Bacteriological and immunological study associated with patients of Urinary Bladder carcinoma

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Abstract:

The blood, serum & urine samples are collected from (22) patients with urinary bladder cancer were admitted to Al-Hilla general teaching hospital after diagnosis by helping urology physician. The result appeared that *E.coli* with high percentage (22.7% ,27.2%)in nixed &single infection respectively followed by *Ps.aeuroginosa* (22.7% , 13.6%) and *S.aureus* (18.8% , 9.09%). Interleukin 2 &Interleukin 8 concentration level was detected in serum by enzyme-linked immunosorbent assay(ELISA) and data were compared with control to compare the performance of each cytokins & results show no elevated , no significant decrease in level in two cytokins, this leads to an independent factors for the detection of urinary bladder cancer.

Introduction

Bladder cancer is the ninth most common cancer diagnosis worldwide, with more than 330 000 new cases each year and more than 130 000 deaths per year. (Ploeg *et al*., 2009 ; Zhou *et al*., 2009)

Bacterial infections traditionally have not been considered major causes of cancer. Recently, however, bacteria have been linked to cancer by two mechanisms: induction of chronic inflammation and production of carcinogenic bacterial metabolites**.**

One of the etiological factors implicated in the development and progression of bladder cancer includes urinary tract infections (UTIs) including bacterial, parasitic, fungal, and viral infections; urinary lithiasis and pelvic radiation (Pasin *et al*., 2008).

Bacteria are the primary cause of UTIs, with the vast majority (70–80%) attributed specifically to infection with *Escherichia coli*. A recurring theme in the link between bacterial infection and carcinogenesis is that of chronic inflammation, which is often a common feature of persistent infection (Karin and Greten 2005).

Also Cytokines are important mediators of inflammation and are associated with pathogenesis of many inflammatory diseases. (Shahzad *et al*., 2010).

IL-2 signal plays a key role in promoting development, homeostasis and function of regulatory T cells. IL-2 affects multiple signal pathways, and its deficiency causes the multifacted dysregulation of immune response. (Geng *et al*., 2012). IL-2 also seems to be associated with the malignancy of the tumour .Also Increased expression of IL-2 and IL-2R has been reported in actively proliferating tumours such as stomach, renal and spinocellular cancers , squamous cell carcinomas of the head and neck , melanomas, neuroblastic tumours and prostate cancer.(Tuñón *et al*., 2004).Also Recently, it has been shown that IL-8 plays a critical role in cancer invasion, angiogenesis and metastasis. It is a chemotactic factor for T cells, neutrophils, and basophils besides its pro-inflammatory role, IL-8 has been evaluated as a pro-oncogenic effector in various types of human cancers, including leukemia, astrocytoma, melanoma, breast cancer, ovarian cancer, lung cancer, prostate cancer, colon cancer, urinary system cancer , gastric cancer and pancreatic cancer (Mahdi *et al.,* 2013). IL-8 signaling has been shown to induce the activation of this classic Mitogen Activated Protein Kinases (MAPK) signaling cascade, with downstream phosphorylation of extracellular signal-regulated kinases (Erk) detected in both neutrophils and cancer cells (Luppi *et al*., 2007).

Material and Methods:

Total of 22 patients with Urinary Bladder Carcinoma UBC were admitted to AL- Hilla General Teaching Hospital /Iraq after they diagnosis by helping with Urology Physician were suspected to have UBC according to their clinical manifestations and Ultrasound changes.

Venous blood samples, serum and urine were collected from 22 patients suffering from Urinary Bladder Carcinoma, as well as, patients without taking any chemotherapeutic agents.

The age of the patients are ranging from (45-80) years old including (20 males) and (2 females). Detection bacteria by culturing urine on ordinary and specific media and biochemical test for isolation and differentiation.

The concentration of Interleukin -2 & Interleukin -8 evaluate by using serum from patients and ELISA kits (koma biotech-Korea).

Result and Discussion:

Although, there is no evidence on the role of bacteria in the stimulation of urinary bladder cancer, but some patients complain from sever urinary tract infections UTI .So, the present study investigates on the main bacteria associated with UTI in patients with urinary bladder cancer.

Recently, however, bacteria have been linked to cancer by two mechanisms: induction of chronic inflammation and production of carcinogenic bacterial metabolites. The most specific example of the inflammatory mechanism of carcinogenesis is *Escherichia coli* infection. *E. coli* has been epidemiologically linked to urothelial carcinoma of the urinary bladder by its propensity to cause lifelong inflammation (Gabri *et al*., 2012). Also Shokeir A. (2004) explained that Bladder carcinogenesis is probably related to bacterial and viral infections, commonly associated with bilharzial infestation rather than the parasite itself. It was observed that *E.coli* is predominant among other bacteria, followed by *Pseudomonas* and *Staphylococcus* , The other type of bacteria includes *Klebsiella pneumoniae* . This finding is in agreement with the study performed by Al-Bayati *et al*., (2009) that is obvious that *E. coli* is the most predominant organisms followed by *K. pneumoniae* and *Ps. aeruginosa* . Also El-Mosalamy *et al.,* (2012) that was showed a history of urinary tract infection can be considered as a risk factor for bladder cancer specially infection by *E. coli* may play a major additive and synergistic role during bladder carcinogenesis.

Table (1) The Bacterial isolation from urine of patients with urinary bladder cancer

Mixed Bacterial Isolates			
Bacterial Isolates	**Number**	**Percentage %**	**Total**
Escherichia coli + *Pseudomonas aeroginosa*	5	22.7%	**9** **40.9%**
Escherichia coli + *Staphylococcus aureus*	4	18.18%	
Single Bacterial Isolates			
Bacterial Isolates	**Number**	**Percentage %**	**Total**
Escherichia coli	6	27.27%	**13** **59.09%**
Staphylococcus aureus	2	9.09%	
Klebsiella Pneumonia	2	9.09%	
Pseudomonas aeroginosa	3	13.6%	

The present study shows no elevated in IL-8 level and this may be belong to all cases of have superficial but not invasive cancer. Alteration of cytokine levels is associated with cancer progression. (Lin *et al*., 2004)

Hikmet *et al*., (2004) results who revealed a high IL-8 levels which is related to invasive bladder cancer patients and not to individuals with superficial bladder cancer .also Mahdi *et al*., (2013) show of ELISA test for IL-8 revealed a significantly increase serum IL-8 of patients with urinary bladder cancer in comparison with control group.

Previous studies have documented elevated of IL-8 in patients with urothelial cell carcinoma and this elevated associated with increased stage of disease, disease recurrence and lack of efficacy of intravesical therapies, including bacillus Calmette-Guérin and mitomycin C. (Sagnak *et al*., 2009 ; Kocak *et al*., 2004).
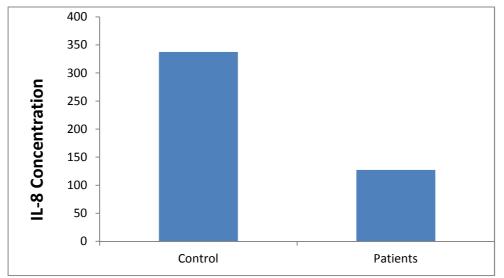
Figure (1) The Interleukin 8 concentration in patients with urinary bladder cancer comparing with control. *P* **0.005048**

Recently, it has been shown that IL-8 plays a critical role in cancer invasion, angiogenesis and metastasis. It is a chemotactic factor for T cells, neutrophils, and basophils besides its pro-inflammatory role, IL-8 has been evaluated as a pro-oncogenic effector in various types of human cancers, including leukemia, astrocytoma, melanoma, breast cancer, ovarian cancer, lung cancer, prostate cancer, colon cancer, urinary system cancer , gastric cancer and pancreatic cancer.(Kuwada *et al*., 2003; Utgaard *et al*., 1998).

Also Decrease IL-2 in serum of patients with urinary bladder cancer might be show refer to that the lower immune system that maintains or regulated tumor activity against malignant bladder tissue. However interleukin-2 (IL-2) may boost the immune system to fight tumors and IL-2 plays a pivotal role in the treatment of patients with metastatic melanoma and renal cell carcinoma. (Liang *et al*., 2012).

This finding has led to some authors to conclude that whereas endogenous IL-2 stimulates cell proliferation, exogenous IL-2 inhibits such a proliferation (Reichert *et al*., 2000).
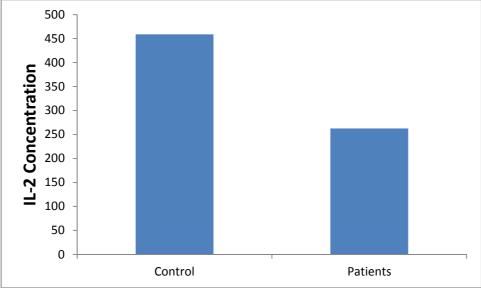

Figure (2) The Interleukin 2 concentration in Patients with urinary bladder cancer comparing with control . *P* **0.003378**

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