Implications of Accurate Interpretation of Carcinoma in Prostate Biopsy

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Prostate carcinoma is the second leading cause of cancer in men in the United States (US). Despite controversies on the efficacy of prostate cancer screening, it has become more common in the US since the early 1990s. Among the screening methods, needle biopsy is the most powerful and reliable means of diagnosis of prostate adenocarcinoma (PCA) that dictates the management protocol and follow-up regimen.¹

A review of the Surveillance, Epidemiology and End Result Program (SEER) 2019 data shows that PCA survival depends on the extent [stage] of tumor at the time of diagnosis, with 100% survival for localized PCA.² The excellent survival rate is regardless of the management protocol [surgery, radiation or observation].³

Less aggressive observation management of PCAs has become more popular nowadays due to the slow growth of this tumor. Based on the definition by the National Cancer Institute [https://www.cancer.gov/], observation management is divided into two categories:

Active Surveillance (AS): is used to avoid or delay the need for more aggressive treatments such as radiation therapy or surgery, which can cause side effects or other problems. During AC, certain exams and tests are done in a regular schedule.

Watchful Waiting (WW): is referred to closely watching patients with documented low to intermediate risk PCAs by tests and examinations but not giving definite treatment unless symptoms appear or change. In addition to slow growing conditions, WW is sometimes used in conditions when the risks of treatment are greater than the possible benefits.

Based on the successful experience with AS, it is currently recommended in management of low risk PCAs. The morphological criteria defining low risk PCAs include: grade group 1 [Gleason score ≤6], low volume disease (<2-3 cores involved by adenocarcinoma, involving ≤50% of each core], PSA ≤10 ng/ml and clinical stage ≤T2a.⁴,⁵ Studies have revealed that despite a potential risk of delaying treatment and missing the window of curability, AS and [in certain cases] WW are the preferred option for management of patients’ quality of life.⁶ This mandates an accurate interpretation of the Gleason score.

There are controversies in the interpretation of prostate biopsies between general and genitourinary pathologists, including overgrading of Gleason pattern 4 and undergrading Gleason pattern 5 in needle biopsies.⁷,⁸,⁹,¹⁰ Among these, overgrading of pattern 4 appears to be of significant implication, especially because it can deprive the patient of AS and result in overtreatment.¹⁰

Several morphological subtypes of Gleason pattern 4 PCAs have been introduced, including [in decreasing order of frequency] poorly formed glands, cribriform, glomeruloid and hypernephromatoid subtypes. These subtypes are usually identified admixed with each other. Studies have revealed a worse outcome associated with cribriform and glomeruloid subtypes,¹¹,¹² but there is not enough data to support the behavior of other subtypes, especially the poorly formed glands. It appears that the most discrepancy in diagnosis of Gleason pattern 4 stems from detection and quantity of poorly formed Gleason pattern 4.¹³

Some studies recommend radical treatment procedure for PCAs containing a significant amount of Gleason pattern 4 with cribriform morphology¹⁴; however, others report that AS is an acceptable management method when confronting limited Gleason pattern 4 in grade group 2 PCAs (<50% Gleason pattern 4 limited to a single area).¹⁵ This mandates a systematic and careful grading of PCAs by the pathologists with quantitating the higher grade component.¹⁶ Epstein et al have advised practicing caution in overcalling Gleason pattern 4 in suspected poorly formed glands.¹⁷ Other experts have provided more objective criteria to facilitate diagnosis of poorly formed pattern 4, including practicing caution in calling limited [≤5] poorly formed glands immediately adjacent to well-formed glands.¹³

In our practice, we have confronted discrepancies in the interpretation of Gleason score where our review altered the management in up to 8% of the cases.¹⁰ Some of the most common discrepancies we identified included overcalling adenocarcinoma in foci with high grade prostatic intraepithelial neoplasia (HGPIN) and outpouching of atypical small acinar proliferation (ASAP) next to HGPIN, overcalling limited poorly formed glands admixed with well-formed glands as pattern 4, overcalling branching glands as Gleason pattern 4 and overcalling pattern 5 in intraductal spread of acinar PCAs. Similarly, it is unnecessary to provide confusing information like numerical Gleason grade to mimickers of PCA [i.e. ASAP].

In order to provide a standard format of reporting PCAs
in needle biopsy, the College of American Pathologists [https://www.cap.org/], Genitourinary Pathology Society [https://www.gupathsociety.org/] and International Society of Urological Pathologists [https://isupweb.org/isup/] provide up-to-date standard protocol templates and guidelines that can reduce discrepancies in interpretation. It is essential that pathologists and men’s health caregivers follow the guidelines in diagnosis and grading of PCa to facilitate proper management and prevent potential liability.

References

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