ELSEVIER

Urologic Oncology: Seminars and Original Investigations ▮ (2015) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

ERG overexpression and multifocality predict prostate cancer in subsequent biopsy for patients with high-grade prostatic intraepithelial neoplasia

Rajal B. Shah, M.D.[a,*], Jianbo Li, Ph.D.[b], Nadeem Dhanani, M.D.[c], Savvas Mendrinos, M.D.[a]

[a] *Division of Urologic Pathology, Miraca Life Sciences Research Institute, Miraca Life Sciences, Irving, TX*
[b] *Cleveland Clinic Foundation, Cleveland, OH*
[c] *Division of Urology, The University of Texas at Houston, Houston, TX*

Received 2 August 2015; received in revised form 8 October 2015; accepted 11 October 2015

Abstract

Purpose: The most important clinical significance of an isolated high-grade prostatic intraepithelial neoplasia (HGPIN) diagnosis is the risk of missed prostate cancer (PCa) in subsequent biopsies. Because most patients with HGPIN do not harbor or develop PCa, clinical, pathological, or molecular markers that predict of PCa risk are of clinical significance.

Materials and methods: Overall, 155 men with a diagnosis of isolated HGPIN, which was based on the results of extended biopsy, and who underwent at least one repeat biopsy were analyzed for ERG oncoprotein (ERG) expression and clinicopathological parameters to determine the risk of finding PCa in subsequent biopsies.

Results: Of 155 patients diagnosed with HGPIN on initial biopsy, 39 (25%) had PCa on subsequent biopsies. For men with only one repeat biopsy, the cancer detection rate was 22%. Most (54%) PCas were detected in ≤6 months of rebiopsy. ERG expression was present in 15 patients with HGPIN (9.6%). Patients with ERG expression in HGPIN were more likely to have PCa in repeat biopsy, with 9 (60%) ERG-positive and 30 (21%) of ERG-negative patients having PCa ($P = 0.001$). Multifocal involvement ($P = 0.0001$), cribriform morphology ($P = 0.004$), and bilaterality ($P = 0.0075$) of HGPIN were other significant risk factors. On multivariable analysis, only the presence of ERG positivity and multifocality remained significant parameters in detecting PCa on a repeat biopsy. The presence of ERG-negative focal HGPIN involving one core, which accounted for 46% of patients, had minimal (16%) PCa risk on subsequent biopsy. In total, 8 patients (89%) ERG-positive HGPIN had PCa identified at identical sites on subsequent biopsy, of which 5 (71%) were ERG positive.

Conclusions: The status of ERG expression in HGPIN along with other histological parameters stratifies patients into low- and high-risk groups for having PCa on subsequent biopsy. Our results further support molecular characterization of HGPIN as a means to improve risk stratification and optimize surveillance strategies.

Keywords: High-grade prostatic intraepithelial neoplasia (HGPIN); ERG; Multifocality; Prostate cancer

1. Background

High-grade prostatic intraepithelial neoplasia (HGPIN) is widely accepted as a putative neoplastic precursor lesion of prostate cancer (PCa) [1,2]. The clinical importance of HGPIN stems from its association with PCa in concurrent or subsequent prostate needle biopsies [3,4]. Historically, a diagnosis of HGPIN based on the results of needle biopsies had been associated with a high likelihood of finding a cancer on repeat biopsy (~40%); however, the diagnosis rates of PCa after an initial diagnosis of HGPIN have significantly decreased in recent years (~25%) as more aggressive extended biopsy templates have reduced the number of cancers missed on initial biopsy [3,5]. Based on emerging data, some protocols now defer repeat biopsy within the first year if HGPIN, specifically isolated HGPIN, is made on extended biopsy template [3,6,7]. However, there is considerable heterogeneity in practices regarding

* Corresponding author. Tel.: +1-214-596-7075; fax: +1-214-596-2274.
E-mail addresses: rshah@Miracals.com, rajalbshah@gmail.com (R.B. Shah).

http://dx.doi.org/10.1016/j.urolonc.2015.10.008
1078-1439/