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Original contribution

Tumor necrosis in radical prostatectomies with high-grade prostate cancer is associated with multiple poor prognostic features and a high prevalence of residual disease☆

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Summary The Gleason grading system and the recently defined Grade Groups are strong, well-established predictors of outcome in prostate cancer. Each Gleason score, however, is the result of a sum of categories (Gleason patterns or GPs) that are intrinsically heterogeneous, as each individual pattern encompasses several tumor morphologies. Although the prognostic value of specific morphologic components of GP4 has recently been demonstrated, the significance of the different patterns of GP5 is largely unknown. We reviewed 344 consecutive prostatectomies performed at the Hospital of the University of Illinois at Chicago between 2011 and 2016 and selected 56 cases with primary or secondary GP5 with archival material available for review. Subsequently, we sorted the cases according to the presence or absence of tumor necrosis in invasive adenocarcinoma GP5—designated G5 (+N) and G5 (−N), respectively—for comparison of histopathologic and clinical characteristics. The GP5 (+N) group demonstrated higher prevalence of biochemical recurrence ($P = .0006$) and seminal vesicle invasion ($P = .02$), with a trend toward a higher frequency of lymph node metastases ($P = .07$) and multifocal surgical margin involvement ($P = .09$). Also, G5 (+N) patients showed higher preoperative prostate-specific antigen values ($P = .005$) and a larger percentage of submitted tissue involved by tumor ($P < .0001$). Our results show that GP5 with tumor necrosis is associated with poor prognostic histopathologic features and high rates of residual disease after prostatectomy.

1. Introduction

The Gleason grading system, originally described by Dr Donald F. Gleason in 1966 [1], has successfully passed the test of time. Undoubtedly, its prevailing role as a powerful

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predictor of outcome is tightly related to its original validation on a large clinical cohort [2]. Since its inception, this grading system has undergone 2 significant modifications in 2005 and 2014, respectively [3,4]. During the International Society of Urological Pathology (ISUP) consensus meeting held in Chicago in 2014, scoring of the different architectural patterns found in prostate cancer was thoroughly revised. Agreement was reached by an overwhelming majority of attendants (94%) to assign a Gleason pattern (GP) 5 to cribriform lesions with unequivocal comedonecrosis. In contrast, consensus was not reached about the grading of discrete glands with intraluminal necrotic debris.

In the 2014 ISUP meeting, Dr Jonathan Epstein also proposed the adoption of a 5-tiered Grade Group system, where tumors containing primary or secondary GP5 correspond to 1 of the 2 highest-risk categories: Grade Group 4 and Grade Group 5. Support for this proposal stems from the significant differences in biochemical progression–free survival between Grade Groups demonstrated in 2 large studies and from the counterintuitive nature of the original grading system, which classifies low-risk disease as Grade 6 [5,6]. Although the categories of both the Gleason score (GS) and the newly introduced Grade Group system are unquestionably powerful as clinical predictors, they are also intrinsically heterogeneous. Internal variation can be explained in part by the structure of the GS, a summative score where every addend—ie, GP—consists of a spectrum of tumor morphologies rather than a uniform histologic pattern. In this study, we evaluate the significance of tumor necrosis (TN) in patients with prostate cancer containing primary or secondary GP5. To this end, we reviewed all radical prostatectomies performed at the Hospital of the University of Illinois at Chicago from January 2011 to December 2016 and selected those with primary or secondary GP5. Cases were then assigned to 1 of 2 groups depending on the presence or absence of TN in GP5 for comparison of histopathologic and clinical data.

2. Materials and methods

This study was performed with approval from the Institutional Review Board of the Office for the Protection of Research Subjects (Research Protocol #2017-0640).

2.1. Case selection

A search for all radical prostatectomies performed at the Hospital of the University of Illinois at Chicago between January 2011 and December 2016 was conducted using the intradepartmental PathNet Anatomic Pathology: Pathology Case Retrieval software (build: 2016.05.1.89), identifying a total of 344 cases. All reports were reviewed, and cases with GP5 were initially selected. Specimens with >5% GP5 corresponding to either the primary or secondary pattern of the tumor were included in the study provided that they met the additional qualifiers detailed below.

Histology slides of cases with GP5 were reviewed by 5 authors (A. M. A., M. R. H. A. R., E. V., A. S., K. S. M.). All cases with possible TN were presented at a consensus meeting, and only those for which agreement was reached about the presence of TN as defined below were further evaluated by

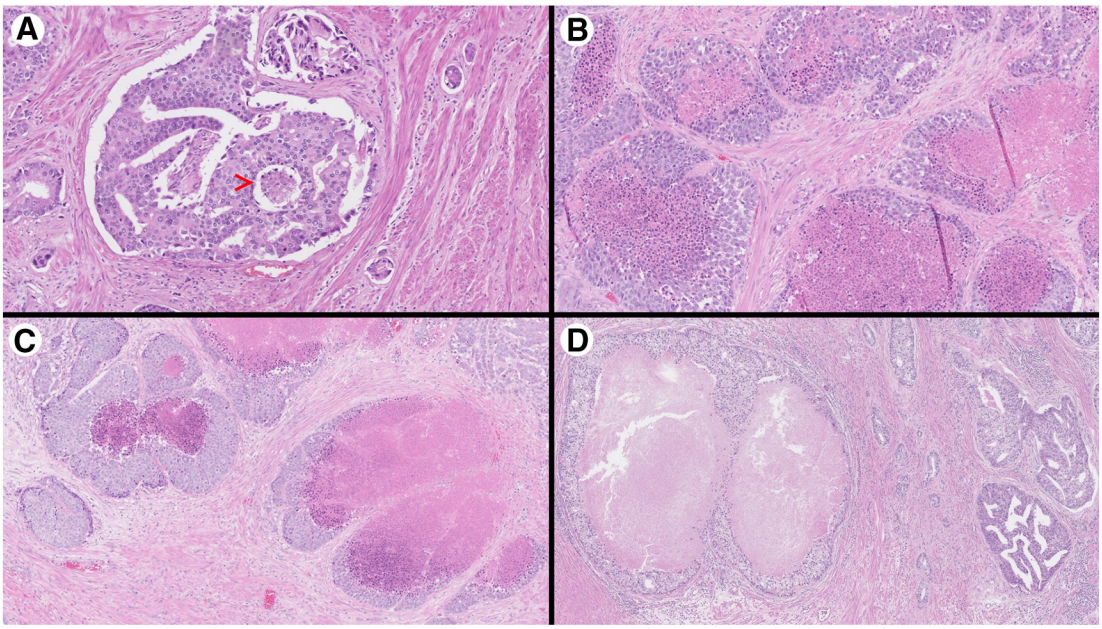

Fig. 1 A, Cribriform tumor with small focus of "punctiform" TN (red arrowhead) consisting of 4-10 karyorrhectic cells and necrotic debris (hematoxylin and eosin stain, original magnification ×150). B, Focal necrosis (hematoxylin and eosin stain, ×150). C, Diffuse necrosis consisting of confluent necrotic foci (hematoxylin and eosin stain, ×100). D, Eosinophilic debris without clear evidence of karyorrhexis, interpreted as secretions (hematoxylin and eosin stain, ×70).