Expression Of E-Cadherin And Ki-67 (MIB-1) In Transitional Cell Carcinoma Of The Urinary Bladder

Thesis

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BY

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Aim of the work:

The aim of the present study is to evaluate the expression of E-cadherin and Ki-67 (MIB-1) in urothelial transitional cell carcinoma and to compare the immunoreactive results with the standard histopathological measures including the grade as well as the stage of the tumor.

INTRODUCTION:

Bladder cancer has a high incidence in many developed countries. In the United State, bladder cancer is reported as the 4th cancer in incidence among male patients, whereas it ranks the 11th among female patients with cancer (Wong-You–Cheong et al, 2006).

In Egypt, bladder cancer is considered as one of the most common cancers. Transitional cell carcinoma constitute only 31% of bladder cancer in Egypt, however, this incidence is increasing annually compared to other pathological types (Mokhtar, 1991).

Urinary bladder carcinoma is characterized by a high recurrence rate after the initial treatment by endoscopic resection. In fact, about 70% of the patients showed tumors recurrence after tumor resection and some of these patients eventually showed progression towards invasive and more aggressive disease (Stein et al, 1998, Droller, 1998 and Schultz, 2006).

The ability of molecular markers to predict tumor recurrence or progression has been investigated intensively over the last two decades. A substantial number of potential molecular markers for the prediction of clinical course and outcome have been identified in recent studies of molecular biology and genetics.

Disruption of cell–cell and cell–extracellular matrix junctions is an important key for tumor cells growth, migration, invasion into surrounding tissues, and metastasis. The majority of studies in this area focus on the role of E-cadherin in

malignant cell transformation and progression. In general, E-cadherin expression was most often decreased in the undifferentiated “aggressive” carcinomas that have high invasive potential (Takeichi, 1993, Ivanov et al, 2001, and Pienado et al, 2004). However, data from variable sources showed no correlation between down expression of E-cadherin and tumor aggressiveness.

Loss of E-cadherin expression, among other factors, was associated with a poor prognosis and disease recurrence in both univariate and multivariate analysis (Fromont et al, 2005).

Bryan and Tselepis, (2010) found that cadherin switching (from E-cadherin to P- and N-cadherins) was important process late in the molecular pathogenesis of bladder cancer. It might hold some of the answers to the development of muscle invasive and metastatic disease. This finding may open the way for researchers to study the phenomenon of cadherin switching rather than expression alone.

Anti Ki-67 antibody MIB-1; a proliferative biomarker, has been widely used in histopathologic studies to estimate the growth fraction of human neoplastic tissue samples. This marker has shown promise as an independent prognosticator of patient outcome in several malignancies (Li et al, 2004, Morinaga, et al 2005 and Gimott, et al 2005).

Ki-67 over expression was studied to diagnose difficult cases with flat bladder lesions as CIS, and urothelial dysplasia. Sun et al, (2002) studies 30 cases with urothelial dysplasia and

found a significant increase in Ki-67 expression among cases with high grade dysplasia as well as cases with CIS.

In a huge recent multicenter study by Margulis et al, (2009) Ki-67 expression was assessed in tumor tissue from 713 patients treated with radical cystectomy and bilateral lymphadenectomy at six centers. The study showed that a high Ki-67 labeling index was independently associated with established features of aggressive urothelial carcinoma, disease recurrence, and cancer-specific survival. The authors concluded that routine assessment of Ki-67 expression status along with assessment of other established predictors of urothelial carcinoma outcome has the potential to improve identification of patients who are at increased risk for disease progression after radical cystectomy and thus may benefit from perioperative systemic chemotherapy.

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