

Pan-Urethral Condylomata Acuminata in an Immunocompromised Patient



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CASE PRESENTATION

A 59-year-old African American male was referred for urologic evaluation of symptomatic anogenital warts. The patient was initially diagnosed with anogenital warts 1 year prior, however he did not seek further evaluation at that time. Subsequently, the lesions grew in size and number resulting in pain and occasional bleeding ultimately prompting him to seek medical attention. Additionally, he noted worsening postvoid dribbling but denied other lower urinary tract symptoms (LUTS) or hematuria. The patient has a past medical history of benign prostatic hyperplasia (BPH) treated with Tamsulosin and Acquired Immune Deficiency Syndrome (AIDS) treated with Highly Active Antiretroviral Therapy. He has no history of smoking and has not been sexually active since being diagnosed with AIDS 6 months prior.

Physical examination revealed an uncircumcised phallus with multiple verrucous lesions of the dorsal penile shaft, glans, and prepuce causing mild phimosis. Urethral meatal involvement was also noted. Multiple perianal lesions were also observed. There were no ulcerations, vesicles, or inguinal lymphadenopathy.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of genital lesions includes benign, infectious, inflammatory, and neoplastic pathology. Common benign cutaneous conditions include acrochordon (ie, skin-tags), pearly penile papules, and seborrheic keratosis. Common infectious genital lesions include condyloma acuminatum caused by Human Papilloma Virus (HPV), molluscum contagiosum caused by Poxvirus, and syphilitic lesions including chancres and condyloma lata. Inflammatory conditions that can manifest with genital involvement include lichen planus, lichen sclerosus, psoriasis, or drug eruption. Neoplasms

are an important consideration when evaluating genital lesions. Buschke-Lowenstein tumor, a benign but locally destructive tumor, Bowen's disease, and Bowenoid papulosis, as well as squamous cell carcinoma are associated with HPV infection and must be ruled out when evaluating patients with genital neoplasms.

This patient also presented with symptoms consistent with urinary obstruction, which have a broad differential diagnosis including bladder outlet obstruction secondary to BPH, prostate cancer, urethral stricture, or meatal stenosis especially in patients undergoing repeated urethral instrumentation, and primary urethral neoplasm. Although our patient's symptoms could easily have been attributed to BPH, the history of worsening LUTS and physical exam findings demonstrating meatal condylomata raised the index of suspicion for possible urethral involvement.

DIAGNOSTIC ASSESSMENT, MANAGEMENT, AND OUTCOMES

At initial evaluation the patient reported being compliant with Highly Active Antiretroviral Therapy, which was corroborated on laboratory evaluation with an undetectable viral load and a CD4 count of 206 cells/mm³. Urinalysis and urine culture were negative as was work-up for Chlamydia, Gonorrhea, and Syphilis. The appearance of the cutaneous lesions on physical exam was consistent with condylomata acuminata. Given the symptomatic nature of these lesions, including preputial involvement with resultant phimosis, surgical excision of condylomata and circumcision were recommended. Additionally, cystourethroscopy was recommended to evaluate for urethral condyloma. After obtaining informed consent, the patient was taken to the operating room. Cystourethroscopy demonstrated multifocal papillary lesions of the pendulous, membranous, and prostatic urethra, with no evidence of bladder involvement (Fig. 1 A,B; supplementary video). Circumcision and resection of meatal condyloma with meatoplasty was performed. The remaining external cutaneous condylomata of the phallus were laser ablated. Biopsy of a urethral lesion was performed, however the remaining intraurethral lesions were too numerous to ablate endoscopically.

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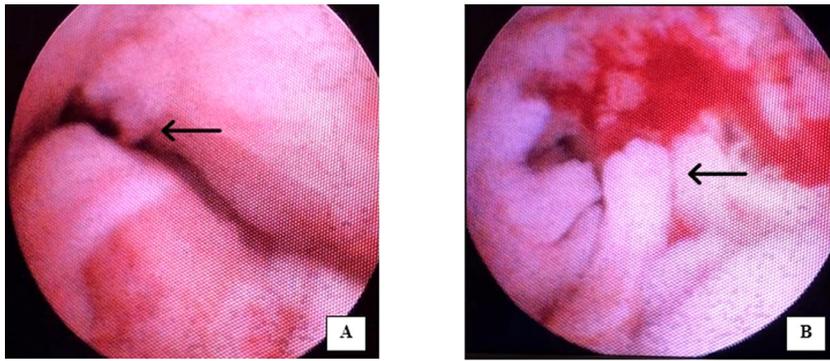


Figure 1. (A) Urethroscopic finding of condylomata acuminata of the prostatic urethra. (B) Urethroscopic finding of conylo-mata acuminata of the pendulous urethra. (Color version available online.)

Pathology of the cutaneous and urethral lesions demonstrated high-grade condylomata acuminata strongly positive for p16 indicating that the lesions were HPV-related.

The patient had an uneventful postoperative course and at 1-month follow-up reported resolution of pain associated with the cutaneous lesions and improvement in his LUTS likely related to the prepuce lesions previously causing extrinsic obstruction of the meatus. Physical examination revealed satisfactory cosmetic result with no new verrucous lesions. An extensive discussion was held with the patient regarding the pathology results, cystourethroscopy findings, and treatment options for urethral condylomata. He was informed about the risk of oncologic progression associated with anogenital warts, obstructive potential of the untreated urethral lesions, as well as the high risk of recurrence after surgical management. Treatment options for urethral condylomata acuminata including 5-fluorouracil (5-FU) urethral instillation and surveillance were reviewed. Due to substantial symptomatic improvement the patient opted for surveillance. At 3 and 6-month follow-up the patient reported satisfactory voiding and offered no complaints while examination demonstrated no new cutaneous lesions. Given this satisfactory postoperative outcome and the plan to continue surveillance irrespective of endoscopic findings in this asymptomatic patient, the decision was made to defer repeat endoscopic examination until 1-year follow-up.

DISCUSSION BY ANDREW WINER, M.D

Condylomata acuminata also known as anogenital warts are benign proliferative lesions caused by HPV, the most common sexually transmitted infection in the United States.¹ There are over 40 HPV serotypes that can be sexually transmitted, with the low oncogenic risk serotypes 6 and 11 recognized as the most prevalent causative agents of condylomata acuminata.² In the United States, the prevalence of genital HPV was 42.5% among a cohort of screened adults aged 18-59 during 2013-2014.³ Importantly, only 1% of patients with positive HPV genital swab have detectable genital warts.⁴

Anogenital warts are skin-colored, soft papules that typically exhibit a multifocal distribution. In uncircumcised

men lesions often occur at the glans penis, coronal sulcus, frenulum, and inner prepuce while the most commonly affected site in circumcised men is the penile shaft. The lesions can also affect the anal canal, urethra, as well as vulva, vagina, and cervix in women. Extragenital involvement is common and fingers and arms are frequently affected. Although most patients with anogenital warts are asymptomatic at presentation, some may develop pruritus, pain, or bleeding. Psychological distress is reported by 25% of patients presenting for management of anogenital condylomata.⁵

Although external genital lesions are commonly seen in general practice, lesions extending into the urethra are uncommon and require a high index of suspicion for timely diagnosis. It has been reported that up to 5% of patients with cutaneous lesions also have urethral involvement.⁶ Urethral condylomata are most often located in the distal pendulous urethra or fossa navicularis, with most lesions within 10 mm of the urethral meatus. Patients with extensive urethral disease typically complain of obstructive LUTS, dysuria, hematuria, or hematospermia.

The use of endoscopic examination during the initial evaluation of a patient with anogenital warts is controversial as some authors believe this risks seeding the proximal urethra.⁷ Despite this theoretical risk, a review of the literature has failed to elicit reports of prostatic urethral or bladder seeding from urethroscopy.⁸ In patients with distal penile involvement, early urethroscopy may facilitate timely diagnosis of urethral involvement, with 1 study demonstrating urethral condylomata in 43% of such patients. Based on these findings careful physical exam including meatal inspection should be performed in all patients with genital condylomata, with lesions of the meatus and glans being an indication for urethroscopy.⁸ In patients who do not meet these criteria, presence of dysuria, urethral discharge, or obstructive LUTS should heighten the index of suspicion and prompt endoscopic evaluation.

The patient's immune status has a significant impact on disease course. Patients with HIV commonly present with larger, more numerous warts that may be less responsive to treatment, have a higher intralesional viral load, and

increased prevalence of coinfection with high-risk HPV serotypes, particularly HPV-16. Immunocompromised state allows for frequent reactivation of latent HPV, reducing the likelihood of disease clearance. They also develop urethral lesions at a higher frequency and suffer more recurrences after treatment compared to HIV-negative patients. Additionally, as HIV/AIDS progresses there are fewer T-lymphocytes reacting to HPV oncoproteins E6 and E7, creating a potential for disease progression and malignant transformation. Given the high oncologic risk in these patients, biopsy of anogenital condylomata in immunocompromised patients is recommended before treatment.⁹

There are no specific guidelines for management of urethral condylomata acuminata, as the disease is relatively uncommon. For the sake of this discussion we will classify treatment modalities as surgical or nonsurgical, however they can also be classified as provider- or patient-applied. Most treatment modalities used for genital lesions are not easily applied to urethral condylomata because of the difficulty administering therapy and the potential for adverse sequelae. The goal of treatment is to eradicate the lesions, palliate symptoms, and achieve extended disease-free intervals. Several topical and surgical therapies including 5-FU,¹⁰ photodynamic therapy with 5-aminolaevulinic acid, topical Bacillus Calmette-Guerin,¹¹ surgical excision, electrocautery, cryotherapy, and laser therapy¹² have been reported. To date few groups have attempted treating urethral lesions with topical therapy either as monotherapy or an adjunct to resection or ablation. One study of 20 patients with urethral lesions treated with 5-FU instillation reported complete response in 90% of patients at 6-month follow-up.¹⁰ Treatment was applied after each void and nightly for 7 days. Case reports have suggested efficacy of this treatment modality in HIV patients as well. Others have reported success with a single instillation using a penile clamp to optimize urethral dwell time.¹³ Side effects seen with this type of treatment were scrotal or meatal irritation and dysuria.^{10,13}

Ablation of urethral condylomata using (Nd): YAG laser, has demonstrated a 13% recurrence rate at 3-month follow-up in 1 study of 38 patients, suggesting that ablation alone may be insufficient for disease eradication.¹² Another study of 25 patients treated with Holmium: YAG laser ablation followed by 1% 5-FU instillation demonstrated complete response in all patients at 6-month follow-up.¹⁴ Instillation of cidofovir in conjunction with surgery was recently proposed as a treatment option for immunocompromised patients with urethral condylomata. Two patients treated with this approach had variable results, with 1 patient recurring within 6 months of treatment and the other disease-free at 3.5-year follow-up.¹⁵ The limited evidence available on treatment of patients with urethral condylomata acuminata forces practitioners to rely on clinical judgment until better quality studies defining optimal therapy in these patients become available.

The case presented illustrates a patient at high risk of urethral involvement with several indications for urethroscopy, prompting endoscopic evaluation and subsequent diagnosis of urethral condylomata acuminata. Although presence of meatal lesions noted on physical exam suggested possible involvement of distal urethra, the finding of condylomata in the proximal urethra was atypical and may be associated with the history of AIDS. Without sufficient data to define optimal therapy, clinical judgment is needed to determine how best to manage patients with urethral condylomata acuminata. Given the symptomatic improvement after surgical treatment and desire to avoid additional treatment, surveillance is a reasonable strategy, but more research is warranted in this area.

Video: Urethroscopy showing extensive urethral condylomata acuminata.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.urology.2019.05.002>.

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