<td>.30</td>
</tr>
<tr>
<td>Extensive</td>
<td>6/16 (37.5)</td>
<td>11/53 (20.75)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Frequency of Subtypes of Prostatic Atrophy in Groups A (Without Inflammation) and B (With Inflammation)

<table>
<thead>
<tr>
<th>Prostatic Atrophy*</th>
<th>Group A, No. (%)</th>
<th>Group B, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only S</td>
<td>4/22 (18.18)</td>
<td>10/66 (15.15)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Only SC</td>
<td>2/22 (9.09)</td>
<td>15/66 (22.72)</td>
<td>.22</td>
</tr>
<tr>
<td>Only H</td>
<td>0/22</td>
<td>5/66 (7.57)</td>
<td>.33</td>
</tr>
<tr>
<td>Combined subtypes</td>
<td>16/22 (72.72)</td>
<td>36/66 (54.54)</td>
<td>.13</td>
</tr>
<tr>
<td>S + H + SC</td>
<td>6/16 (37.50)</td>
<td>13/36 (36.11)</td>
<td>.24</td>
</tr>
<tr>
<td>S + SC</td>
<td>4/16 (25.00)</td>
<td>8/36 (22.22)</td>
<td>.89</td>
</tr>
<tr>
<td>S + H</td>
<td>6/16 (37.50)</td>
<td>4/36 (11.11)</td>
<td>.06</td>
</tr>
<tr>
<td>H + SC</td>
<td>0/16</td>
<td>11/36 (30.55)</td>
<td>.03</td>
</tr>
</tbody>
</table>

* S indicates simple atrophy; H, hyperplastic atrophy; and SC, sclerotic atrophy

(group A), and atrophy with inflammation (or inflammatory atrophy) (group B).

The median age for patients was 58 years in group A and 64 years in group B. There was a trend for higher age in patients with atrophy with inflammation (P = .06).

Sixteen (72.72%) and 6 (27.27%) of the 22 patients in group A, and 49 (74.24%) and 17 (25.75%) of the 66 patients in group B were white and African Brazilian, respectively.

Histologic carcinoma was found in 24 (24%) of the 100 prostates examined, including 3 (25%) of the 12 cases without atrophy, 5 (22.72%) of the 22 cases in group A, and 16 (24.24%) of the 66 cases in group B. In 1 (20%) of the 5 patients with HC in group A and 1 (6.25%) of the 16 patients with HC in group B, involvement was extensive.

High-grade prostatic intraepithelial neoplasia was found in 78 (78%) of the 100 prostates examined, including 9 (75%) of the 12 cases in the group without atrophy, 16 (72.72%) of the 22 cases in group A, and 53 (80.30%) of the 66 cases in group B. In 6 (37.5%) of the 16 patients with HGPIN in group A and 11 (20.75%) of the 53 patients with HGPIN in group B, involvement was extensive.

There was no statistically significant difference between groups A and B with respect to race (P = .89), HC (P = .89), extensive HC (P = .43), HGPIN (P = .65), and extensive HGPIN (P = .30) (Table 1).

There was no topographical relation of inflammatory atrophy with either HGPIN or HC. Morphologic transition between atrophic acini with or without inflammation and HC or HGPIN was not seen in any case. Of the total of 78 patients with HGPIN, we found a continuum between HGPIN and invasive adenocarcinoma in only 2 (2.56%) (Figure 4).

According to the subtypes of prostatic atrophy, simple atrophy was seen in groups A and B in 4 (18.18%) of 22 patients and 10 (15.15%) of 66 patients, respectively; sclerotic atrophy was noted in 2 (9.09%) and 15 (22.72%) patients, respectively; hyperplastic atrophy was observed in 0 and 5 patients (7.57%), respectively; and combined subtypes were seen in 16 (72.72%) and 36 (54.54%) patients, respectively.

There was no statistically significant difference between groups A and B according to the subtypes of prostatic atrophy (Table 2); however, sclerotic atrophy was seen more frequently in group B (prostatic atrophy with inflammation) and this difference was statistically significant (P = .03) when combined with the hyperplastic subtype. A striking topographic relationship of focal inflammation and sclerotic atrophy was seen in areas with erosion of the epithelium (Figure 3).

**COMMENT**

The term proliferative inflammatory atrophy was proposed by De Marzo et al. to designate discrete foci of proliferative glandular epithelium with the morphologic appearance of simple atrophy or postatrophic hyperplasia occurring in association with inflammation. According to these authors, the morphology of PIA is consistent with McNeal’s description of postinflammatory atrophy, with that of chronic prostatitis described by Bennett et al. and with the lesion referred to previously as “lymphocytic prostatitis” by Blumenfeld et al.

De Marzo et al. and Putzi and De Marzo suggested that PIA may indeed give rise to carcinoma directly, as hypothesized previously, or that PIA may lead to carcinoma indirectly via development into HGPIN. This hypothesis is based on 3 separate findings providing supportive evidence: (1) morphologic merging between PIA and HGPIN in 34% of the PIA lesions; (2) the phenotype...
of many of the cells in PIA is most consistent with that of an immature secretory-type cell, similar to that for the cells of HGPIN; and (3) PIA, HGPIN, and carcinoma all occur with high prevalence in the peripheral zone and low prevalence in the central zone of the human prostate.

Three articles are at odds with the findings of De Marzo et al. and Putzi and De Marzo. In the only study done in Brazil, in which 100 prostates were examined in autopsies, no relation, including topographical, was found between prostatic atrophy of any subtype and HC or HGPIN. In this latter study, no reference was made to atrophy with inflammation. Anton et al., studying radical prostatectomies, concluded that postatrophic hyperplasia is a relatively common lesion that is present in about one third of prostates, with or without prostate carcinoma. The authors found no association between the presence of postatrophic hyperplasia and the likelihood of cancer and no topographic association between postatrophic hyperplasia and prostate carcinoma foci. This finding held true for both clinical cancer in a radical prostatectomy specimen and incidental cancer in a cytoprostatectomy specimen. In a recent report, Bakshi et al. studied 79 consecutive prostate biopsies. Fifty-four percent of initial biopsies were benign, 42% of the cases showed cancer, and 4% demonstrated HGPIN or atypia. Postatrophic hyperplasia was seen in 17% of benign initial biopsies with available follow-up. Of these, 75% had associated inflammation. There was no significant difference in the subsequent diagnosis of prostatic cancer for groups with postatrophic hyperplasia, partial atrophy, atrophy, or no specific abnormality. The authors concluded that the subcategories of atrophy did not appear to be associated with a significant increase in the risk of diagnosis of prostate cancer subsequently.

The purpose of the present study was to find any relation of inflammatory atrophy to either HC or HGPIN. Of a total of 100 prostates examined, 66 showed chronic inflammation of any of the subtypes of atrophy (simple, hyperplastic, or sclerotic). When compared with 22 prostates with no inflammation of any subtype, no significant difference was found for age, race, HC, or HGPIN.

No significant difference was found between atrophy and HC (P = .61) or HGPIN (P = .96), even considering the hyperplastic subtype of atrophy (present as the only lesion or combined with other subtypes). It is noteworthy that only a few cases demonstrated hyperplastic atrophy as the only subtype (5/88, 5.68%). In most of the cases, this lesion was seen combined with the other subtypes of atrophy (40/88, 45.45%). This finding supports the hypothesis that prostatic atrophy is a morphologic continuum and that hyperplastic subtype (or postatrophic hyperplasia) seems to be at the extreme end of this morphologic continuum seen in this series.

The group with inflammation (group B) was equally seen associated with extensive HC or HGPIN. No case demonstrated morphologic transition between prostatic atrophy with or without inflammation and HC or HGPIN. The only continuum seen in this series was a morphologic transition between HGPIN and invasive adenocarcinoma in 2 (2.56%) of 78 patients with HGPIN (Figure 4).

So far, HGPIN is the only and earliest morphologically recognizable precursor lesion of prostate cancer; however, the demonstration of a continuum between HGPIN and microinvasion is rare. Such microinvasion is seen in about 2% of high-power microscopic fields of HGPIN.

Considering the subtypes of prostatic atrophy, a higher frequency of sclerotic atrophy either alone or combined with other subtypes was seen in group B, and the difference was statistically significant (P = .03) when combined with the hyperplastic subtype. A striking finding was a topographical relation of focal inflammation to sclerotic atrophy in areas with erosion of the epithelium (Figure 3). This finding suggests that the inflammatory infiltrate may be secondary to prostatic secretion extravasated in areas of eroded epithelium frequently seen in this subtype of atrophy. Sclerotic atrophy is a peculiar subtype of prostatic atrophy. It shows simultaneous atrophy of the epithelium and proliferation of the fibroblasts about the acinus. Continued proliferation results in hyalinization of the collagen. With higher degrees of hyalinization the acini dilate, sometimes prominently, and the epithelium becomes extremely flattened; eventually it disappears completely (Figure 3). This subtype of prostatic atrophy was described in detail by Moore in 1936.

In conclusion, atrophy with chronic inflammation (or inflammatory atrophy) was seen in 66 (66%) of 100 prostates examined at autopsy. In this study, we found no statistically significant difference between prostatic atrophy without inflammation (group A) and prostatic atrophy with inflammation (group B) in relation to age, race, or presence of HC and HGPIN. Likewise, no difference was seen when the extent of involvement of HC and HGPIN was taken into account. Considering the subtypes of prostatic atrophy, no significant difference was seen between group A and group B, but sclerotic atrophy either alone or combined with other subtypes was more frequent in the group with inflammation. A striking morphologic finding was a topographical relation of focal inflammation with sclerotic atrophy in areas with erosion of the epithelium. This finding suggests that the inflammatory infiltrate may be secondary to prostatic secretion extravasated in areas of eroded epithelium, which frequently occurs in this subtype of atrophy.

References


