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Original Article

Immunohistochemical differential diagnosis between urothelial carcinoma and prostate adenocarcinoma among Egyptian patients

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ABSTRACT

The aim of the present study was to differentiate between prostate adenocarcinoma and urothelial carcinoma among Egyptian patients by immunohistochemical methods. Two groups of patients were used: urothelial group, consisted of 9 cystitis, 21 transitional cell carcinoma (TCC) and 5 urinary bladder mucoid adenocarcinoma (MAC) and prostatic group, consisted of 9 nodular prostatic hyperplasia (NPH) and 21 prostatic adenocarcinoma (PAC). H–E stained sections were performed to confirm the diagnosis and evaluate the histopathological characteristics of the tumor. Immunohistochemical techniques were used for detection of P63, CK7, CK10 and PSA. The results showed that in urothelial group, positive p63and CK7 immunostaining was observed in all cases of cystitis, transitional cell carcinoma and urinary bladder mucoid adenocarcinoma. All cases of cystitis, transitional cell carcinoma and urinary bladder mucoid adenocarcinoma were CK10 and PSA negative. In prostate group, positive p63 immunostaining was observed in all cases of NPH and in prostatic adenocarcinoma. Positive CK7 immunostaining was observed in all cases of NPH while all cases of prostatic adenocarcinoma were CK7 negative. Positive CK10 immunostaining was observed in all cases of NPH. In prostatic adenocarcinoma, 11 cases were CK10 positive and 10 cases were CK10 negative. All cases of NPH and prostatic adenocarcinoma were PSA positive. In conclusion, the result of the present work proved that p63 and CK7 can be used along with other markers to differentiate between adenocarcinoma of prostate and urothelial carcinoma of the bladder. Also, CK10 and PSA are useful for distinguishing prostate cancer from urothelial carcinoma.

1. Introduction

Bladder cancer is a common neoplasm around the world. Bladder cancer has been the most common cancer during the past 50 years [1]. Almost all bladder cancers originate in the urothelium, which is a 3- to 7-cell mucosal layer within the muscular bladder. It is often described as a polyclonal field change defect with frequent recurrences due to a heightened potential for malignant transformation. However, bladder cancer has also been described as resulting from implantation of malignant cells that have migrated from a previously affected site. This occurs less often and may account for only a small percentage of cases [2]. Incidence of bladder cancer increases with age, with the median age at diagnosis being 68 years, and is about 4 times higher in men than in women. Over the past 2 decades, the rate of bladder cancer has been stable in men but has increased in women by 0.2% a year. The male predominance in bladder cancer in the United States reflects the prevalence of transitional cell carcinoma (TCC). With squamous cell carcinoma (SCC) – in contrast to TCC – the male-to-female incidence ratio is 1:2 [2].

Bladder cancer is the most common malignancy among Egyptian males and previously has been attributed to *Schistosoma* infection [3]. It represents a global health problem, in Egypt, carcinoma of bladder is the most prevalent cancer, accounting for as many as 31% of all cancer cases currently, and it ranks first in males representing 16.2% of male's cancer [4]. In 2002, Egypt's world-standardized bladder cancer incidence was 37/100,000, representing approximately 30,000 new cases each year [5].

Cancer of the prostate is now recognized as one of the principal medical problems facing the male population [6]. Rates of prostate cancer vary widely across the world. Although the rates vary widely between countries, it is least common in South and East Asia, more common in Europe, and most common in the United States. According to the American Cancer Society, prostate cancer is least common among Asian men and most common among black men, with figures for white men in between. However, these high rates

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may be affected by increasing rates of detection [7]. Prostate cancer develops primarily in men over fifty. It is the most common type of cancer in men in the United States, with 186,000 new cases in 2008 and 28,600 deaths [8]. It is the second leading cause of cancer death in US men after lung cancer. In the United Kingdom, it is also the second most common cause of cancer death after lung cancer, where around 35,000 cases are diagnosed every year and of which around 10,000 die of it. The Prostate Cancer Prevention Trial found that finasteride reduces the incidence of prostate cancer rate by 30%. There had been a controversy about this also increasing the risk of more aggressive cancers, but more recent research showed this may not be the case [9].

Immunohistochemistry has been described as helpful for distinguishing bladder carcinoma from prostate adenocarcinoma. p63 is a recent discovered molecule, which is part of p53 family and plays an essential role in the normal development and stratification of many epithelia (oral, gastric and cervix mucosae), including urothelium [10]. p63 is a transcription factor that localizes to the nucleus, and has been shown in several studies to be a marker of urothelial origin of tumors [11] and is used to differentiate prostate cancer from benign mimickers [12]. Cytokeratins are typical epithelial cell markers expressed in a tissue-specific and differentiation-dependent manner. It has been reported that cytokeratins were extensively present in many malignant epithelial cells [13,14] and tended to be altered in association with increases in metastatic ability and malignancy [15]. CK7 (Cytokeratin 7) is a basic cytokeratin, which is expressed in the epithelial cells of ovary, lung, and breast but not of colon, prostate, or gastrointestinal tract [16] and is found in urothelial neoplasia of the urinary bladder [17]. Cytokeratin 10 (CK10) is a heterotetramer of two type I and two type II keratins. CK10 is typically associated with cytokeratin 1 (CK1). CK10 is expressed in all suprabasal cell layers, and it is part of the acidic/high molecular weight keratin subfamily [18]. Prostate specific antigen (PSA) is a single-chain 34-kd glycoprotein of 237 amino acids containing approximately 8% carbohydrate. It is a serine protease produced almost exclusively by prostatic epithelial cells [19]. Immunohistochemical staining with PSA is widely used to aid in the diagnosis of metastatic prostatic carcinoma [20].

Distinction between prostate carcinoma (PC) and urothelial carcinoma (UC) is important due to the potential therapeutic and prognostic implications. Whereas hormone therapy may be used in treatment of PC, chemotherapy is used for UC. However, discriminating between these two cancers can be a diagnostic challenge especially in high-grade tumors and in the presence of limited tissue. The aim of the present study was to differentiate between prostate adenocarcinoma and urothelial carcinoma among Egyptian patients by immunohistochemical methods.

2. Patients and methods

This study was carried out on sixty-five specimens of Egyptian patients (65 male patients) from Pathology Department, Faculty of Medicine, Menoufia University during the period between 2009 and 2011, that is divided into:

- urothelial group: consisted of 9 cystitis, 21 transitional cell carcinoma (TCC) and 5 urinary bladder mucoid adenocarcinoma (MAC);
- prostatic group: consisted of 9 nodular prostatic hyperplasia (NPH) and 21 prostatic adenocarcinoma (PAC).

2.1. Clinical data

Clinical data related to the selected cases were obtained from the patients' medical records including patient's age, grade of tumor and Type of biopsy.

2.2. Histological examination

For histological examination, samples were fixed in 10% formalin. Following fixation, specimens were dehydrated through ascending series of alcohol, cleared in xylene and embedded in molten paraplast. Sections of 5-micron thickness were cut using rotary microtome, mounted on clear glass slides and stained with hematoxylin and counter stained with eosin. Stained sections were performed to confirm the diagnosis and evaluate the histopathological characteristics of the tumor.

2.3. Immunohistochemical analysis

Immunohistochemical reaction was performed using an avidin biotin complex immunoperoxidase technique on paraffin sections. p63 was detected using a purified Mouse Monoclonal Antibody (clone BC4A4, dilution 1:100–1:200) raised against p63. For CK7, the primary antibody was a purified Mouse Monoclonal Antibody (clone OV-TL 12/30) raised against CK. For CK10, the primary antibody was a purified Mouse Monoclonal Antibody (clone DE-K10) raised against CK and for PSA (Prostate Specific Antigen), the primary antibody was a purified Mouse Monoclonal Antibody (clone ER-PR8 + PA05) raised against PSA.

2.3.1. Scoring and evaluation of p63

Immunohistochemical expression was assessed semi-quantitatively for staining intensity and percentage of positive tumor cells with brown nuclear staining (for p63). Only moderate or strong staining in at least 5% of the tumor cells was considered positive [11].

2.3.2. Scoring and evaluation of cytokeratins

Each case in which more than 10% of the cancer cells reacted positively for an antibody, immunostaining was scored based on the intensity of staining and the percentage of cells that stained positively. Staining scores were calculated by multiplying the percentage of positive tumor cells per section (0% to 100%) by the immunohistochemical staining intensity. The sections were classified according to staining intensity as negative if staining was faint or negative and positive if staining was moderate to intense [21].

2.3.3. Scoring and evaluation of PSA

In scoring the expression of PSA, the extent and intensity of immonopositivity were considered, using the method of Zhao et al. [22].

The intensity of positivity was scored from 0 to 3 as follows: 0 as non-stained, 1 as weak, 2 as moderate, and 3 as strong as positive control. The percentage of positively stained cells for each staining intensity was estimated. The final composite score was determined after multiplying the intensity of positivity and percentage of positivity in the respective lesions.

2.4. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences, SPSS 16.0 statistical software (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Clinicopathological data

3.1.1. Urinary bladder group

This group consisted of [9 cystitis, 21 transitional cell carcinoma (TCC) and 5 urinary bladder mucoid adenocarcinoma (MAC)]. The