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ORIGINAL ARTICLE

The expression of p63 in bladder cancer vs. chronic bilharzial bladder

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KEYWORDS

P63;
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Bladder

ABBREVIATIONS

SCC, squamous cell carcinoma;
CIS, carcinoma *in situ*;
TCC, transitional cell carcinoma

Abstract ***Objective:*** To investigate the immunohistochemical expression of p63 in bladder cancer and the variation of expression in relation to histological type, grade and stage of the tumour, and whether bilharziasis (endemic in Egypt) has an effect on its expression, in an attempt to better understand the tumour behaviour and the possibility of using p63 as a prognostic marker.

Patients and methods: In a prospective study, biopsies were taken from the bladders of 70 patients, who were divided into three groups; group A comprised 10 with a normal urothelium, group B comprised 20 with chronic cystitis (bilharzial and non-bilharzial) and group C contained 40 with bladder cancer. The biopsies were examined for the expression of p63, using immunohistochemical techniques.

Results: The mean (SD) ages of groups A, B and C were 45.2 (9.5), 50.5 (11.7) and 60.5 (9.9) years, respectively. There was a statistically significant decrease in the expression and immunoreactivity in group C ($P < 0.05$), and a significant decrease with advancing tumour stage and grade ($P < 0.01$). In cases of squamous cell

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carcinoma there was a statistically significant lower immunoreactivity than in transitional cell carcinoma ($P < 0.05$). There was a tendency for a statistically significant decrease in the immunoreactivity in bilharzial cystitis ($P < 0.05$), but in the malignant group, bilharziasis had no apparent effect on the pattern of expression.

Conclusion: p63 might be a helpful biomarker and adjunct in predicting the biological behaviour and progression of tumours. Further studies are recommended to elucidate more clearly its role as a prognostic indicator and its utility as a tumour marker.

Introduction

In Egypt, bladder cancer is intimately related to the parasitic blood fluke *Schistosoma*, which has been endemic in Egypt at least since 1900 BCE, and is endemic in 74 countries throughout the world [1,2].

Carcinoma of the bladder is the foremost oncological problem in Egypt, constituting 30.3% of all cancers, 40.6% of male cancers and 14.3% of female cancers, as recorded at the National Cancer Institute [3]. Worldwide it is an important health problem, with 386,300 newly diagnosed cases and 150,200 deaths in the year 2008 [4].

Various methods are currently used for detecting bladder cancer, of which the most recent is the use of tumour markers as a complement to the tumour grade and stage, to reflect the potential behaviour of the tumour and the possibility of its progression or recurrence [5].

The gene *p63* is a homologue of the p53 tumour-suppressor gene located at 3q27–3q29 [4]. It is expressed selectively in the basal cells of stratified epithelium, including the urothelium [6]. It is suggested to play a critical role in the normal development and maintenance of the human urothelium [7].

Several studies have assessed the role of p63 in malignant transformation, as well as tumour progression. Some of these studies showed a downregulation in muscle-invasive tumours, and others proposed an impaired expression with biological aggressiveness, and of being a common feature of high-grade invasive carcinomas, suggesting a role in tumour progression and biochemical differentiation [8,9]. Considering the urothelium as a unit acting in the same manner throughout the urinary tract, similar studies on the upper urinary tract transitional cell carcinoma (TCC) showed a significant decrease in immunoreactivity with advancing tumour stage, and an association with a poor prognosis [10]. By contrast, other studies showed that the designation of *p63* as an oncogene or a tumour-suppressor gene might be difficult, because its isoforms might have opposing functions [11].

Thus we evaluated the immunohistochemical expression of p63 in bladder cancer and the variation of expression in relation to histological type, grade and stage of the tumour, and whether bilharziasis has an effect on its expression.

Patients and methods

The study included 70 patients admitted to the Urology department of Theodor Bilharz Research Institute, Egypt. The patients were prospectively enrolled in the study and divided into three groups; a control group (A) of 10 patients who underwent cystoscopy for any urological disease other than cystitis or bladder tumour; a cystitis group (B) of 20 patients with chronic cystitis (bilharzial and non-bilharzial); and a malignancy group (C) of 40 patients with bladder cancer. According to the results of the biopsy, group B patients were retrospectively divided into bilharzial and non-bilharzial, and group C into those with TCC or squamous cell carcinoma (SCC).

All patients had a detailed history taken, a full clinical examination, routine laboratory investigations, urine cytology, and imaging in the form of abdominal and pelvic ultrasonography, intra-venous urography (IVU) and computed tomography scan (CT) of the abdomen and pelvis in selected cases. There were no patients with associated upper tract TCC in the study.

After signing an informed consent, all patients underwent cysto-urethroscopy and biopsy. For groups A and B the biopsies were taken from the urothelium using a cold-cup biopsy forceps, while for group C we used a resectoscope to take biopsies from the tumour and from the surrounding apparently normal urothelium. In patients with invasive bladder cancer who had a radical cystectomy, the biopsy was taken from the cystectomy specimen after surgery.

The biopsy specimens were immediately fixed with formalin 10%, and assessed histopathologically after staining with haematoxylin and eosin, and for the immunohistochemical study of p63 expression. Schisto-