EXPRESSION OF CYCLOOXYGENASE-2 IN MALIGNANT EPITHELIAL TUMORS OF THE URINARY BLADDER; HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

THESIS SUBMITTED IN PARTIAL FULFILLMENT OF M.D. DEGREE IN PATHOLOGY

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Abstract

The malignant urothelial tumors of the urinary bladder represent 95% of the malignant tumors of this organ.

Aim of the work: is to evaluate the expression of cyclooxygenase-2 (COX-2) in the precancerous and malignant epithelial tumors of the bladder and its correlation with the different prognostic factors.

Material and methods: this study included 60 bladder carcinoma specimens obtained by radical cystectomy and 5 control bladder specimens from the mucosa away from the tumors.

Results: there was no statistically significant relationship between COX-2 expression and most of the different clinico-pathological factors while there was statistically significant relationship between COX-2 expression and the stage of the tumors.

Conclusion: there was statistically significant relationship between COX-2 expression and the stage of the tumors. Further studies are needed to determine the possibility of considering COX-2 expression in the malignant bladder tumors as a prognostic factor.

Key words: Urinary bladder, malignant epithelial tumors, COX-2, and prognostic factors.

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A.A.	Arachidonic acid
A. fangchi	Aristolochia fangchi
CAP	College of American Pathologists
CIS	Carcinoma in situ
COX-2	Cyclooxygenase-2
CYT 1A2	Cytochrome P450 1A2
DAB	Di-Amino-Bezidinetetrahydrochloride
H&E	Haematoxylin and Eosin
ISUP	International Society of Urological Pathology
IUC	Invasive urothelial carcinoma
NAT2	N- acetyltransferase-2
NCI	National Cancer Institute
NSAIDs	Non-steroidal Anti-inflammatory Drugs
PUNLMP	Papillary urothelial neoplasm of low malignant potential
PBS	Phosphate-Buffered Saline
P Value	Probability value
Sq C C	Squamous cell carcinoma
TCC	Transitional cell carcinoma
TNM	Tumor-Node-Metastasis
WHO	World Health Organization

Introduction

Urinary bladder tumors comprise a heterogeneous group of lesions. About 95% of the bladder tumors are of epithelial origin (D' hallewin et al., 1996, Volante et al., 2001).

Urothelial carcinomas represent approximately 90% of all primary tumors of this organ (Kutarski et al., 1993, Mhawech et al., 2002). Primary squamous cell carcinomas represent about 5% of the bladder cancers (Frank et al., 2003). In Egypt, the incidence of squamous cell carcinoma of the urinary bladder is increased due to urinary schistosomiasis (Koraitin et al., 1995). The urinary bladder adenocarcinoma constitute approximately 2% of the malignant tumors of this organ (Fukushima et al., 1989). Other malignant epithelial tumors as small cell carcinomas are very rare (Cheng et al., 2000).

The biological behavior of the urinary bladder carcinomas is unpredictable and the morphological methods are often insufficient to predict the clinical outcome of patients with these tumors (Billerey et al., 1999).

This discrepancy in the behavior of these tumors from recurrence to progression has encouraged the research for prognostic markers; one of these markers is cyclooxygenase-2 (Shirhama, 2000).

Cyclooxygenase (COX) exists in two isoforms, COX-1 and COX-2, and catalyzes the conversion of arachidonic acid to prostaglandins (Sulma et al., 1999). Whereas COX-1 is expressed constitutively in most normal tissues and is required for the normal physiological functions, cox-2 usually is not detectable but induced in response to various stimuli such as oncogenes and tumor promoters (Tsutomu et al., 2001).

Cyclooxygenase-2 (COX-2) overexpression was observed in various malignant tumors as well as in urinary bladder carcinoma (Pruthi et al., 2004). Although there is abundant evidence pointing to the role of (COX-2) expression in tumorigenesis, the mechanisms by which (COX-2) expression exerts its effects on tumorigenesis is not clear, but recent studies have shown that COX-2-derived prostaglandins display their effects through cellular apoptosis and steps of metastasis, thus contributing to the prognosis of these patients with bladder cancer (Kim et al., 2002).

In vitro and animal studies demonstrated a decreased incidence and decreased growth of bladder cancer when administrating non-selective and selective COX-2 inhibitors (Mohseni et al., 2004). Moreover, a large case-control study demonstrated an overall decreased risk of bladder cancer in regular users of non-steroidal anti-inflammatory drugs (Castelao et al., 2000).

Aim of the work

1- Histopathological study of different types of urinary bladder carcinomas, their variants, grade and stage.

2- Evaluation of cyclooxygenase-2 (COX-2) expression in different types of urinary bladder carcinomas and precancerous lesions.

3- Correlation between the expression of cyclooxygenase-2 (COX-2) and different prognostic features in different types of urinary bladder carcinomas.

TUMORS OF THE URINARY BLADDER

WHO Histological classification of tumors of the urinary tract (2004):

I- Urothelial tumors

Infiltrating urothelial carcinoma

With squamous differentiation

With glandular differentiation

With trophoblastic differentiation

Nested

Microcystic

Micropapillary

Lymphoepithelioma-like

Lymphoma-like

Plasmacytoid

Sarcomatoid

Giant cell

Undifferentiated

Non infiltrating urothelial neoplasms

Urothelial carcinoma in situ

Non invasive papillary urothelial carcinoma, high grade

Non invasive papillary urothelial carcinoma, low grade

Non invasive papillary urothelial neoplasm of low malignant potential

Urothelial papilloma

Inverted urothelial papilloma

II- Squamous neoplasms

Squamous cell carcinoma

Verrucous carcinoma

Squamous cell papilloma

III- Glandular neoplasms

- Adenocarcinoma

Enteric

Mucinous

Signet ring cell