Case report:

Multifocal primary tumour with lesions in prostate gland and urinary bladder: clinical case

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Abstract

In some cases a combination of several malignant tumours in one person can be observed. In such case it is the multifocal primary tumour (MPT). The tumours combination in genitourinary system is rare phenomenon, including a rare combination of prostate and urinary bladder cancers. These pathologies can be caused by both the endogenous factors - age, gender, heredity, inflammatory and proliferative processes, abnormal inclusions (calculi and amyloids) and exogenous factors, among which the leading cause is the environmental pollution (heavy metals salts and others), bad habits, occupational hazards, oncogenic viruses and ionizing radiation.

A 76 - year- old male patient, Ukrainian, was hospitalized at urology department with complaints on pollakiuria, frequent urinary retention, haematuria appeared about 1 month before.

After examination of patient the preliminary diagnosis was made: «Urinary bladder cancer, acute urinary retention, macrohematuria and posthemorrhagic anemia».

Based on the histological and immunohistochemical examinations, the final diagnosis was determined: combined malignant tumours - acinar adenocarcinoma of prostate index 9 (5 + 4) accordimg to D.F. Gleason and invasive urothelial carcinoma of the urinary bladder.

This clinical case demonstrates that the probability of combined oncologic cancer pathology with lesions in one system is rather high. Therefore, in order to exclude the cancer combinations, the patients with malignant tumour in the genitourinary system should undergo a complex examination.

Keywords: Cancer; prostate; urinary bladder; multifocal primary tumour; case report; immunohistochemical examination.

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Introduction.

Urinary bladder cancer (UBC) is highly ranked among oncologic pathologies and accounts up to 3.3% of all malignant tumours. And this figure increases annually[1]. In Europe it is the fifth common cancer in male – 14.4 cases per 100 000 population (mortality rate - 4.5). 5-year survival in non-invasive UBC is 96%, but it is sharply reduced to 70% if the tumour spreads through the organ and up to 5.5% with the presence of distant metastases [2,3].

Prostate cancer (PC) is a tumour that is more common in men aged over 70 years. In Europe the incidence of

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prostate cancer is 96.0 cases per 100 000 population (mortality rate - 19.3) that constantly increases [3,4]. As the diagnosis and treatment methods are constantly improved, the 5-year survival of patients with prostate and urinary bladder cancers has increased[5]. In most cases the prostate and urinary bladder cancers can be diagnosed by clinical, laboratory and instrumental examinations[6,7]. Depending on the stage of the disease, tumour dissemination, grade of differentiation and immunophenotype, the treatment of prostate and urinary bladder cancer is carried out by surgical procedures (transurethral resection, cystectomy, prostatectomy, etc.), polychemotherapy, immunotherapy, hormonal treatment, radiotherapy and symptomatic treatment [5,8].

In some cases a combination of several malignant tumours in one person can be observed. In such case it is the multifocal primary tumour (MPT). Although the lesions of both organs are observed, the survival of patients is higher compared with patients with one tumour, due to the presence of differentiated tumours in patients with MPT[9]. The tumours combination in genitourinary system is rare phenomenon [10], including a rare combination of prostate and urinary bladder cancers [6]. These pathologies can be caused by both the endogenous factors - age, gender, heredity, inflammatory and proliferative processes, abnormal inclusions (calculi and amyloids) and exogenous factors, among which the leading cause is the environmental pollution (heavy metals salts and others), bad habits, occupational hazards, oncogenic viruses and ionizing radiation [6,11-14].

Case presentation

A 76 - year- old male patient, Ukrainian, was hospitalized at urology department with complaints on pollakiuria, frequent urinary retention, haematuria (blood in the urine) appeared about 1 month before.

During examination the anemia was revealed, the erythrocyte sedimentation rate was increased and macrohematuria was present. The pelvic ultrasound revealed the tumour on the back wall of the urinary bladder, which invades in all its layers. The cystoscopy revealed the round mass on the back wall of the urinary bladder that was 5.0 cm in diameter, pink colored and tightly adjoined to the urinary bladder neck. Erosions were present on the surface of tumour, bleeding at the touch. After examination of patient the preliminary diagnosis was made: «Urinary bladder cancer, acute urinary retention, macrohematuria and posthemorrhagic anemia». Preoperative treatment was determined: detoxification (saline, Ringer's solution), antibiotics, analgesics and spasmolytics.

By transurethral resection, the tumour and adjoining tissues were removed. The fragments were fixed in 10% formaldehyde solution and sent to histological laboratory. The histological examination of patterns, stained with hematoxylin and eosin revealed the tumour infiltrates in smooth muscle stroma. Most of them were round, irregular shaped complexes with cribriform and solid architecture of growth. In solid patterns, almost complete loss of glands lumen was observed. Tumour cells were atypical epithelial complexes, delineated by pale eosinophilic cytoplasm, with moderately polymorphic rounded-oval nuclei and significantly enlarged nucleoli (Figure 2A). In smaller area of tumour tissue an adenocarcinoma was present with spreading small glands or chains and strands of epithelium that merged together and infiltrated the prostate gland tissue (PGT). In most cases the infiltrate cells had large, irregularly shaped nuclei with distinct nucleoli, eosinophilic or amphiphilic cytoplasm was around in different ratio. In some tumour lesions the necrosis was present. The changes were determined as acinar adenocarcinoma of high grade of malignancy, with 9 (5 + 4) index according to D.F. Gleason.

In other areas of specimens the diffuse infiltrates were revealed, consisting of rounded-oval cells, some of them were spindle-shaped. Tumor cells had nucleus of different shapes with dispersed and rough-dispersed chromatin without clear nucleoli (Figure 2B). Around the nucleus there was moderately and low expressed eosinophilic cytoplasm. High rate of mitosis was observed in tumour cells (more than 5 in 5 fields of view with microscope magnification - 400). In some areas the histologic features of tumour were similar to lymphoma with plasmacytic differentiation of cells (eccentrically located nuclei with densely eosinophilic cytoplasm). The changes in the determined part of the tumour were defined as undifferentiated malignant neoplasia.

To verify the diagnosis, the immunohistochemical study was carried out. Screening panel of antibodies included cytokeratin pan (PCK), CD45 (leukocyte common antigen - LCA) and vimentin. The results were the following: both types of malignant tumours were positive for CK pan, but receptors LCA and vimentin didn't expressed (Figure 3).

It should be noted that vimentin-positive cytoplasmic reaction was observed in stromal sells of all tumours and the positive membrane reaction on expression of LCA - in leucocytes, singly-scattered in tumour. Based on the results, the epithelial origin of both malignant tumours was determined.

Later the immunohistochemical study with other antibodies was carried out: CK LMW (8, 18), CK HMW (5, 14), CK 7 and CK 20. The results were the following: adenocarcinoma tissue had positive heterogeneous reaction on CK LMW, it was the CK HMW « - », CK 7 « - » and CK 20 « - ». The tissue of undifferentiated tumour expressed all types of CK (Figure 4).

At the last stage of immunohistochemical study the identification of specific receptors (androgen (AR), prostate-specific antigen (PSA) and AMACR) was carried out. The adenocarcinoma tissue had a distinct positive nuclear reaction on AR and cytoplasmic reaction on PSA and AMACR receptors. The tissue of undifferentiated tumour had heterogeneous expression on AMACR receptors and was negative on AR and PSA receptors (Figure 5).

Based on the histological and immunohistochemical studies, the final diagnosis was determined: combined malignant tumours - acinar adenocarcinoma of prostate index 9 (5 + 4) accordimg to D.F. Gleason and invasive urothelial carcinoma of the urinary bladder (Table 1).

Table 1. Immunohistochemical characteristic of tumours.

	CK pan	LCA	Vimentin	CK LMW	CK HMW	CK 7	CK 20	AR	PSA	AMACR
Acinar adenocarcinoma	+	-	-	+/-	-	-	-	+	+	+
Urothelial carcinoma	+	-	-	+	+	+	+	-	-	+/-

Medicinal postoperative treatment included the third-generation cephalosporin and fluoroquinolones antibiotics, analgesics and antiseptics.

Discussion

According to Warren and Gates in case of MPT the probability that a tumour is a metastasis of another one should be completely excluded [10.15]. Based on the clinical picture of the patient, that was typical for malignant tumour of urinary bladder, the first diagnosis was urinary bladder cancer. This diagnosis was also confirmed by cystoscopy. During the surgery the part of prostate with adjoining tissues were removed and together with the urinary bladder tumour tissues were sent to histological laboratory. The histological and immunohistochemical studies revealed the combined malignant tumour that emerged from transitional epithelium of urinary bladder and acinar epithelium of prostate.

In world literature there are some cases of combined neoplastic lesions of urinary bladder, prostate, kidney, thyroid and others. [6,10,15]. The combination of urinary bladder and prostate cancers is rather often phenomenon among cases of MPT of genitourinary system. If one of these malignant tumours is present the risk of pathologies combination increases in 18-19 times [6,16,17]. The risk of second malignant tumour is caused by general carcinogenic affect of substances, place of residence and work in environmentally polluted areas, genetic predisposition, a side effect of chemotherapy or radiation therapy [1,11,15,16]. In given case, a combination of several factors is present: age, living on environmentally polluted territory with a high content of heavy metals salts and chronic smoking.

Due to the fact that prostate cancer is observed in a significant number of patients with UBC it is important to make a blood test for PSA in preoperative period to exclude the lesion of prostate gland. Moreover, in postoperative period, the increased level of serous prostate-specific antigen up to 22 ng / ml (reference value 0-4 ng / ml) was revealed that can be considered as the result of prostate gland traumatizing during the surgery or influence of malignant tumour. It is important to study the specimen by using the modern immunohistochemical and cytomorphological methods that finally determines the histogenesis of tumour growth.

The further treatment of patient should be adjusted; the prostatectomy, polychemotherapy, radiotherapy and hormonal treatment should be carried out. Taking into account that the tumour didn't invade into nearby organs and distant metastasis were absent, in case of appropriate treatment, the prognosis for the patient is relatively favorable. This case report is ethically approved.

Conclusion

This clinical case demonstrates that the probability of combined oncologic cancer pathology with lesions

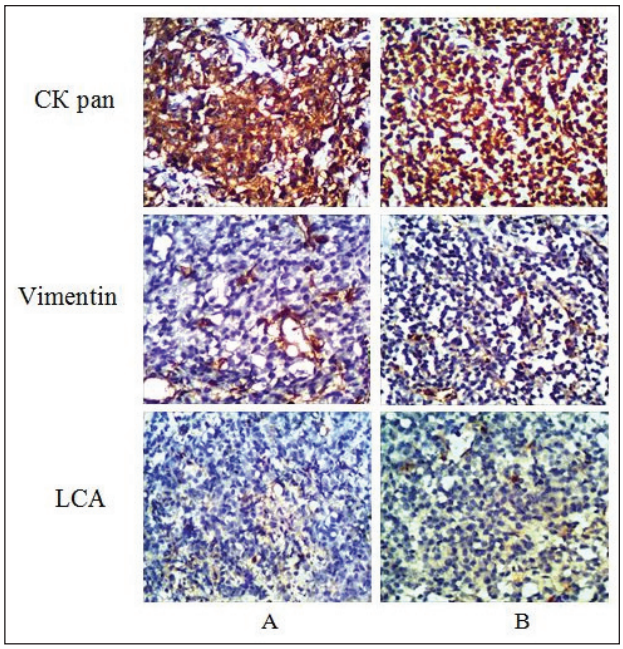

Figure 2. A - adenocarcinoma tissue, B- undifferentiated tumour tissue.
Immunohistochemical study of CK pan, vimentin and LCA receptors. Magnification - 400.

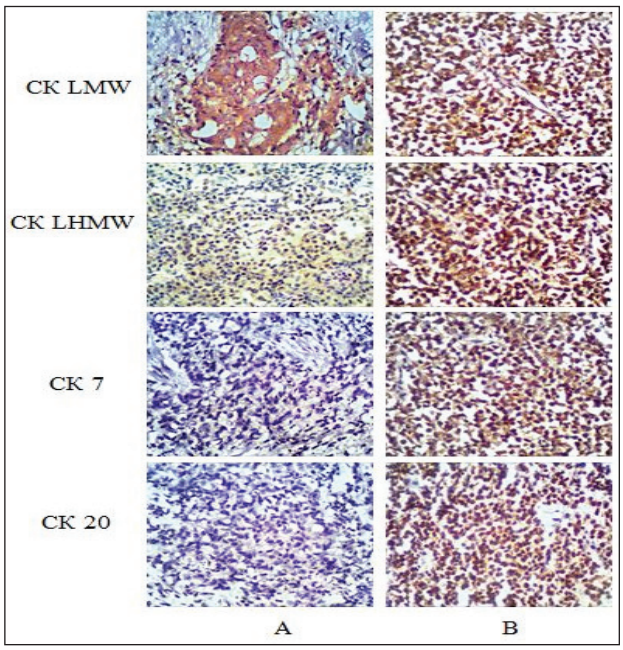

Figure 3. A - adenocarcinoma tissue, B- undifferentiated tumour tissue.
Immunohistochemical study of CK LMW, CK HMW, CK 7 and CK 20 receptors.
Magnification - 400.

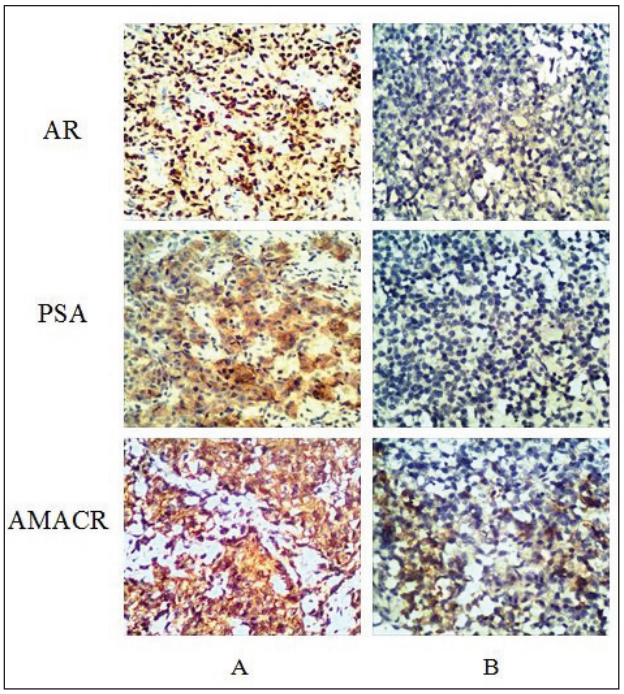

Figure 4. A - adenocarcinoma tissue, B- undifferentiated tumour tissue.
Immunohistochemical study of AR, PSA and AMACR receptors. Magnification - 400.

in one system is rather high. Therefore, in order to exclude the cancer combinations, the patients with malignant tumour in the genitourinary system should undergo a complex examination. If the histological study didn't reveal the tumour histogenesis, the additional examinations of tumour should be carried out, including immunohistochemical determination of the receptors in neoplastic cells.

Conflictof intetrest: None

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