Original Article

Morphological characterization of prostatic ductal carcinoma and impact on tumor grade

Faraz Ahmed Baig,[1] Amna Hamid,[2] Talat Mirza,[3] Serajuddaula Syed [1]

[1] Department of Pathology, Ziauddin University Karachi, Pakistan.
[2] Department of Medicine, Ziauddin University Hospital Karachi, Pakistan.
[3] Department of Pathology, Dow University of Health Sciences Karachi, Pakistan.

Keywords: *Prostate; adenocarcinoma; ductal; Gleason score*

Abstract

Objective: The clinical significance and impact of ductal prostatic carcinoma on overall tumor grade has been controversial. We therefore characterize the ductal and non-ductal subtypes of prostate adenocarcinoma and studied their impact on biological aggressiveness of tumor.

Method: We utilized tumor bearing prostate biopsies reported during 2010-2014 from Dow Diagnostic Research & Reference Laboratory to identify cases of Prostatic ductal and non-ductal acinar adenocarcinoma. Clinicopathologic variables of age and Gleason scores were analyzed and statistical analysis performed.

Result: A total of 140 non-ductal acinar cases and 10 ductal cases were identified. Ductal cases were predominantly high grade with advanced histopathological features. (90%; $p<0.03$). There was no significant statistical difference with patient's age.

Conclusion: In the limited series of this histologic subtype, ductal cancers were more likely to present with advanced grade cancer, suggesting that timely detection of the disease is vital.

***Corresponding author:**
Dr. Faraz Ahmed Baig
Tel.: +92-345-3316575; E-mail: fabaig@yahoo.com

Introduction

Prostate cancer is the second most common malignancy in men globally.[1] The major proportions of prostate carcinomas are acinar adenocarcinoma, although several rare morphologic variants coexist. [2] Ductal carcinoma is the most frequent among all rare variants of prostate cancer. It accounts for 5 % of total prostate carcinoma cases. [3] Ductal tumors typically arise from large periureteral prostatic ducts as well as peripheral prostatic ducts. [4]

The vast majority of these tumors comprise of variable volume of ductal component accompanied with acinar component. Tumors with absolute ductal component are extremely rare. [2, 5] Histologically, ductal adenocarcinomas are composed of columnar cells arranged in papillary or cribriform pattern whereas acinar adenocarcinomas exhibit cuboidal cells arranged in acini. [6, 7] The papillary pattern of ductal tumors consist of true papillary fronds lined by columnar cells exhibiting a variable degree of nuclear pleomorphism and hyperchromasia. The other pattern consists of proliferating large, back-to-back cribriform glands with central necrosis. [6, 7] In both patterns, the surrounding stroma is fibrotic or altered. Based on the morphological features the ductal component is graded as 4 on Gleason scoring system. [2]

The presence of ductal component was reported to be associated with an aggressive disease, although the impact of ductal component on the overall Gleason score of tumor remains controversial. [8, 9] We therefore first characterized the cases of prostate ductal adenocarcinoma and non-ductal tumors based on tumor morphology, and then compared the impact of ductal and non-ductal carcinomas on cumulative tumor grade. We also sought to examine the association of ductal adenocarcinoma with patient's age on diagnosis.

Materials and Methods

The ethical approval was sought from the institutional review board of Dow University of Health Sciences to examine biopsies of patients who underwent transurethral resection of prostate (TURP) resulting in prostatic adenocarcinoma diagnoses at Dow Diagnostic Research & Reference Laboratory from 2010-2014. The informed consent along with patient data regarding age and pertinent clinical history were obtained. A panel of consultant histopathologists evaluated the morphological features, Gleason scores, and the percentage of the ductal adenocarcinoma component. We also reviewed the pathological features of the non-ductal adenocarcinoma cases, their Gleason scores and the patient's age on diagnosis.

The statistical analysis was performed by SPSS 21.0 (The Statistical Package for the Social Sciences, Chicago, USA) package program. The research parameters were divided into two groups; age (patients aged ≤ 65 years and those with >65 years of age) and pathological tumor grade (≤7 Gleason's score and >7 Gleason's score). Correlation between categorical variables with prostatic ductal and non-ductal adenocarcinoma was evaluated by Binary Logistic Regression. In all tests, minimum limit of significance was determined as 0.05 ($p<0.05$).

Result

Ten out of 150 cases (6.6%) exhibited morphological features of ductal adenocarcinoma. Six out of these ten cases were aged ≤65 years while the rest were >65 years of age at the time of diagnosis. All ductal carcinoma cases were characterized by distinctive pseudostratified columnar epithelial cells in papillary or cribriform architecture. (Figure 1) The ductal component coexisted with conventional acinar adenocarcinoma in all ten cases. Nine ductal adenocarcinoma cases were graded as >7 and only one scored ≤7 on Gleason scoring system. Overall, there were no significant differences except for ductal carcinomas were significantly aggressive (Gleason score >7) than non-ductal tumors. The clinicopathological characteristics and statistical estimates of cases are summarized in table 1.

Discussion

The ductal adenocarcinoma is a rare variant of prostatic cancer, exhibiting columnar cell morphology. The ductal component coexists with acinar component. [2, 3] In the present study, we were able to document ten ductal prostatic adenocarcinoma cases, which accounted for 6.6% of the total prostate adenocarcinomas reported. Similar frequencies were reported in previous studies. [10-12] Historically, ductal carcinoma was believed to be a less aggressive tumor, however recent studies have found that the presence of any amount of ductal histology is a predictor of an aggressive nature of the tumor. [8, 13] Moreover, Morgan et al. reported greater than two-fold increased risk of mortality of ductal carcinoma compared to patients with acinar carcinoma. [3]

In agreement to recent studies, we have also determined that tumor grade was significantly higher in ductal cases and these cases were therefore more likely to be poorly differentiated and have metastatic

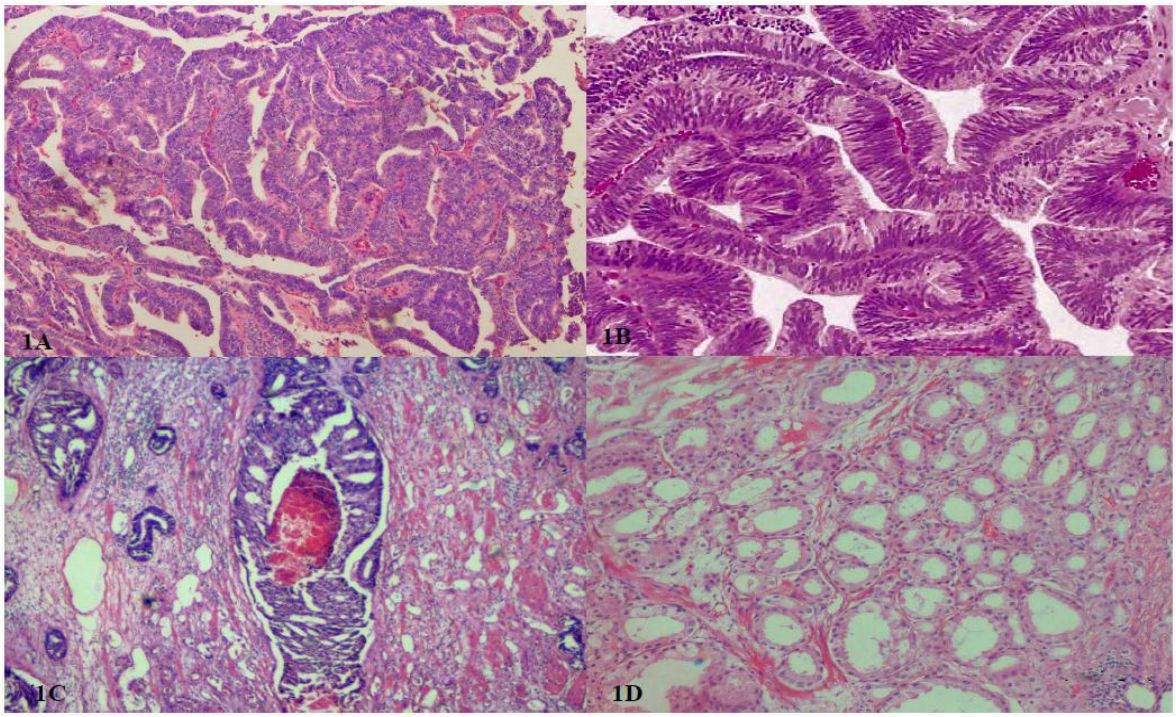

Figure 1. A. Prostatic ductal adenocarcinoma with papillary morphology (10x). B. Papillary proliferation lined by tall columnar cells (40x). C. Cribriform prostatic ductal adenocarcinoma with central necrosis (40x). D. Non-Ductal acinar adenocarcinoma exhibiting small round crowded glands lined by a single layer of cuboidal cells (40x).

Table 1: Histopathology comparison of ductal prostatic adenocarcinoma and non-ductal prostatic adenocarcinoma with statistical estimates.

Tumor (Adenocarcinoma) n = 150	Morphology	Age			Gleason Score		
		≤65	>65	p-value [a]	≤7	>7	p-value [b]
Ductal n =10	Papillary or cribriform architecture with absent basal layer	6	4	0.53*	1	9	0.03*
Non-Ductal (Acinar) n = 140	Atypical glands lined by cuboidal cells having round nuclei with absent basal layer	59	81	0.06*	63	77	0.23*

[a] p-values for comparisons between age and tumors; [b] p-values for comparisons between Gleason score and tumors;
* Binary Logistic Regression test.

disease at the time of diagnosis than did acinar or non-ductal adenocarcinomas. We therefore suggest that the detection of ductal carcinoma on pathology independently predicts a bad overall prognosis, thus early detection of the tumor is important for the patient's survival.

Papillary and cribriform architectures were the two predominant morphological patterns in ductal cases. Similar patterns were observed in previous investigations as well. [6, 7] Additionally, like previous studies, we have also determined that cancers with ductal histology are generally found to have an acinar component as well. [2, 3, 5]

Morgan et al. reported a significant relationship of age >70 years with ductal carcinoma. [3] Contrary to these findings, we have noticed that majority of ductal cases were aged <65 years. However, we were unable to document a significant statistical link between them. Limited number of ductal cases included in the present study could explain this discrepancy. We therefore, suggest further research with a larger series of samples to confirm the relationship between age and ductal carcinoma.

There are several limitations in this study. First, the cases we analyzed were selected from the transurethral resection of prostate (TURP) specimens. So, more advanced ductal or acinar adenocarcinoma cases that were considered to be non-surgical candidates were not included in our analysis. Secondly, TURP specimens further limit us to consider other parameters such as tumor stage and PSA levels for comparative analyses. Third, the cases of ductal carcinoma were limited in number and that all ductal cases we examined showed more than 60% of the ductal component, thus we could not determine whether cases that contain lesser volume of ductal component would also show more advanced pathological features comparing to non-ductal acinar adenocarcinoma or not.

Conclusion

In the present study, we characterize a rare but important subtype of prostate cancer. The findings in this study favor a more aggressive natural history of ductal adenocarcinomas when compared to non-ductal acinar adenocarcinomas. Ductal adenocarcinomas are more likely to present with high pathological grade. Further prospective research will be required to confirm the findings reported in this study, and will therefore be potentially helpful to identify the factors responsible for the observed differences between ductal and non-ductal acinar prostate cancers.

Acknowledgements

We thank Dr. Nadeem Khan, Mr. Manzoor Ahmed Asi and the whole histopathology team for their professional assistance whenever needed. Special thanks to the Vice Chancellor Prof. Dr. Masood Hameed Khan and all members of BASR, Dow University of Health Sciences for approving this research.

Funding

None.

Competing Interests

None declared.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA: a cancer journal for clinicians. 2011;61(2):69-90. Epub 2011/02/08.
2. He Huang FC. Prostatic Ductal Adenocarcinoma Exhibits More Advanced Histopathological Features than Acinar Adenocarcinoma. North American Journal of Medicine and Science. 2012;Vol 5(4):208-11.
3. Morgan TM, Welty CJ, Vakar-Lopez F, Lin DW, Wright JL. Ductal adenocarcinoma of the prostate: increased mortality risk and decreased serum prostate specific antigen. The Journal of urology. 2010;184(6):2303-7. Epub 2010/10/19.
4. Epstein JI. Prostatic ductal adenocarcinoma: a mini review. Medical principles and practice : international journal of the Kuwait University, Health Science Centre. 2010;19(1):82-5. Epub 2009/12/10.
5. Epstein JI, Allsbrook WC, Jr., Amin MB, Egevad LL. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. The American journal of surgical pathology. 2005;29:1228-42. Epub 2005/08/13.
6. Humphrey PA. Histological variants of prostatic carcinoma and their significance. Histopathology. 2012;60:59-74. Epub 2012/01/04.
7. Grignon DJ. Unusual subtypes of prostate cancer. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2004;17:316-27. Epub 2004/02/21.
8. Samaratunga H, Duffy D, Yaxley J, Delahunt B. Any proportion of ductal adenocarcinoma in radical prostatectomy specimens predicts extraprostatic extension. Human pathology. 2010;41:281-5.
9. Amin A, Epstein JI. Pathologic stage of prostatic ductal adenocarcinoma at radical prostatectomy: effect of percentage of the ductal component and associated grade of acinar adenocarcinoma. The American journal of surgical pathology. 2011;35(4):615-9.
10. Epstein JI, Woodruff JM. Adenocarcinoma of the prostate with endometrioid features. A light microscopic and immunohistochemical study of ten cases. Cancer. 1986;57(1):111-9. Epub 1986/01/01.
11. Bostwick DG, Kindrachuk RW, Rouse RV. Prostatic adenocarcinoma with endometrioid features. Clinical, pathologic, and ultrastructural findings. The American journal of surgical pathology. 1985;9(8):595-609. Epub 1985/08/01.
12. Greene LF, Farrow GM, Ravits JM, Tomera FM. Prostatic adenocarcinoma of ductal origin. The Journal of urology. 1979;121(3):303-5. Epub 1979/03/01.
13. Aydin H, Zhang J, Samaratunga H, Tan N, Magi-Galluzzi C, Klein E, et al. Ductal adenocarcinoma of the prostate diagnosed on transurethral biopsy or resection is not always indicative of aggressive disease: implications for clinical management. BJU international. 2010;105(4):476-80. Epub 2009/08/28