Adenocarcinomas of the prostatic duct in necropsy material

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The general consensus about prostatic duct adenocarcinomas is that they have a rather aggressive biological behavior. In addition, studies or reports of latent adenocarcinoma of the prostatic duct in necropsy material are scarce in the literature. We report here three cases of adenocarcinoma of the prostatic duct that were found incidentally among 39 cases of latent acinar prostate adenocarcinomas in necropsy material. We examined the morphologic and histological features of these prostatic duct adenocarcinomas, in order to better understand their biological behavior. We identified two cases of mixed ductal-acinar adenocarcinoma and one case of pure ductal adenocarcinoma. The pure form had a favorable histological differentiation, while the mixed forms had intermediate histological differentiation patterns. Invasiveness was related to both volume and histological differentiation. The finding of prostatic ductal adenocarcinomas among autopsy material, as well as some of their histological features, suggest that these tumors might have a similar biological potential as prostatic acinar cancer.

Key Words: prostate cancer, ductal carcinomas, autopsy, biological behavior, necropsy material

Introduction

To the best of our knowledge, in the current medical literature there is no report of prostatic ductal adenocarcinoma found in autopsy specimens from men who died from causes other than prostate cancer. The incidental finding of three cases of prostatic ductal carcinoma (one purely ductal and two mixed acinar-ductal carcinomas) among latent acinar prostate adenocarcinomas in necropsy material prompted our analysis to determine the clinical and pathological stage and tumor grade of the ductal tumors and compare this to the latent acinar adenocarcinomas, in an attempt to improve our understanding of the biological behavior of prostatic ductal cancer.

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Materials and methods

We examined 39 prostates with latent cancer that were found in 200 consecutive autopsies of men between 40 and 98 years of age who had died of causes other than carcinoma of the prostatic gland. None of the men had a history suggesting prostate cancer or an abnormal post-mortem, pre-necropsy digital rectal examination (DRE). The whole prostates and seminal vesicles were sectioned for a histopathological examination to determine the exact size, location, and number of foci; histological grade (Gleason score); and local invasion (capsular, perineural, and perivascular penetration). Morphometric analysis was done on the 39 totally embedded specimens using an image analysis system. For statistical analysis, the two mixed forms of acinar ductal carcinomas and the pure ductal form were assessed as a single ductal group.

Results

Most (36) of 39 latent carcinomas found upon autopsy of 200 men were pure acinar carcinomas. In the remaining three cases, two were mixed ductal-acinar carcinomas and one was a papillary ductal carcinoma. The two mixed ductal-acinar carcinomas consisted of separate foci of adenocarcinoma found among foci of acinar prostatic adenocarcinomas in the prostates of two men over age 76. Both prostate specimens were enlarged but not hard, firm, or fixed, in the pre-necropsy DRE. The papillary ductal carcinoma was found in the prostate of a 92-year-old man and was visible upon macroscopic examination as a small, single lesion arising from the verumontanum into the prostatic urethra lumen.

Twenty-four of 39 tumors detected were multifocal. Most of these multifocal tumors were comprised of small neoplasms with a volume less than 0.5 ml, except for the multifocal tumors that contained the two mixed ductal-acinar carcinomas. Those tumors were composed of more than five separate foci of ductal and acinar adenocarcinomas that were adjacent to each other. It proved to be extremely difficult to make an accurate determination of the exact number of foci and size of the tumors; the foci of adenocarcinomas of the prostatic duct in both cases had a volume that was greater than 0.5 ml but less than 1 ml, while the overall tumor volumes were greater than 2 ml.

TABLE 2. **Correlation between local invasiveness and tumor volume for acinar, ductal, and mixed carcinomas**

	Capsular	Neural	Vascular
Tumor < 1 ml n = 28	1	1	1
Percentage	3.57%	3.57%	3.57%
Tumor > 1 ml n = 11	3	5	2
Percentage	27.2%	45.45%	18.18%

Most of the latent acinar carcinomas found in autopsy (21 of 39; 53.85%) had a favorable histological grade: 7 (17.9%) had a Gleason score of 3, and 14 (35.89%) had a Gleason score of 4, Table 1. A total of 17 of 39 (43.58%) had an intermediate histological differentiation (Gleason score 5 or 6). Only one carcinoma (2.56%) had a Gleason score of 7.

The two mixed ductal-acinar carcinomas had an intermediate histological pattern (Gleason scores 5 and 6), and the one pure ductal carcinoma had a favorable histological pattern (Gleason score 3). No statistically significant difference in the histological differentiation was found between the 36 acinar and 3 ductal adenocarcinomas ($p > 0.05$).

Most of the latent acinar cancers (28 of 39, or 71.79%) were carried either by single or multifocal carcinomas with total volumes of less than 1 ml, and most (53.85%) were of favorable histological type, so the rate of invasiveness was low, Table 2. Perineural invasion, the most common indicator of aggressive behavior, was observed in six carcinomas (five pure acinar patterns and one mixed acinar-ductal pattern) and always correlated with an elevated Gleason score (mostly Gleason score 6). Capsular penetration alone was observed in

TABLE 1. **Gleason scores of three ductal* and 39 acinar carcinomas**

	2a	3	4	5	6	7
Ductal*	0	1	0	1	1	0
Rate	0%	33.3%	0%	33.3%	33.3%	0%
Acinar	0	7	14	12	5	1
Rate	0	17.9%	35.89%	30.76%	12.82%	2.56%

*Ductal carcinomas consist of one pure ductal and two mixed ductal-acinar carcinomas

TABLE 3. **Distribution of latent prostate cancers in 200 autopsies**

Age at death years	Number of men (prostate specimens)	Acinar cancer detected number of men	Ductal cancer detected number of men
> 86	42	19	1
76-85	37	12	2
66-75	30	5	0
56-65	35	2	0
46-55	31	1	0
40-46	25	0	0
Total	**200**	**39**	**3**

*Ductal cancers consist of one pure ductal and two mixed ductal-acinar cancers

three carcinomas and correlated with a tumor volume greater than 1 ml. Both capsular and neurovascular invasion together were found in one carcinoma; this was a mixed acinar-ductal carcinoma with an overall volume of 2.2 ml and a Gleason score of 6.

Ductal and acinar carcinomas with a volume of less than 1 ml did not exhibit aggressive behavior unless they were dedifferentiated. There was no statistically significant difference in capsular penetration, or perineural and perivascular invasion for acinar versus ductal (mixed and pure form) adenocarcinomas ($p > 0.05$). It is also worth noting that adenocarcinomas of the prostatic duct were all found among men over age 75, where the higher aggregation of latent carcinomas was also observed, Table 3.

Discussion

Most cases of carcinoma involving the prostate gland show characteristic acinar histologic features; nevertheless, histologic variants of adenocarcinoma are common.[1] Adenocarcinoma of the prostatic duct, although initially believed to represent an endometrial carcinoma arising from a Müllerian remnant,[2] is now considered to be of prostatic origin and accounts — in its pure form — for 0.2%[3,4] to 0.8% (or more)[5] of all prostatic adenocarcinomas.

Adenocarcinomas of the prostatic duct usually occur with two patterns of disease.[7] The first pattern consists of tumors of primary ducts, arising from large, central periurethral prostatic duct spaces that are lined with a distinct basement membrane. Typically, these tumors exhibit papillary fronds supported by branching fibrous connective tissue cores that are usually lined with a single layer of tall, columnar epithelial cells. When deeply invasive, they usually grow as a single gland.[7]

The second pattern of disease consists of tumors arising from more peripheral or secondary periurethral ducts that show a histologic similarity to the invasive portion of the central prostatic duct carcinomas. Adenocarcinomas of secondary prostatic ducts denote multicentric involvement and are characterized by areas in which growth is contained within intermediate and small ducts. Small papillary projections are common and many of the lumina are filled with eosinophilic debris. Involvement of the secondary ducts is mostly characterized by an extensive invasion of the prostatic gland, sometimes resulting in carcinoma that is clinically indistinguishable from acinar carcinoma. Usually, secondary duct tumors are mixed with standard acinar carcinoma, and they often lack a urethral component.[4,6] Patients with the second pattern of disease usually have an extensive, advanced, terminal pathologic stage of cancer. In one study, the incidence of positive margins in specimens with carcinoma of secondary ducts was reported to be higher than in acinar carcinomas.[6] Similarly, the incidence of capsular penetration in clinical, stage-B ductal carcinomas was reported to be much higher than in acinar carcinomas of the same clinical stage.[6]

Coexisting ductal and acinar adenocarcinomas are much more common than pure ductal adenocarcinomas, but the actual incidence is not well established. In our study, the two mixed ductal-microacinar carcinomas were found among multifocal tumors in variant proportions (1/3 and 1/6 respectively).

Rotterdam and Melicow[8] reported a high rate for adenocarcinomas of the prostatic duct that contain additional components of acinar adenocarcinoma of the prostate. Millar et al,[9] however, reported that only half of the prostatic duct cases in their clinicopathological study contained mixed ductal-acinar carcinomas.

Dube et al[10] reported that real dual primary lesions are relatively rare and account for only close to 5% of all cases of ductal prostatic carcinoma.

Since the prognosis for patients with prostatic cancer is greatly influenced by tumor multifocality,[11] and, since the invasive pattern of mixed acinar-ductal carcinoma was found among foci of acinar carcinoma of intermediate or pure differentiation in our study, it is possible that the aggressiveness of the mixed acinar-ductal tumors was derived from such additional components of acinar carcinoma. Indeed, in our study, the two large, multifocal latent cancers that carried mixed acinar-ductal tumors showed variability in Gleason grade among individual tumors. The correlation of the Gleason grade of every single focus (acinar or ductal) of multifocal latent cancers with the Gleason grade of the index tumors was moderate (56.4%). Furthermore, high Gleason grade foci can express their aggressive attitude independently from their presence rate in the whole tumor: both neurovascular and capsular invasion were observed in a multifocal tumor of six foci that showed variety in histological differentiation (Gleason scores of 2 through 7).

A literature review of prostate cancer cases reported that mixed ductal-acinar tumors showed a wide range of differentiation, as opposed to uniform cytological appearance. This characteristic is most likely determined by the acinar tumor components, since acinar tumors have intermediate or poor differentiation when they present at the same time.[12]

In a clinical study by Bostwick et al, a microacinar carcinoma was reported as clinically more aggressive than the coexistent ductal carcinoma.[5] In addition, Millar et al[9] referred to well-documented cases of mixed ductal and acinar carcinomas in which the acinar component had a Gleason score of at least 5. The natural history of solitary endometroid carcinoma appears to be that of a low-grade malignancy with low biological aggressiveness. According to a study of 16 cases by Walther et al,[12] most adenocarcinomas of the primary prostatic ducts, arising over the prostate utricle region, were found at a low stage of cancer; they concluded that more aggressive lesions appear to be prostatic adenocarcinoma of the acinar rather than the endometroid (ductal) type.

Invasion of the prostatic stromal tissue was not observed in the single case of carcinoma of the primary ducts that we found. This may be explained by the central location of these tumors. It is notable that most transition zone tumors are noninvasive, even when they are large or have an advanced cancer grade. If invasive, they show much less capsular penetration than peripheral zone cancers of comparable possible volume; this is due to the transition zone boundary, which provides a barrier to tumor spread through the peripheral zone.

Finally, in the present study, the age-related prevalence of adenocarcinomas of the prostatic duct was similar to that for acinar cancer, a finding that agrees with other studies.[13,14]

Study limitations

The data presented here were collected from a relatively small sample of latent adenocarcinomas of the prostatic duct, which were found accidentally in autopsy specimens. It is important to note, however, that such tumors are relatively rare and the rate of occurrence among ordinary acinar carcinomas in this study is similar to that reported by other clinical studies. These findings may improve our understanding and point the way to further investigation of the behavior of ductal adenocarcinoma.

Conclusions

It is generally accepted that prostatic duct adenocarcinomas are in an advanced pathologic stage by the time they are diagnosed, and that compared to acinar cancers, they are linked with much higher short-term treatment-failure rates. Some studies[6,10,15] have demonstrated that patient age, symptoms, findings on DRE, levels of serum PSA, and alkaline phosphatase in patients with adenocarcinomas of the prostatic duct, are similar to those found in patients with acinar adenocarcinomas. Furthermore, the same authors[6] reported that DNA analysis in ductal and acinar tumors did not reveal striking differences between these cancers.

In this study, the finding of latent prostatic ductal adenocarcinoma in autopsy material from men who did not die from prostate cancer and also the finding of no special morphometric differences between ductal and acinar tumors suggests that these two types of carcinoma might have a similar biologic behavior that is related to tumor histological differentiation, volume, location, and multifocality. □

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