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SURVIVIN AND CASPASE-3 AS A DIAGNOSTIC AND PREDICTIVE BIOMARKERS OF RECURRENCE FOR URINARY BLADDER CARCINOMA AFTER TURBT

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Background: Bladder cancer even in early stage develop recurrence. Poor sensitivity of cytology and invasiveness of urethrocytostcopy have generated interest in non-invasive tools to monitor for recurrence. Caspase-3 and survivin have central role in regulation of apoptosis. Survivin can aid early diagnosis, determine prognosis in multiple cancer types and predict response to anti-cancer therapies. Its combination with other biomarkers as caspase-3 enhance prognostication and prediction of treatment response in UBC.

Methods: Immunohistochemical expression of survivin and caspase-3 were assessed in 44 Egyptian consecutive patients with UBC and 7 cystoscopic biopsies of cystitis as control reactive benign urothelium. Relationships between their expression, clinicopathological characteristics, diagnostic and prognostic performance were statistically analyzed.

Findings: No survivin immunoreactivity was identified in non-neoplastic bladder tissue. Expression of survivin and caspase-3 was altered in 42(95.5%) and 10(22.7%) cases, respectively. There was statistically significant moderate positive correlation between survivin and caspase-3 expression among whole studied cases ($p=0.006$). Expression of either survivin or caspase-3 protein individually significantly differ ($p=0.000$) in cancer status from control cases. Survivin was an independent predictor of UBC in multivariable analyses. Diagnostic accuracy of survivin alone was significantly better than caspase-3 alone (sensitivity 81.82% vs. 68.18%, $p=0.027$). Addition of survivin immunoreactivity to model including caspase-3 expression improved diagnostic accuracy with a sensitivity of 93.18%. Addition of gender to the previous model improved more diagnostic accuracy with sensitivity of 100%.

Interpretation: Survivin alone is very promising marker and reliable indicator in UBC. Survivin and caspase-3 antigens have a cooperative effect on bladder cancer, their simultaneous evaluation augments diagnostic sensitivity.



Figure 1: (a) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for survivin (brown color). (b) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for caspase-3 (brown color). (c) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for survivin (brown color). (d) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for caspase-3 (brown color). (e) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for survivin (brown color). (f) High grade papillary urothelial carcinoma (HGPUC) showing strong immunohistochemical staining for caspase-3 (brown color).



Figure 2: (a) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for survivin (brown color). (b) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for caspase-3 (brown color). (c) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for survivin (brown color). (d) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for caspase-3 (brown color). (e) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for survivin (brown color). (f) Low grade papillary urothelial carcinoma (LGPUC) showing weak immunohistochemical staining for caspase-3 (brown color).

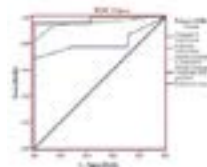


Figure 3: ROC curve comparing the performance of survivin expression alone, survivin expression plus gender, and survivin expression plus caspase-3 expression in predicting urinary bladder cancer. The curve for survivin expression plus caspase-3 shows the highest area under the curve (AUC) of 0.9318, indicating the best diagnostic performance.

Biography

Vivian G D Rouston obtained her MBBCh in 2004 and Masters in Pathology in 2015 from Faculty of Medicine Alexandria University. She was trained for Histopathology and Cytopathology at Histopathology Division of the Department of Pathology, St James's University Hospital, the Leeds Teaching Hospitals, NHS Trust, United Kingdom. She is working as a Histopathology Specialist in a general hospital in Egypt.

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