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Urologic Oncology: Seminars and Original Investigations 32 (2014) 941–945

UROLOGIC ONCOLOGY

Original article

Self-reported acne is not associated with prostate cancer

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Received 16 January 2014; received in revised form 21 February 2014; accepted 24 February 2014

Abstract

Objective: Some studies have suggested an inverse association between acne vulgaris and the acne-related bacterium *Propionibacterium acnes* and prostate cancer (PCa). Self-reported acne might be an easily obtainable marker to identify men at relatively low risk of PCa and might be incorporated into PCa risk calculators. This study aimed to evaluate the association between self-reported acne and PCa in a large case-referent study.

Methods and materials: The case group comprised 942 patients with PCa recruited from a population-based cancer registry in 2003 to 2006, 647 of whom met the criteria for aggressive PCa. The referents (n = 2,062) were a random sample of the male general population. All subjects completed a questionnaire on risk factors for cancer, including questions about acne. Odds ratios (ORs) and 95% confidence interval (CI) were calculated using multivariable logistic regression for PCa and aggressive PCa as separate end points, while adjusting for age and family history of PCa.

Results: A history of acne was reported by 320 cases (33.9%) and 739 referents (35.8%). Self-reported acne was significantly associated neither with PCa (adjusted OR = 0.95, 95% CI: 0.80–1.12) nor with aggressive PCa (adjusted OR = 0.97, 95% CI: 0.80–1.18).

Conclusion: Self-reported acne is not suitable as a marker to identify men at low risk of aggressive PCa.

Keywords: Prostate cancer; Aggressive prostate cancer; Acne vulgaris; Risk factor; Marker; *Propionibacterium acnes*

1. Introduction

Early detection of prostate cancer (PCa) is possible by testing serum prostate-specific antigen (PSA) [1]. Population-based PSA screening is not adopted, though, as this would coincide with considerable overtreatment [2]. Therefore, the global research community is evaluating new (bio)markers that may identify men at increased risk of (aggressive or "clinically significant") PCa, in whom the benefits of screening might outweigh the adverse effects. Established PCa risk factors are African descent, older age, and a positive family history of PCa, but none of these has sufficient discriminative power to be used in a public health setting.

Androgens play an important role in PCa growth and development and have been a target for PCa treatment since the 1950s. Although the exact relationship between androgens and the risk of PCa is still to be unraveled, androgen status is an obvious target to serve as a marker for PCa [3]. Several

Dr Cremers was supported by contract number 202059 (ProMark) from the Seventh Framework Program of the European Union and by an Agiko stipend (number 92003573) of the Netherlands Organisation for Health Research and Development, The Netherlands.

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http://dx.doi.org/10.1016/j.urolonc.2014.02.019
1078-1439/

proxies for androgen status, e.g., acne vulgaris and male-pattern baldness, have been investigated as possible markers for PCa [4–9]. The associations between either acne or male-pattern baldness and PCa were most often of inverse nature but were also often not statistically significant.

Recently, besides this suggested link with acne as a proxy for androgen status, another possible mechanism to underlie an association between acne vulgaris and PCa was studied. *Propionibacterium acnes*, a skin bacterium associated with acne, is known to be prevalent in prostate tissue and has been suggested to be associated with prostatic inflammation and PCa carcinogenesis [10,11]. In a large case-referent study, an association was found between higher concentrations of circulating *P. acnes* antibodies and a decreased risk of PCa, particularly locally advanced and metastatic PCa [12]. The authors hypothesized that the higher antibody titers may reflect an increased immune response against *P. acnes*, providing cross-immunity against its possible carcinogenic effects.

In theory, the identification of men at relatively low risk of PCa by simple phenotypes such as a history of acne could result in screening policies with a better balance between intended and unintended effects. This might be achieved by incorporating information about acne history into PCa risk calculators and decision aids. In this article, we describe a large case-referent study on the association between self-reported acne and PCa.

2. Methods and materials

The study population and study design have been described in detail before [13,14]. In brief, the case group was recruited for an ongoing study on genetic susceptibility of (prostate) cancer (Polygene study; www.polygene.eu). All patients diagnosed with PCa in the period 2003 to 2006 and registered by the regional cancer registry held by the Comprehensive Cancer Centre the Netherlands (IKNL), Nijmegen, were included. Eligibility criteria were age at diagnosis of 75 years or younger, alive at the date of invitation to the study, and living in the catchment area of the IKNL. Overall, 1,330 patients met these criteria and were invited for the study between September 2006 and June 2007. In total, 1,020 patients stated to be willing to participate (77%). Participation consisted of donation of a blood sample and completion of a risk factor questionnaire. Finally, 956 patients (72%) actually completed the questionnaire. The registration staff of the IKNL had already collected clinical and pathology data of all patients in the cancer registry. These standard data were supplemented with more detailed information obtained from the medical files in the 7 hospitals where the patients were treated.

The referents were recruited for the Nijmegen Biomedical Study (NBS; www.nijmegenbiomedischestudie.nl), a population-based survey conducted in 2002 by the Department of Epidemiology and Biostatistics and the Department of Clinical Chemistry of the Radboud University Nijmegen Medical Centre. A total of 21,756 (49% of whom were men) age and sex-stratified randomly selected inhabitants of Nijmegen, the Netherlands, were invited to fill a questionnaire and donate 2 tubes of blood for a study on gene-environment interactions in multifactorial diseases such as cancer. In total, 9,350 people returned a completed questionnaire (response 43%), 46% of whom were men. The NBS participants who had completed the NBS questionnaire, had given consent for further research, were still alive and had known addresses ($n = 7{,}950$ of whom 3,625 were men) were contacted again in 2008 and invited to fill an additional questionnaire containing, among others, questions about acne. A total of 5,613 individuals (2,552 men) completed the questionnaires (response 71%). Participants with a history of PCa at the time of recruitment in 2002 were excluded from the analyses.

The questions about acne inquired whether the subject ever had acne, at what age the acne had started and ended, and the location of the acne (face, shoulders/neck, back, and chest). All non-Western, nonwhite subjects were excluded from the analyses, as it is known that acne patterns differ between different races and because non-Western, nonwhite subjects comprise only a small minority in this part of the Netherlands [15]. Referents younger than 43 years (the youngest age of diagnosis among the PCa cases) were excluded to improve the comparability of the age distributions of cases and referents.

All participants in the Polygene and NBS studies were fully informed about the goals and procedures of the study and gave written informed consent. The study protocols were approved by the institutional review board of the Radboud University Nijmegen Medical Centre.

2.1. Statistical analysis

The association between acne and PCa was evaluated by cross-tabulation. For participants who reported a history of acne, the location of the acne was specified, including the proportion of participants reporting that location within the participant group.

Odds ratios (ORs) and corresponding 95% CI were calculated to quantify the strength of the association between acne (all locations) and PCa. Multivariable logistic regression modeling was used to calculate the association between acne and PCa adjusted for positive family history (dichotomized, i.e., ≥ 1 first-degree relative with PCa, included in the model as a nominal variable) and age at the time of completing the questionnaire (continuous linear variable). Acne was included in the models as a dichotomous (nominal) variable, using no acne as reference category.

Additional analyses were performed using aggressive and nonaggressive PCa as separate end points. Aggressive PCa was based on D'Amico et al.'s [16] criteria for PCa progression and defined as PCa with any of the