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The articles: "Detection of loss of heterozygosity in patients with urinary bladder carcinoma: neoplastic tissue vs. urine sedime nt cells" and "Significance of *CDKN2A* gene A148T variant in patients with bladder cancer"

Toward a better understanding of bladder cancer – Genetic aspects are key

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Clinical urology critically relies on answers to questions regarding the biology of bladder cancer because of its influence on patient management. The first question is related to the origin of muscle invasive bladder cancer. Is muscle invasiveness developing as a simple consequence of continued growth of NMIBC (non-muscle invasive bladder cancer)? The second question is related to oncological characteristics of bladder cancers, i.e. infiltrative growth, metastatic potential, and resistance to systemic treatment. It is difficult to answer these two crucial questions, but we hope that genetic analysis will help shed light on this topic. Clinical practice shows that one marker will not be indicated, but rather different and characteristic biochemical pathways can be connected with particular superficial or infiltrative tumor growth features.

Two original papers related to genetic and biochemical aspects of bladder cancer included in this issue of the Journal are trying to find answers on the above-mentioned questions. In the first paper entitled "Detection of loss of heterozygosity in patients with urinary bladder carcinoma: neoplastic tissue vs. urine sediment cells". The authors presented an occurrence of LOH (Loss of Heterozygosity) in regions very important for bladder cancer development, like 17p13 (*P53*), 13q14 (*RB1*), and 9p21 (*CDKN2A/ARF*) [1]. There are two important conclusions arising from this study. First of all, that LOH on chromosome 17, 17p13 locus (*P53*) is more frequently found in high-grade bladder cancers. In low stage and grade cancers, LOH is most often observed on chromosome 9 (*CDKN2A/ARF*). This observation is consistent with two possible molecular and clinical pathways of bladder carcinoma development. One form begins from flat lesions quickly converted to invasive cancers and the second rises on the basis of gradual changes leading to "benign" features of superficial papilloma looking tumors. Secondly, authors of this study showed that analysis can be performed on cancer tissue and urine sediment cells as well, making this technique advantageous in non-invasive methods for detection and screening of bladder cancer.

In the next paper entitled "Significance the *CDKN2A* gene A148T variant in patients with bladder cancer", the authors showed that A148T polymorphism of *CDKN2A* gene was identified in men older a 60, in whom the disease was diagnosed with higher clinical stages and higher grades of malignancy [2]. *CDKN2A* gene product influences on proteins responsible for proper cell divisions. This has attempted to show a potential association between A148T alterations (changes of *CDKN2A* gene) and an increased risk for bladder cancer development. Authors claimed that the A148T variant of the *CDKN2A* gene can be associated with an increased risk for bladder cancer development and with the coexistence of other factors may lead to carcinogenesis.

The above-mentioned issues are of the utmost importance for every urologist who wants to know which non-muscle invasive bladder cancer (NMIBC) can be safely treated by TUR, but which NMIBC will be quickly converted into MIBC (muscle invasive bladder cancer). Do all bladder cancers belong to one homogenous entity? It seems, they do not, but we have to wait for a conclusive answer.

REFERENCES

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2. Borkowska E, Jędrzejczyk A, Kruk A, al: *Significance of CDKN2A gene A148T variant in patients with bladder cancer.* CEJUrol 2011; 64: 168-174

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