EDITORIAL COMMENT

Maciej Salagierski

Department of Urology, Medical University of Łódź, Poland

Bladder cancer (BCa) remains a commonly occurring disease [1]. Multiple risk factors of BCa have been identified, the most important of which are cigarette smoking and various occupational exposures. As a matter of fact, a thorough understanding of the epidemiology of bladder cancer can assist in the prevention and early detection of the disease. Approximately 75–80% of bladder tumors present as non–muscle invasive (NMI) disease and the remainder present as muscle–invasive disease (MI). Proper staging, grading, and risk stratification are critical for determining the most appropriate management strategies for NMI based on risk of recurrence and progression. Although the family predisposition to BCa is uncertain, the possibility of an inherited subtype of bladder cancer could not be excluded.

The manuscript by Monika Banaszkiewicz et al. [2] represents the second study recently published in CEJU being the continuation of work of the same author [3]. The article brings up an intriguing issue of genetic and environmental factors in BCa patients that might be responsible for the neoplastic transformation. According to the authors, the aim of the manuscript was to find a better way to diagnose BCa in its early stage.

What can we learn from this study? The authors analyze a group of 131 patients with BCa, diagnosed for the first time and demonstrating different clinical stages (Ta–T4) and grades (G1–G3). Altogether 11 mutations (8.4%) of CHEK2 gene were detected, the polymorphism of CYP1B1 gene occurred in 18 patients (12.9%), and oncogenic HPV was found in 36 (29.3%) patients. The authors conclude that the coexistence of CHEK2 gene mutations or the 355T/T polymorphism of the CYP1B1 gene together with the presence of oncogenic HPV types demonstrates a statistically significant correlation with histologically malignant grades of BCa. Importantly, HPV infections, according to the recent publications [4], are not only responsible for oncogenic transformation in penile squamous cell carcinoma but also appear to be associated with other urological malignancies.

The article, though presenting relevant data, has some major flaws. First of all, the study lacks the control group the author used before to compare the study results [3]. According to the previous study, both CHEK2 gene mutations and/or 355T/T polymorphism of CYP1B1 gene were also present in healthy individuals (however, they occurred less frequently than in cancer patients). Furthermore, the study group represents a very mixed and heterogenous population of BCa patients. It is difficult, at least from a clinical point of view, to understand why, as most of the patients had T1a or T1 disease (82%), the authors include a very small number of patients with pT3 (n = 2) and pT4 (n = 1) BCa. Is the intention of authors to early detect a premalignant condition, a pTa or a pT4 tumor? Additionally, over 91% (n = 120) of examined patients were smokers. Could there be an influence of this smoking habit on the described genomic changes? What could have been the results of the study in non–smokers (n = 11)?

Banaszkiewicz et al. reasonably point out the value of prophylactic measures (in the preclinical phase of the neoplasm) and the need for diagnosing the neoplasm in its early non–invasive stage – factors which allow for much better treatment results and patient survival. Regardless, even with the current state of knowledge, only a small percentage of NMI tumors (20%) progress and most of the invasive BCa are identified as de novo lesions without a previous history of NMI disease. Nevertheless, knowing the deleterious potential of progressing tumors, it remains a very important issue to be raised. The authors also state that "In the performed studies, a statistically significant and positive correlation was found between the simultaneous occurrences of: genetic (CHEK2/CYP1B1 mutations/polymorphisms) and environmental (HPV) factors on one hand and the histopathological grade of urinary bladder carcinoma on the other, regardless of pT. In this way, it was possible to find out that non–invasive cancers of the urinary bladder, in which the above–mentioned factors coexisted, were associated with an increased risk of progression towards invasive changes", but do they have arguments to support this theory? Do they know the history of all lesions? Would it be possible to predict, based on the result of the present study, which tumors are more likely to progress or recur? Will patients with mutations certainly have the worst prognosis? What happened during the follow–up of patients with mutations/polymorphism? Was there any progression of the disease in this group? How many patients with mutations died? Unfortunately, Banaszkiewicz et al. do not provide the follow–up data. We only know that, according to the study results, most patients with the coexistence of mutations had G3 tumors. The statistical significance of obtained results might also be questioned due to the small number of individuals with mutations/polymorphism/HPV infection. Finally, do we know exactly how many cases all of the mo-

lecular events co–existed in the present study? The reader can only guess that the amount of coexistent mutations was very small.

It is also unclear why the authors added the results of the UroVysion test in their study. Does it bring any relevant information to the manuscript? Do the authors suggest that new diagnostic tests based on the genetic changes in BCa described in the manuscript could overcome the limitations of UroVysion?

In conclusion, Banaszkiewicz and colleagues, in an interesting study, describe the molecular changes that might be related to an aggressive BCa phenotype. Due to some methodological drawbacks, the study appears more relevant for researchers than clinicians. Importantly, the authors underline that "these studies require continuation in order to put research questions into clinical context". The future will definitely bring an answer to many currently intriguing oncological issues.

References

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Correspondence
Dr. Maciej Salagierski, FEBU, MD, PhD
m.salagierski@yahoo.com