



Incidence and Clinicopathological Characteristics of Gleason Pattern 5 Prostate Cancer in Contemporary Needle Biopsies Series: A Prospective Study

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Background

- Management of patients with prostate adenocarcinoma (PCa) heavily depends on the Gleason score assigned on prostate needle biopsy (NBX).
- The presence of a Gleason pattern 5 (GP5) PCa is associated with disease progression and the worst clinical outcome. Patients with GP5 are often not amenable to surgical intervention, instead receiving hormonal and radiation therapy.
- Previous studies have demonstrated that GP5 is underdiagnosed by pathologists.
- Due to its poor clinical significance, the 2005 International Society of Urologic Pathologist (ISUP) modification of Gleason grading system recommends upgrading of tertiary GP5 in prostate NBX to a secondary Gleason pattern regardless of how small the amount of GP5 might be.

Aims

- To formally assess incidence, pattern distribution, and pathological variables associated with GP5 PCa in NBXs settings, especially after introduction of the 2005 ISUP modified Gleason grading system.
- To assess morphological spectrum of GP5 PCa in relation to its pattern distribution.

Methods

- A total of 1557 consecutive and prospectively collected prostate NBX cases were evaluated to determine incidence and pathological variables of GP5 PCas.
- Gleason grading was performed according to the 2005 ISUP modified Gleason grading system. All cases with tertiary GP5 component were upgraded to secondary pattern to assign final Gleason score.
- All GP5 cases were prospectively re-reviewed in the departmental consensus conference by study authors. As a rule, high threshold was utilized before diagnosing GP5. Cases where tangential sectioning of poorly formed Gleason pattern 4 glands could not be ruled out were interpreted as Gleason pattern 4.

Results

Incidence of Gleason Pattern 5 Prostate cancer

Of 1557 NBXs, PCa was detected in 664 cases. GP5 was present in 94 (6%) of all NBX cases. Of 664 PCa cases, GP5 represented 14% of cases.

Table 1: Clinicopathological Characteristics of 94 PCa Cases with a Component of GP5

Mean age, years (range)	71 (47-92)
Mean pre-biopsy PSA, ng/ml (range)	39 (2.5-1469)
Mean number of biopsy cores (range)	8 (6-14)
Mean percent positive cores (range)	68 (6-100)
Mean core with highest tumor volume (range)	60 (5-100)
Mean percent core involvement by GP5 (range)	12 (5-65)
Perineural invasion (%)	65 (69)
Extraprostatic extension (%)	12 (13)
Intraductal spread of PCa (IDC-P) (%)	29 (31)
Highest Gleason score (%)	
3+5=8	34 (36)
5+3=8	1 (1)
4+5=9	58 (62)
5+4=9	1 (1)

Distribution of GP5 PCa

The distribution for GP5 was as follows: primary component (n=2, 2%), secondary component (n=30, 32%), and tertiary component (n=62, 66%).

Table 2: Morphological Presentations Based on Distribution of Gleason Pattern 5

Architectural Pattern	Primary pattern 5 (n=2)	Secondary pattern 5 (n=30)	Tertiary pattern 5 (n=62)
Cords	1 (50)	29 (97)	61 (98)
Single cells	1 (50)	21 (70)	50 (81)
Solid sheets/Nests	1 (50)	14 (47)	12 (19)
Comedonecrosis	-	-	2 (3)

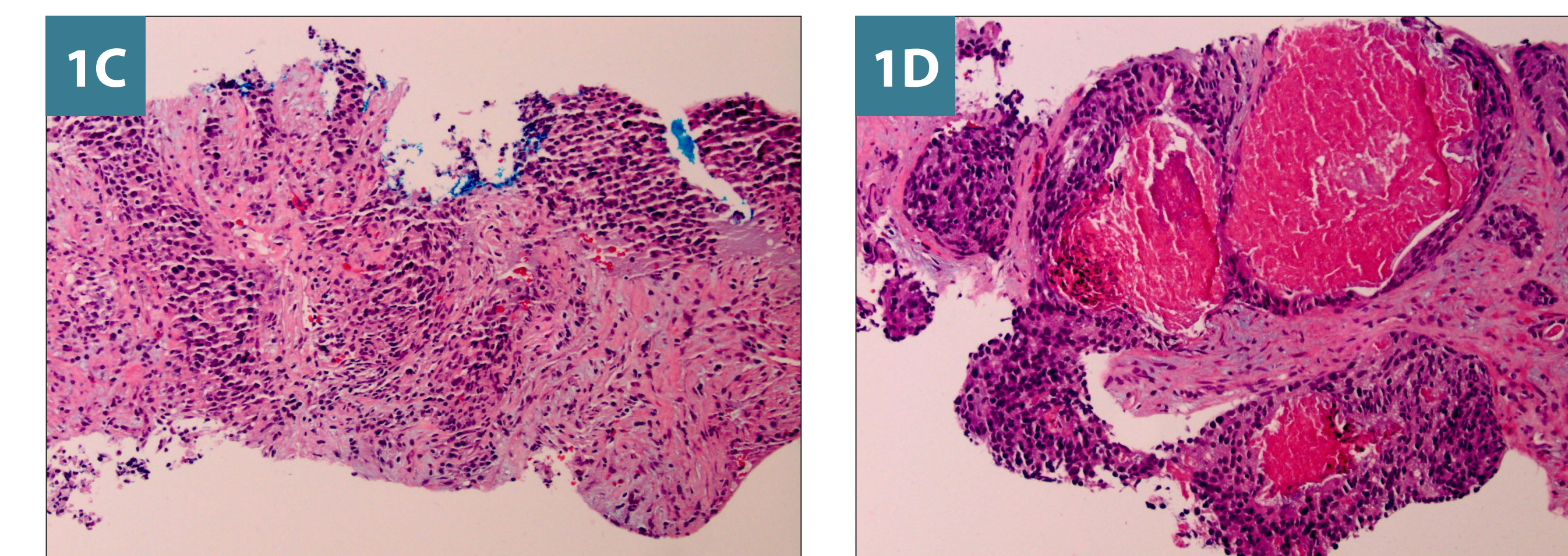
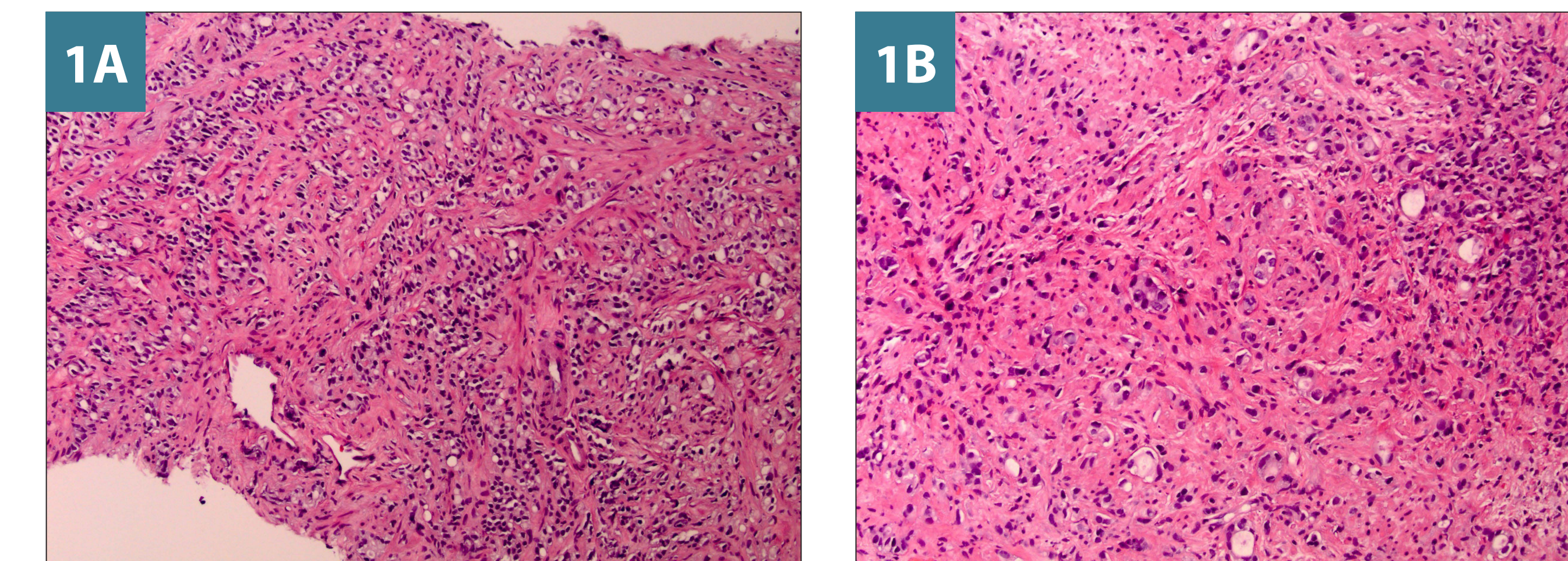


Figure 1. A-D. Morphological spectrums of GP5 PCa and relation to pattern distribution. GP5 composed of infiltrative tumor cords (A) and single cells (B). These two architectural patterns are most frequently encountered when GP5 is present in secondary or tertiary distribution pattern. GP5 composed of tumor in solid nests and sheets architecture (C). GP5 composed of comedonecrosis pattern (D). Comedonecrosis GP5 was least frequently encountered.

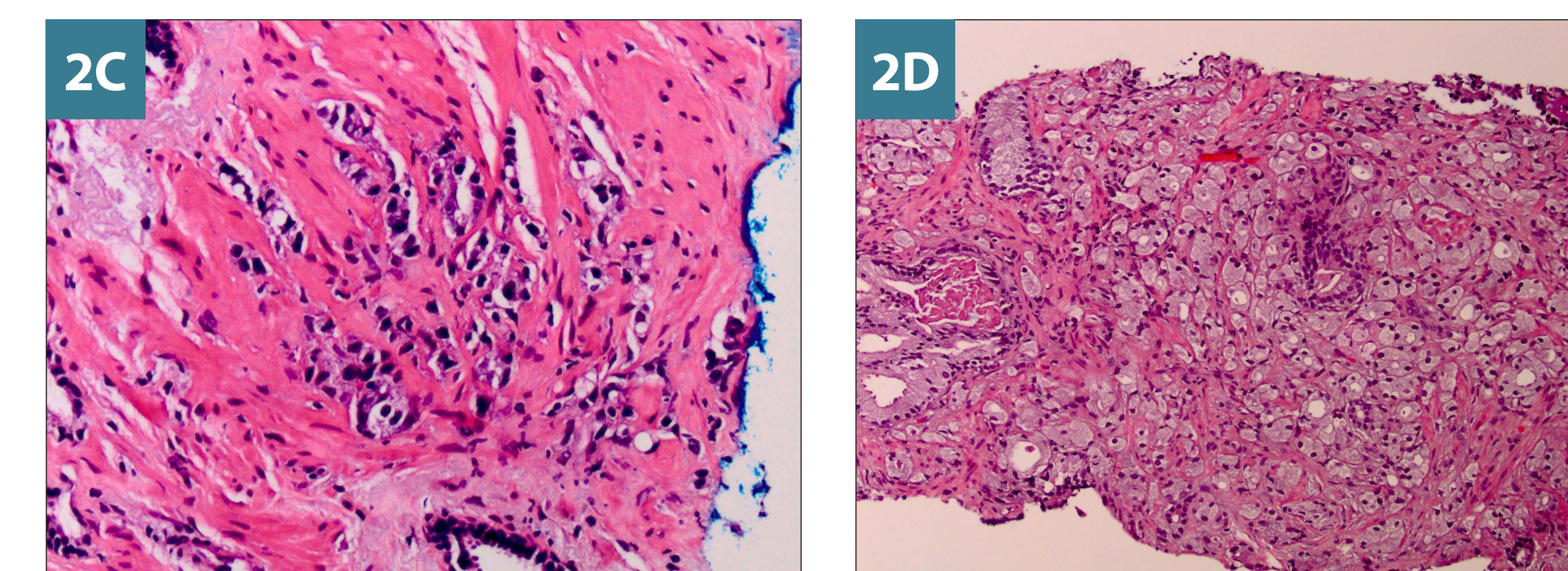
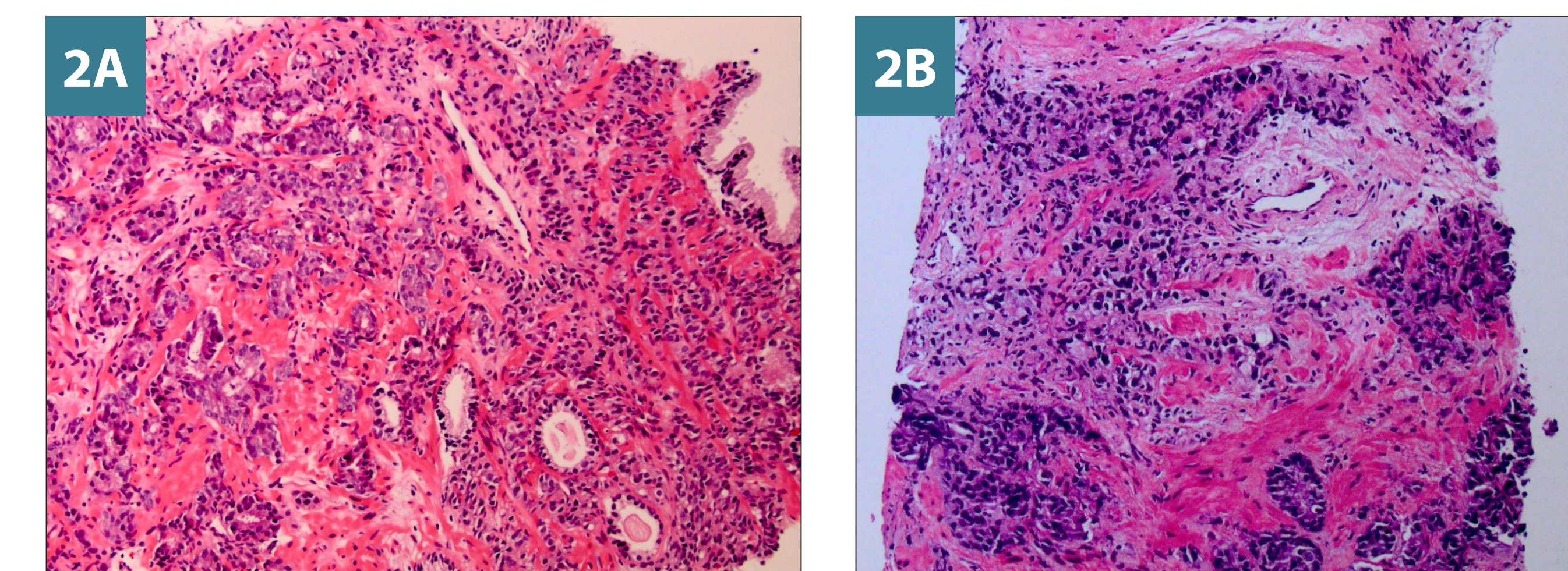


Figure 2. A-D. Examples of GP5 presenting as a tertiary component of PCa in prostate NBX. A prostate NBX demonstrating primary pattern 3, secondary pattern 4 (poorly formed glands), and tertiary pattern 5 (infiltrative cords); such a case is assigned as Gleason score 3+5=8 (A). Examples of infiltrating cords of PCa (B-C) and individual cells (D) diagnosed as tertiary component GP5 (primary and secondary Gleason pattern not shown). Cords and single cells could be misinterpreted as poorly formed glands of Gleason pattern 4. The presence of many cords and/or single cells, high N:C ratio of the tumor cells (A-C) and maintenance of cords and single cells architecture at multiple levels support the diagnosis of GP 5 component. In panel D, the cells have foamy features resulting in low N:C ratio (D).

Study Highlights

- Gleason pattern 5 (GP5) is a relatively frequent presentation in the contemporary NBX practice setting and is associated with several high-risk clinicopathological features.
- The majority of GP5 represent tertiary or secondary component of carcinoma
- Infiltrating tumor cords and single cells are the two most frequently encountered morphological presentations, specifically when GP5 PCa is present as secondary or tertiary component of PCa in NBXs. Comedonecrosis is the least common morphological presentation.
- While considering tertiary or secondary GP5 PCa in NBX, multiple levels should be evaluated to differentiate tangentially sectioned poorly formed glands of pattern 4 from cords and single cells pattern of GP5. This diagnostic pitfall specifically in the setting of tertiary distribution pattern of GP5 may account for its under recognition.
- Due to the important prognostic and therapeutic implications of GP5, pathologists must be aware of its varied morphological presentations, clinicopathological spectrum and the fact that the majority of GP5 represent a tertiary or secondary component of carcinoma.

References

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