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Immunohistochemical detection of hTERT in urothelial lesions: a potential adjunct to urine cytology

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Abstract

Background: Urine cytology has a critical role in evaluation for bladder carcinoma. Due to the low sensitivity of this technique, ancillary modalities such as the detection of markers of malignancy by immunochemistry are desirable. Promising factors in this context are components of the human telomerase enzyme complex. Telomerase repairs and extend telomeres, which when eroded beyond a critical limit trigger a senescence checkpoint. Accordingly, while absent in normal somatic cells, telomerase activity has been detected in the great majority of malignant tumor specimens tested, and so has potential value for the recognition of malignant cells in clinical specimens.

Methods: In this study, we investigated whether the immunohistochemical detection of the catalytic subunit of telomerase (hTERT) can aid cytology in the diagnosis of bladder lesions. Findings from the retrospective evaluation of over 100 cell blocks, including urine sediments from confirmed malignant and benign conditions, were compared with routine urine cytology data.

Results: The presence of hTERT protein was indicative of the transformation of urothelia to a malignant phenotype. Nucleolar hTERT was expressed in 27 (93%) of 29 samples obtained from patients with confirmed primary bladder cancer. Conversely, hTERT was detectable in only 3 (0.8%) of 39 samples from benign conditions. The hTERT assay showed higher diagnostic sensitivity (84.8%) than published urine cytology data (~65%) for confirmed bladder carcinoma, however, the hTERT assay was less specific than cytology (65.2% vs. ~95% respectively).

Conclusion: As a highly sensitive marker, immunohistochemical hTERT detection in urine sediments represents a reliable adjunct to cytology in the accurate diagnosis of urothelial neoplasms.

Background

The diagnosis of suspicious bladder lesions is, in part, dependent on the demonstration of atypical cells in the cytological examination of voided urine or bladder washings. However, the relatively low diagnostic sensitivity of urinary cytology warrants the development of improved non-invasive diagnostic techniques [1]. Furthermore, one of the major problems in daily cytology practice is to distinguish benign/reactive cells from malignant cells. Additional techniques, such as immunocytochemistry and flow cytometry, may provide significant help in this differential diagnosis. A number of antibodies directed against specific cell type antigens have been used in urine cytology to enhance the cytological diagnosis, including