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Condyloma Acuminata Presenting as Isolated Papillary Lesions in the Prostatic Urethra

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Patient: Male, 62
Final Diagnosis: Condyloma acuminatum
Symptoms: Urinary retention
Medication: —
Clinical Procedure: Cystoscopy
Specialty: Urology

Objective: Unusual clinical course

Background: A condyloma acuminatum is a sexually transmitted, human papillomavirus (HPV) associated, neoplasm. In men, it is predominantly found on external genitalia and rarely progresses more proximally than the distal penile urethra. Condyloma acuminata of the prostatic urethra are rare and are usually seen as an extension of, or in association with external lesions. Therefore, it is not typically considered in the differential diagnosis of isolated papillary lesions limited to the prostatic urethra.

Case Report: A 62-year-old male with rheumatoid arthritis treated with abatacept presented to urology due to a history of intermittent bladder self-catheterization for urinary obstruction. He underwent a transurethral resection of the prostate and had incidental findings of papillary lesions restricted to the prostatic urethra that were presumed to be urothelial carcinoma. Microscopic examination established the diagnosis of condyloma acuminata, and low-risk HPV 6 and 11 were detected by in-situ hybridization. Subsequent cystoscopy showed marked growth and extension of condyloma acuminata to near the external meatus. After multiple treatments with intraurethral 5-fluorouracil, several small lesions remained in the bulbous urethra. With follow up for 2 years since diagnosis, the patient has not developed external condylomata.

Conclusions: A condyloma acuminatum might present as an isolated papillary growth in the prostatic urethra without clinical or historical evidence of a visible lesion on external genitalia. Immunosuppression and/or urethral instrumentation might be a risk factor for such a presentation. Urologists and pathologists should be aware of this rare possibility in order to avoid misdiagnosis, and ensure that the patient receives appropriate therapy.

MeSH Keywords: Condylomata Acuminata • Human papillomavirus 11 • Human papillomavirus 6 • Intermittent Urethral Catheterization • Urethral Neoplasms

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Background

A condyloma acuminatum is a highly infectious sexually transmitted papillary lesion caused by human papillomavirus (HPV), a non-enveloped double-stranded DNA virus. HPV is the most common sexually transmitted disease in the world, and although vaccination is now available, there is no cure and the post-treatment recurrence rate is high. The virus belongs to the Papillomaviridae family, with over 200 types identified to date and classified into low and high-risk types based on their risk of progression to cancer. Approximately 90% of condylomata are positive for HPV types 6 and/or 11, but co-infection with high-risk types is possible [1]. Although condyloma acuminata occur in men and women, the majority of available literature is largely focused on female genital infection with HPV due to its link to cervical cancer. However, just like their female counterpart, condylomata in men can cause a variety of uncomfortable clinical and social repercussions that are preventable with vaccination. Condyloma acuminata are most commonly encountered on mucocutaneous surfaces of external male genitalia, sometimes extend into the distal urethra, and very rarely progress more proximally [2].

Case Report

We report the case of a 62-year-old male with a 2-year history of intermittent bladder self-catheterization (ISC) for urinary obstruction who presented for a urological evaluation. Other significant medical history included rheumatoid arthritis for which he has been receiving weekly 125 mg injections of abatacept (Orencia). His initial cystoscopy showed a normal meatus, inflamed urethral mucosa presumed to be secondary to ISC, enlarged prostate, and a distended moderately trabeculated bladder. Approximately one month later, the patient underwent transurethral resection of the prostate (TURP) to relieve his urinary obstruction. At this time, cystoscopy showed extensive papillary lesions around the verumontanum and extending distally to the external urethral sphincter. The lesions were clinically presumed to be papillary urothelial carcinoma and were resected during the TURP. The patient reported no previous history of external genital lesions and did not have any visible lesions on examination.

Microscopically, this was a fragmented papillary neoplasm with obvious cytologic atypia including high nuclear/cytoplasmic ratio, nuclear hyperchromasia and irregular nuclear contours, which in this setting, raised the possibility of high-grade urothelial carcinoma (Figure 1). Careful examination showed the papillary fragments were composed of non-keratinizing stratified squamous epithelium with extensive koilocytosis and proliferation of immature basaloid cells, but without high-grade dysplasia (Figure 2). Reference laboratory testing detected low-risk HPV 6 and 11 by in-situ hybridization in the

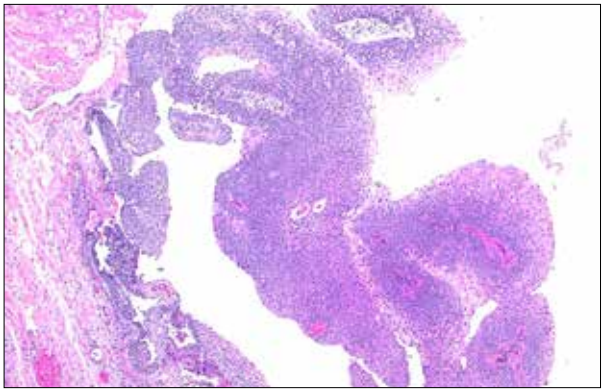

Figure 1. Condyloma acuminatum: low power view of a papillary neoplasm arising in the prostatic urethra. At this magnification, the papillary lesion appears very cellular, and the cells are crowded and show no apparent orientation (hematoxylin and eosin stain 40×).

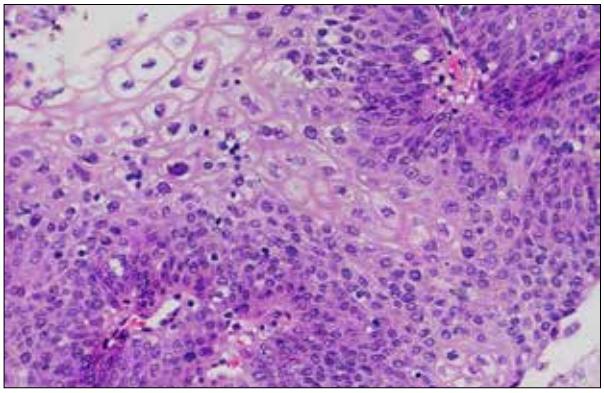

Figure 2. Condyloma acuminatum: higher power view shows non-keratinizing stratified squamous epithelium with extensive koilocytosis (raisinoid hyperchromatic irregular nuclei with cytoplasmic clearing) and a proliferation of basaloid cells. These findings are diagnostic of condyloma acuminatum (hematoxylin and eosin stain 200×).

mature squamous compartment as well as in the immature basaloid cells. High risk subtypes were not detected [3]. The histologic and molecular findings were diagnostic of condyloma acuminata.

Two months following the TURP the patient returned for Holmium laser cauterization of the lesion, however, the lesions were now circumferential in the urethra and extended from their original location in the prostatic urethra to near the meatus. Due to the extent of the condylomata, the procedure was cancelled, and the patient was scheduled for intraurethral chemotherapy with 5-fluorouracil (5FU) to treat the entire urethra.

Following 2 rounds of 6 weekly cycles of 5FU there was a marked reduction in the size and number of condylomata.

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The patient was voiding freely post-TURP and no longer self-catheterizing. On endoscopic examination, only the prostatic urethra had a small amount of residual sloughing lesions. A subsequent cystoscopy 3 months later showed multiple small condylomata in the penile, bulbous and membranous portions of the urethra, as well as recurrent lesions at the external urethral sphincter. A third round of chemotherapy was initiated and increased to 8 weekly cycles. The most recent cystoscopy, 2 years following the initial diagnosis, showed several submillimeter lesions in the bulbous urethra, still without development of external genital condylomata. Mild regrowth of the prostate gland was noted; however, the patient was still voiding freely without the need for resumption of self-catheterization.

Discussion

Condyloma acuminata of the male urethra are relatively rare and is usually seen as an extension of, or at least in association with external genital lesions. Fralick et al. reported that in their study of 114 biopsy proven HPV infected men only 14 (12.3%) had intraurethral lesions, and all of these 14 patients had current or historical evidence of meatal or perimeatal "sentinel" lesions [2]. Specifically, eight patients had a single urethral lesion, the remaining six had multiple lesions in 2 or more locations, but all were confined to the anterior (penile and bulbous) urethra. Olsen et al. presented a case of condyloma of the prostatic urethra without the simultaneous presence of external genital lesions, but the condyloma extensively involved the urethra from the meatus to the verumontanum [4].

Our patient had isolated papillary growths in the prostatic urethra without clinical or historical evidence of visible lesions on external genitalia. This presentation led to the clinical suspicion of a rapidly growing papillary urothelial carcinoma. In this setting, histopathologic examination is key to making the correct diagnosis. The low power impression of a papillary lesion composed of crowded hyperchromatic cells with apparent lack of proper orientation, and with associated scattered larger atypical cells, may appear consistent with high-grade urothelial carcinoma. Careful examination will reveal that the papillary lesion is composed of non-keratinizing squamous epithelium with a marked proliferation of basaloid cells that have fairly uniform nuclei. The nuclear atypia is restricted to the koilocytes and consists of enlarged, hyperchromatic, and crinkled (raisinoid) nuclei that are often multinucleated. These morphologic findings are diagnostic for condyloma acuminatum. HPV studies are usually not necessary to establish this diagnosis, but may be undertaken to confirm it, or if HPV typing is desired.

Another unique feature of our case was the spread of the condylomata from the original site in the prostatic urethra distally towards the meatus. This is in contrast to the typical distal to proximal spread reported in the literature. We were not able to find any previously reported cases with this type of presentation.

Sumino et al. reported development of condylomata following several urological procedures in the anterior urethra of a 70-year-old male without prior history of external genital or urethral lesions. They suggested that the repeated surgical instrumentation of the patient's urethra may have been responsible for the proximal dissemination of HPV and ultimately for the patient's clinical findings [5]. Likewise, we believe that the mucosal disruption from ISC that our patient performed over an extended period of time and other instrumentation are responsible for the introduction of HPV and its spread to the posterior urethra where the lesions were initially identified. Several cases of isolated bladder condyloma acuminata have been reported and appropriately attributed to the patients' primary or therapy induced immunosuppression [6–8]. Similarly, it is possible that our patient's treatment regimen with abatacept may have provided sufficient immunosuppression to have aided in the development of proximal urethral condylomata that otherwise would have been inhibited by the mucosal immune system. Although there is mounting evidence in support of immunosuppression and instrumentation as potential mechanisms for the development and spread of condyloma acuminata to unusual locations, one reported case of isolated bladder condyloma acuminata in an immunocompetent patient without prior history of instrumentation suggests that the complete pathogenesis of these lesions is not yet completely understood [9].

Conclusions

Condyloma acuminata might present as isolated papillary growths in the prostatic urethra without clinical or historical evidence of visible lesions on external genitalia. Urologists and pathologists should be aware of this rare possibility in order to avoid misdiagnosis of a predominantly benign entity as a potentially fatal malignancy such as urothelial or squamous carcinoma. Urethral instrumentation or immunosuppression might be risk factors for such a presentation, but even more likely when combined. The distinction between these neoplasms is crucial due to the different prognosis and treatment modalities employed for these lesions.

Department and Institution where work was done

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Conflicts of interest

None.

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