Borderline Gleason scores: communication is the key

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The biopsy Gleason score (GS) is a critical component of patient management having been demonstrated to be an excellent predictor of patient outcome.[1 2] While the application of Gleason grading is generally straightforward, grading is subject to significant interobserver variation[3] and divergent opinions may confuse clinicians and patients.

Interobserver variation may be due to the application of different grading rules or more commonly different interpretations of borderline morphological appearances. The former is avoidable and multiple consensus conferences have sought to define uniform criteria for grading prostate cancer.[4–7] However, the latter is inevitable in a morphological continuum. We seek to explain why precise grading becomes less important in this scenario, if the findings are effectively communicated by the pathologist and correctly interpreted by the clinician.

Gleason grades commonly represent a morphological continuum from well-formed glands (pattern 3) to increasingly smaller-sized and poorly formed glandular proliferations (pattern 4) and finally to almost no glandular differentiation (pattern 5). Thus, GS is often a continuous variable with arbitrary cut-offs. This is analogous to serum Prostate Specific Antigen (PSA) where arbitrary cut-offs are used to categorise patients into risk groups. However, unlike serum PSA, grade is reported as a discrete variable and it may not be obvious to the clinician whether the reported pattern 4 represents tumour that is bordering on either pattern 3 or pattern 5. Although considerably better defined there may also be difficulty in defining cribriform glands and glomerular glands in terms of size and amount of glandular bridging.[8]

Gleason grades also represent a biological continuum of increasing aggressive behaviour, so it is unlikely that there is a clinically significant difference between tumours at the higher end of GS 6 or lower end of GS 7. Hence, it would be reasonable to treat a patient with such a borderline score as either GS 6 or GS 7. This is like the earlier described scenario with serum PSA. Bone scan examination is recommended for patients with high-risk prostate cancer[9] but serum PSA levels of 19 ng/mL and 21 ng/mL are likely to signify a similar risk even though the former may be categorised as intermediate risk and the latter as high risk. Hence, it could be entirely reasonable to omit this investigation in patients with PSA 21 ng/mL if the tumour is GS 6 and stage T1c.

Although precision of grading is not critical in a morphological and biological continuum, it is of paramount importance that this information is properly communicated to clinicians in order to enable them to judge where the tumour lies within the biological spectrum. While the outcome of a tumour at the lower end of the GS 7 spectrum would not be different from that of one at the higher end of the GS 6 spectrum, it would be significantly better than that of a tumour at the higher end of the GS 7 spectrum. Unlike radiological data, clinicians generally do not view histopathology material and are hence dependent on the pathology report for this information.

One approach to conveying this information is to report the percentage pattern 4 in GS 7 prostate cancers as recommended by the International Society of Urological Pathology.[6] However, there is no clarity regarding how percentage pattern 4 should be calculated. It is uncertain whether one should compare the area of prostate tissue (including stroma) involved by patterns 3 and 4, the area of each tumour pattern or the number of cells in each pattern. For example, microcystic pattern 3 would occupy a relatively large area but have much fewer cells than dense cribriform pattern 4 (figure 1). Pathologists should appreciate that reporting of percentage pattern 4 in prostate needle biopsies is primarily about communication rather than precision, with a focus on flagging cases near the clinically relevant cut offs of percentage pattern 4 (0%, 50% and 95%). This information could enable a clinician to consider active surveillance as an option for patients with limited pattern 4 in a biopsy or treat a man with about 50% pattern 4 using either GS 3+4 or GS 4+3 treatment protocols, after consideration of other factors such as PSA, tumour size and the patient's risk tolerance. Once the information has been effectively communicated to the clinician, the onus is on the latter to interpret this information correctly. It must be recognised that the biopsy GS is subject to significant sampling error and provides only a rough estimate of the true tumour grade. For example, it has been reported that in about 20% of patients with biopsy GS 4+4=8, tumour in the corresponding radical prostatectomy specimen would be primary pattern 3 (GS 3+3 or 3+4).[10] Percentage pattern 4 in GS 7 tumours should be interpreted in the context of the denominator. For example, 80% pattern 4 in a 2 mm tumour focus is not equivalent to that in a 20 mm focus.

Appropriate communication and interpretation are critical for optimal use of Gleason grading in management of patients with prostate cancer. While a simple proforma-based report would generally suffice, cases with a borderline GS may require a

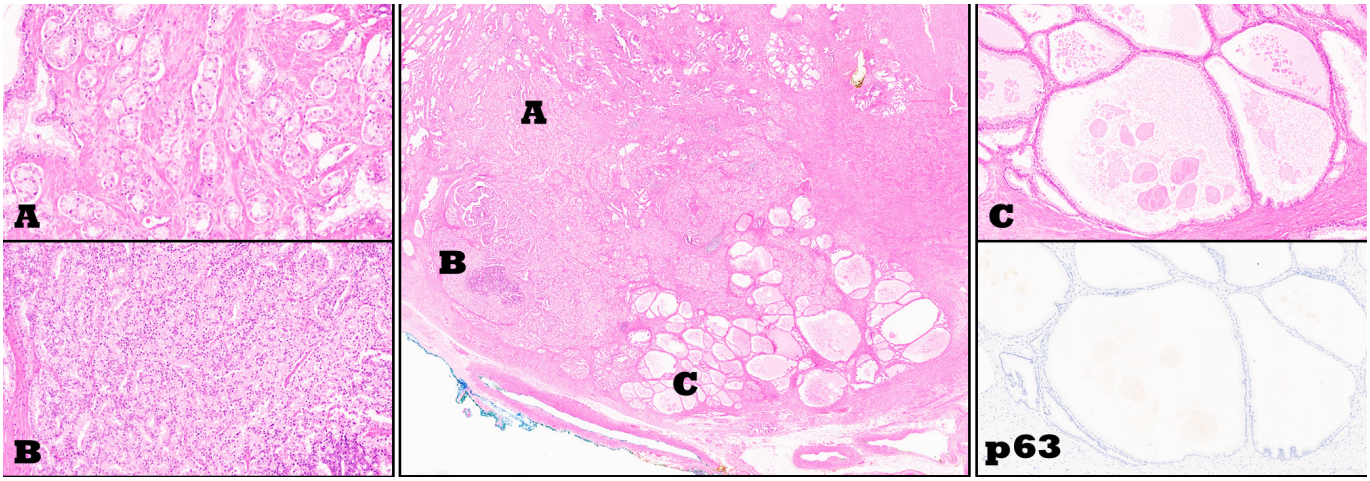

Figure 1 Glandular fusion Gleason pattern 4 prostate cancer (B) would have significantly larger number of cells than comparable area of microcystic (C) or conventional (A) pattern 3 prostate cancer.

short comment clarifying the issue. Gleason grading represents for most subpatterns a morphological and biological continuum, so pathologists should try to avoid changing the GS in cases that are truly borderline, which the same pathologist might interpret differently on different days. In this scenario, an explanatory comment could be provided if necessary.

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