

Verrucous Carcinoma of Urinary Bladder

Mesanenin Verrüköz Karsinomu

Ufuk USTA, Bülent MIZRAK, İclal GÜRSES

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Verrucous carcinoma is a very rare entity in the urinary bladder, and it is usually associated with Condyloma accuminatum and schistosomiasis. Though chronic irritation is accepted as a common etiological factor in few rare cases, bladder stone has not been demonstrated among irritative etiologic agents. Verrucous carcinoma in the bladder of a man of 54 years, who underwent three surgical interventions in the last 20 years because of bladder stone, is presented. The histopathological diagnosis of the specimen from the third operation was verrucous carcinoma of the bladder. Recently the fourth operation; a transurethral resection was performed, as the verrucous carcinoma relapsed.

Key Words: Bladder neoplasms/pathology/surgery; carcinoma, papillary/pathology.

Mesane verrüköz karsinom çok nadir olarak görülür ve sıklıkla kondiloma akkümümatum ve şistozomiazis ile ilişkilidir. Birkaç nadir olguda kronik iritasyon ortak etyolojik faktör olarak kabul edilmiş olsa da, mesane taşı bu iritatif etyolojik ajanlar arasında tarif edilmemiştir. Bu makalede, son 20 yılda mesane taşı nedeniyle üç kez ameliyat edilen 54 yaşında bir erkek hastada görülen mesane verrüköz karsinom olgusu sunulmaktadır. Üçüncü ameliyatı sırasında mesaneden alınan biyopsinin histopatolojik incelemesinde tanı konulan hastaya, tanıdan iki yıl sonra tümörün tekrarlaması nedeniyle trans uretral rezeksiyon uygulanmıştır.

Anahtar Sözcükler: Mesane tümörü/patoloji/cerrahi; papiller karsinom/patoloji.

Verrucous carcinoma is accepted as a distinct variant of well-differentiated squamous cell carcinoma.^[1,2] The most common locations for verrucous carcinoma are oropharynx, lips, and larynx.^[3] Histopathologically verrucous carcinoma is differentiated from ordinary squamous cell carcinoma by its very low grade of atypia and prognostically by its very low

capacity of metastasis.^[1,2-4,5] The verrucous carcinoma of urinary bladder is a very rare entity among the malignant neoplastic conditions of the bladder.^[2] The most common etiological factors for verrucous carcinoma of the bladder are Human Papilloma Virus (HPV) infection, and chronic irritation due to schistosomiasis.^[4,6,7]

CASE REPORT

A man of 54 years had undergone two surgical interventions because of bladder stones, in the last 20 years. Four years ago, he again visited the doctor with complaints of dysuria, polyuria, difficulty in urination, and pelvic pain which had started in the last two weeks. A bladder stone was reported in the intravenous pyelography (IVP), which was supported by the images of the ultrasound. Microscopic urine analysis revealed erythrocytes, a few inflammatory cells and epithelial cells. Microbiological and biochemical urine analysis was performed and there was no crystalline material and no evidence of a parasite or bacteria in the urine. The surgeon planned an operation aiming removal of the stone from bladder. But instead of stone, the bladder was filled with irregular, fleshy tumorous tissue originating from the wall of the urinary bladder. The surgeon resected the tumor tissue and sent the resection specimen to the pathology department.

The patient remained disease-free for two years. In this period, he was routinely screened by pelvic USG and tomography. In his last control USG, the bladder wall was diffusely thickened with a tumorous mass. After the confirmation of the USG diagnosis by pelvic tomography, the surgeon planned a transurethral resection of the mass.

The first biopsy specimen, which was sent to the pathology laboratory two years ago, was composed of seven irregular shaped, tan colored pieces between sizes of 2.5 cm and 1.1 cm. Cut surfaces were gray-white, solid and granular appearing with well formed micropapillary structures (Fig. 1). Five μm thick sections obtained from the formalin-fixed and paraffin-embedded tissues were stained by hematoxylin-eosin (HE). Two sections were taken on polylysine-coated slides, which were later immunohistochemically stained for HPV16-18 (Monoclonal, Neomarkers, Fremont, CA, USA). In this procedure, an external positive control tissue section for HPV was also used.

The latter specimen was a 40 g TUR material, fixed in 10% formaldehyde. This specimen was

processed as described in the first specimen, and sections were stained with HE and immunohistochemically with HPV.

In the microscopic examination of both biopsies, the low power view showed hyperplastic, acantotic squamous epithelium, frequently forming papillomatous structures with characteristics of well-differentiated neoplastic squamous islands of verrucous carcinoma. The high power view showed squamous cells with little atypia and scanty, basally located mitotic figures (Fig. 2a, b). In both biopsies, the tumoral epithelium invaded lamina propria with pushing borders (Fig. 3a, b). There was no individual cell invasion. There was neither vascular, nor perineural invasion. Immunohistochemically, there was no nuclear staining for HPV16-18 antibody in both of the biopsies.

DISCUSSION

Verrucous carcinoma is regarded as a distinct variant of well differentiated squamous cell carcinoma, but it differs from squamous cell carcinoma prognostically, by its very low capacity of metastasis.^[1,2,5]

Histopathologically it is sometimes very difficult to differentiate verrucous carcinoma from well differentiated squamous cell carcinoma.^[2] A few atypical mitotic figures may accompany well differentiated squamous cell carcinoma, whereas in verrucous carcinoma there may be



Fig. 1. Irregular shaped tumorous tissues with micropapillary structures.

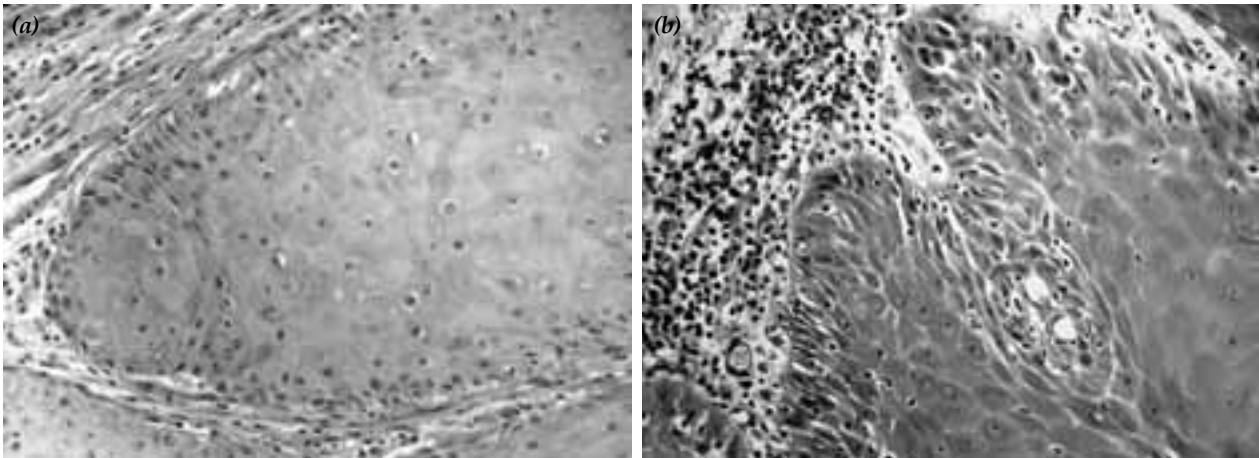


Fig. 2. Absence of cellular atypia in the (a) in the first, (b) in the second biopsy specimen (H-E x 400).

mitosis only in limited numbers and without atypia.^[2-4,6] The invasive borders of verrucous carcinoma show a pushing pattern, while in squamous cell carcinoma it is a tentacled pattern.^[2,3,5] Absence of anaplasia is the prerequisite to discriminate verrucous carcinoma from well-differentiated squamous cell carcinoma.^[1,2]

Another entity in the differential diagnosis is the papilloma of the bladder.^[3,8] But cystoscopically, it can easily be differentiated from verrucous carcinoma by its localization and growth pattern, and histopathologically there is no sign of invasion in squamous papilloma.^[3,8]

Though Condyloma accuminatum is accepted as the most common accompanying lesion in verrucous carcinoma of the bladder, few cases of verrucous carcinoma secondary to

Schistosoma infestation were also reported.^[4,5] In one study, chronic irritation of the bladder was accepted as the most important etiological factor for the metaplastic and malignant transformation of the urothelium, and also development of verrucous carcinoma in the bladder.^[9] However, bladder stone is not described among those irritative agents leading to verrucous carcinoma of the bladder.

In the presented case, HPV and parasitic infestations are excluded by immunohistochemical and microbiological investigations. In both biopsies, HPV16-18 antibody was used immunohistochemically to include or exclude the possibility of Condyloma accuminatum, as HPV16 and HPV18 are known as the most common carcinomatous types of HPV.^[7] Chronic irri-

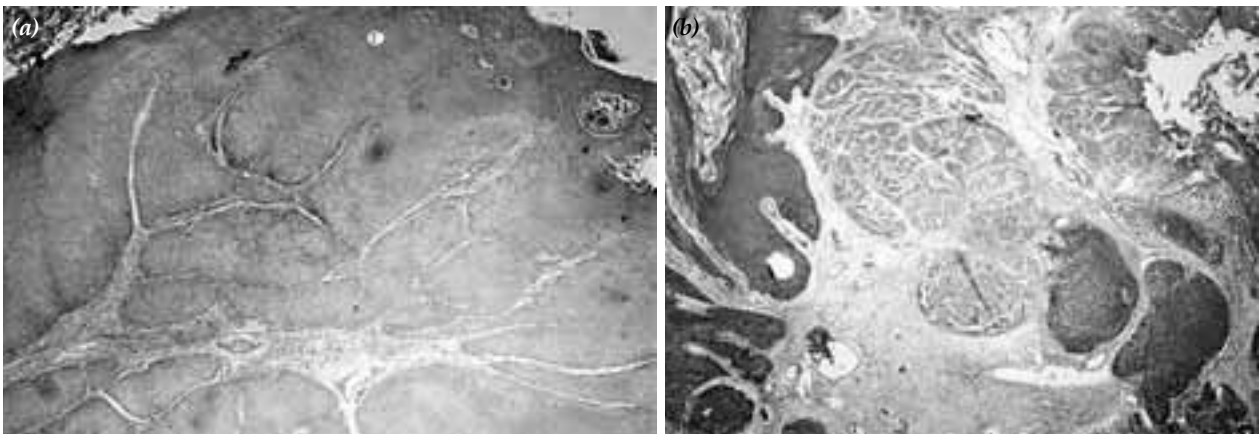


Fig. 3. Invasion of the lamina propria with pushing borders (a) in the first (b) in the second biopsy specimen (H-E x 40).

tation of stones remains to be the most probable etiologic factor for verrucous carcinoma in the presented case.

In one study, focal tumorous transformation into invasive squamous cell carcinoma was observed in 60% of studied verrucous carcinomas.^[5] In the presented case, there is a two year period between both biopsies, and there is no evidence of transformation into squamous cell carcinoma.

Cystectomy is accepted as the first choice for the treatment of verrucous carcinoma.^[5,8] Previous reports revealed neither local invasion nor local recurrence and no distant metastasis of verrucous carcinoma postoperatively. The recurrence of the carcinoma in the presented case may be due to the subtotal resection of the mass, instead of performing a cystectomy.

In conclusion we can say that, in the presented case, irritation is the first possibility for the development of verrucous carcinoma. The second biopsy both supported our first diagnosis of verrucous carcinoma, and showed persistence of the neoplasm, without transforming into other less differentiated forms.

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