Impact of Pathology Review for Decision Therapy in Localized Prostate Cancer

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ABSTRACT

BACKGROUND: The Gleason score is an essential tool in the decision to treat localized prostate cancer. However, experienced pathologists can classify Gleason score differently than do low-volume pathologists, and this may affect the treatment decision. This study sought to assess the impact of pathology review of external biopsy specimens from 23 men with a recent diagnosis of localized prostate cancer.
METHODS: All external biopsy specimens were reviewed at our pathology department. Data were retrospectively collected from scanned charts.
RESULTS: The median patient age was 63 years (range: 46-74 years). All patients had a Karnofsky performance score of 90% to 100%. The median prostate-specific antigen level was 23.6 ng/dL (range: 1.04-13.6 ng/dL). Among the 23 reviews, the Gleason score changed for 8 (35%) patients: 7 upgraded and 1 downgraded. The new Gleason score affected the treatment decision in 5 of 8 cases (62.5%).
CONCLUSIONS: This study demonstrates the need for pathology review in patients with localized prostate cancer before treatment because Gleason score can change in more than one-third of patients and can affect treatment decision in almost two-thirds of recategorized patients.

KEYWORDS: Prostate cancer, Gleason score, pathology, prostate adenocarcinoma

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Introduction

Prostate adenocarcinoma is the most common cancer in men, with increasing incidence of diagnoses at earlier stages of disease in recent years, mainly due to the application of the prostate-specific antigen (PSA) test.[1]

In patients with localized disease, stratification of the risk for disease progression and calculation of life expectancy are fundamental tools in choosing the appropriate treatment for each patient.[2] Currently, this stratification is determined from a group of factors that are based on the TNM staging of the disease, the Gleason score, and levels of PSA.[3–5]

The Gleason score is still an essential tool in the decision to start initial treatment of localized prostate cancer. However, experienced pathologists can classify Gleason score differently than do general pathologists.[6–10]

To illustrate the importance of Gleason score in low-risk patients with a Gleason score of 6 in active surveillance, Fleshner et al[11] found that a repeat biopsy strategy showed a 38% score increase.

We also have evidence that the Gleason score on needle biopsy is an inexact predictor of the final score following prostatectomy, and patients with a biopsy Gleason score of 6 who are undergraded are at significantly higher risk for adverse pathological features and biochemical recurrence.[12]

In some situations, pathology review by a different pathologist results in a new score. Pathology review can affect treatment decision.

Objectives

This article assessed the impact of pathology review of external biopsy specimens from 23 men with a recent diagnosis of localized prostate cancer. These patients were evaluated at the Prostate Cancer Multidisciplinary Clinic for a second opinion from January 2012 to December 2014.

Methods

Data were collected from patients referred to the Prostate Cancer Multidisciplinary Clinic at Albert Einstein Israeli Hospital whose biopsy specimens underwent pathology review with a dedicated urologic pathologist. Patient data and test results were obtained from scanned institutional records.

After comparing pathological results, we evaluated the medical management after review. Only cases of adenocarcinoma of the prostate were evaluated. For cases in which prostatectomy was performed, we evaluated the Gleason score obtained from surgical specimens for simple conference. Specimens were reviewed by our pathology staff.

Because a new prostate cancer grading system was recently proposed,[13,14] we added the new classification (Appendix 1). This project was approved by the institutional review board at Hospital Israelita Albert Einstein (CAAE: 64147617.1.0000.0071).

Results

From January 2012 to December 2014, 50 second-opinion consultations were held at the Prostate Cancer Clinic. A total

of 23 cases of prostate adenocarcinoma had slides for review. These are the subjects of our research.

Patient characteristics are shown in Table 1. The median age was 63 years, and all patients had a Karnofsky performance score of 90% to 100%. The median PSA level was 6.23 ng/mL. Most patients had a T1c or T2a clinical stage.

We found 8 Gleason score changes, corresponding to 34.7% of the sample. The difference in score influenced the treatment in 5 of 8 cases (62.5%) (Appendix 2). After review, the first patient, aged 63 years, PSA of 6.23 ng/mL, and T2a stage with Gleason score 7 (4 + 3) (grade group 3), was upgraded to a Gleason score of 8 (4 + 4) (grade group 4). The other reported patients had a Gleason score of 6 (3 + 3) (grade group 1) that after review had increased to 7 (3 + 4) (grade group 2). Prostatectomy was performed in 4 of them (Table 2).

Table 1. Demographic characteristics.

CHARACTERISTICS	N (23)
Age, y	
Median	63
Interval	46–74
PSA, ng/mL	
Median	6.23
Interval	1.04–13.6
Staging (TNM)	
T1a	2
T1b	1
T1c	11
T2a	5
T2b	1
T2c	1
T3a	1
T4	1

Abbreviations: PSA, prostate-specific antigen; TNM, tumor, node, metastasis.

Discussion

Our study shows the importance of pathology review by an expert pathologist in the diagnosis of localized prostate cancer. Gleason score can change in more than one-third of patients and can affect treatment decision in almost two-thirds of recategorized patients.

The use of Gleason score in risk stratification for treatment of prostate adenocarcinoma is well established.[15,16] The different ways of calculating the score are factors that may result in discordant analysis between pathologists from different services, according to the protocol of each institution.[15]

Currently, the modified Gleason score (International Society of Urological Pathology) makes the standard definition of Gleason pattern 3 extremely rigorous and has led to a reduction in the frequency of Gleason 6 (3 + 3) prostate adenocarcinoma and an increase in the frequency of Gleason 7 (3 + 4).[16,17]

In other words, a Gleason score of 6 has become a diagnosis of exclusion. Thus, the nonrecognition of new standards for defining criteria of Gleason patterns 3 and 4 (Figure 1) can lead to an "upgrade" at the time of histopathology review in reference centers. Another pathological factor contributing to the discrepancy in Gleason grading between primary centers and referral centers is the low frequency with which Gleason pattern 5 is recognized in prostate biopsy specimens (Figure 2).[17–19]

According to the series of Fajardo et al, of the total number of cases that were referred for second opinion in a reference center and featured Gleason pattern 5 on biopsy, about 48% had not been identified by general pathologists in the initial

Table 2. Discordant cases with histopathologic analysis and established treatments.

PATIENT NO.	AGE, Y	cTNM	PSA, NG/DL	GLEASON [GRADE GROUP]	GLEASON REVISED [GRADE GROUP]	TREATMENT DOUBT	ESTABLISHED TREATMENT
1	63	T2a	6.23	7 (4+3) [3]	8 (4+4) [4]	Radiotherapy and hormonal blockade or prostatectomy	Prostatectomy
2	71	T2a	7.0	6 (3+3) [1]	7 (3+4) [2]	Active surveillance or prostatectomy	Prostatectomy
3	55	T1c	11.5	6 (3+3) [1]	7 (3+4) [2]	Radiotherapy and hormonal blockade or prostatectomy	Radiotherapy and hormonal blockade
4	58	T1b	8.6	6 (3+3) [1]	7 (3+4) [2]	Active surveillance or prostatectomy	Prostatectomy
5	68	T1c	8.84	6 (3+3) [1]	7 (3+4) [2]	Active surveillance or prostatectomy	Prostatectomy

Abbreviations: PSA, prostate-specific antigen; cTNM, clinical tumor, node, metastasis.

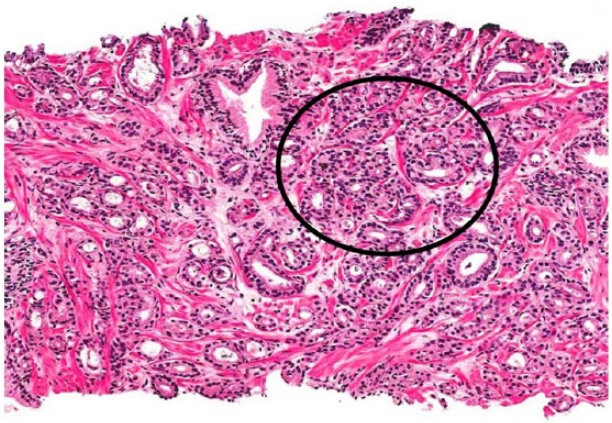

Figure 1. Patient 2 usual adenocarcinoma Gleason 7 (3+4) [grade group 2] (hematoxylin-eosin, original magnification ×200). In the previous scheme, the Gleason grade in this case would have been graded as Gleason 6 (3+3). In the present scheme, however, this case is graded as 7 (3+4). The areas marked in the figure have infiltrative, confluent acini, without stroma to each other, which sets the default as 4. The other areas of the photo illustrate pattern 3.

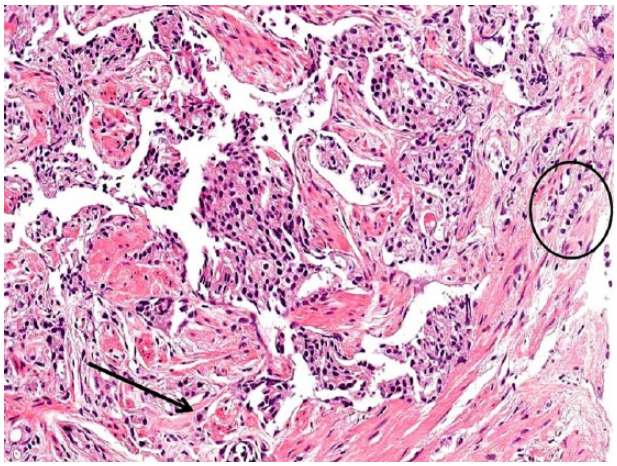

Figure 2. Usual adenocarcinoma Gleason 9 (4+5) [grade group 5] (hematoxylin-eosin, original magnification ×400). In this case, Gleason pattern 4 is predominant, but the circled area shows linear arrangement, and the arrowhead depicts isolated neoplastic cells. These characteristics are standard diagnostic features of Gleason pattern 5.[18,19]

assessment. Similar findings are reported by Fajardo et al and Al-Hussain et al.[18,19] The authors of both studies recommend that urologists forward their cases initially diagnosed as high grade for second opinion in specialized centers, and pathology societies should educate pathologists to recognize Gleason pattern 5 in prostate biopsy specimens because of the prognostic and therapeutic implications associated with the presence of this pattern.[18,19]

Another evaluation bias, well-documented in the literature and in several studies is based on the Gleason score from only one biopsy fragment as opposed to obtaining a consensus of all the fragments. This can explain differences in Gleason scores by different pathologists.[20]

The pathology analysis is also directly related to the amount and size of biopsied fragments. It has been demonstrated that the collection of more fragments as well as the greatest extent of fragment increases the diagnostic accuracy.[20] Even with these details, the Gleason score remains an important risk marker for the disease, mainly because of its strong association with development and prognosis.[21]

Pathology review is a method used to adjust the real risk of the patient, and it also presents benefits in the case of a confirmed Gleason 6; it allows such patients to be categorized as low risk and permits the choice of an active surveillance strategy.[22]

Conclusions

This study demonstrates the need for pathology review in patients with localized prostate cancer before initial treatment; this review can affect treatment decision in almost two-thirds of the recategorized patients. Limitations of our study include limited sample size and retrospective nature of data collection, but the findings echo those of studies from other institutions.[23,24]

Author Contributions

All the authors contributed equally to the development of the study.

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Appendix 1. New grading system.

TRADITIONAL GLEASON SCORE	NEW GRADING SCORE
Gleason score ≤6	Grade group 1
Gleason score 3+4=7	Grade group 2
Gleason score 4+3=7	Grade group 3
Gleason score 8	Grade group 4
Gleason score 9-10	Grade group 5

Appendix 2. Histopathological evaluation.

Cases	23
Concordant Gleason	15
6 (GG 1)	12
7 (GG 2-3)	2
8 (GG 4)	1
Discordant Gleason	8
Increase score	7
6→7 (GG 1→GG 2)	5
7→8 (GG 3→GG 4)	1
7→9 (GG 3→GG 5)	1
Decrease score	1
9→8 (GG 5→GG 4)	1

Abbreviation: GG, grade group.