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Case Report

Urethral condyloma acuminata in a male patient refractory to common topical treatments: A case report

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Abstract Condyloma acuminata is one of the most prevalent sexually transmitted diseases caused by human papilloma virus (HPV). Urethral involvement of condyloma acuminata is uncommon and more challenging to treat. Despite more condylomas are associated with the low-risk HPV (e.g., types 6 and 11), histopathologic examination is sometimes needed to exclude malignant process, especially in a lesion with atypical form or unresponsive to the standard therapy. Here we report a unique case of urethral condyloma acuminata in a male patient that refractory to the common condyloma topical treatments.

Key words
Condyloma acumianta, urethral, HPV, genital warts treatment.

Introduction

Condyloma acuminata (CA) is one of the most prevalent sexually transmitted diseases.[1,2] CA is caused by human papilloma virus (HPV) which can develop either in cutaneous or mucosal epithelial cells. The majority of CA (up to 90% of cases) are associated with the low-risk type of HPV (types 6 and 11), although co-infection with the high-risk HPV (e.g., type 16 and 18) was also observed.[3,4] Meatal/ urethral involvement of CA is uncommon (0.5–5% of all HPV infections). In such conditions, treatment options are limited and the eradication of lesion is more difficult.[1,5-7] Here we report a unique case of CA involving the urethral meatus of a male patient which was not improved after the application of common topical treatments.

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Case report

A 19-year-old homosexual male patient presented to our clinic with a pinkish mass developed at the center of his urethral meatus in the last 7 months prior to the consultation, with a slight dysuria and without any difficulty in voiding. The patient initially consulted to some other dermatologists and the mass was assessed as a CA and treated with Trichloroacetic Acid (TCA) solution twice (once in a week), but the mass was not improved. The patient then decided to buy TCA 80% solution by himself from an online marketplace and self-applied the solution at home for twice, with an interval of 10 days between each application. A few days after the second application, the mass was still not improved, while a painful erosion developed at the rim of urethral meatus and subsequently evolved into a new larger thick whitish mass surrounding the older mass. Since the masses were getting bigger and became more painful, the patient then came to our clinic.

Figure 1 A pinkish "cauliflower-like" mass at the center of urethral meatus, surrounded by a whitish thicker mass at the navicular fossa of urethra (A). The central mass became white on acetowhite test (B).

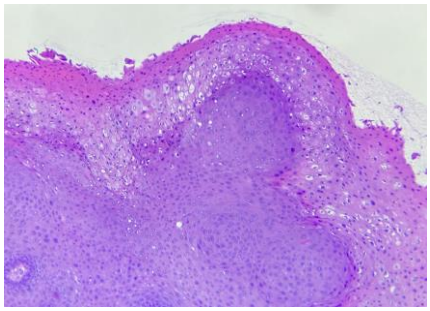

Figure 2 Microscopy examination showed a papillomatous proliferation of the epithelium with many koilocytes with large nuclei and perinuclear clearing appearance; no malignant cells observed.

Physical examination revealed a thick whitish mass at the navicular fossa of urethra which surrounded a pinkish "cauliflower-like" mass at the central of urethral meatus (**Figure 1**). On acetowhite test, the central pinkish mass became white, but no changes were observed on the surrounding navicular fossa mass. We have applied podophylline 25% tincture once and TCA 80% solutions twice on both masses with an interval of 1 week between each application, but the lesion was still not improved. Since the masses remained, we sent the patient to urology clinic to underwent biopsy from both masses to exclude the malignant process. Microscopic examination revealed similar histopathologic changes on both masses: a tissue lined with complex squamous epithelium with hyperplasia and papillomatous proliferation with intact basement membrane. The epithelial cells are still monomorphous with many coilocytes with a large nucleus and "perinuclear clearing" appearance suggesting a condyloma acuminatum, and no malignant cells present (**Figure 2**). HIV and syphilis serologies were also performed and returned all negative. As the patient did not show any improvements to topical treatments, we previously planned to perform cryotherapy or CO_2 laser to the patient but these procedures were temporarily unavailable in our setting due to COVID-19 pandemic. We then referred the patient to the urology clinic to underwent surgical excision.

Discussion

Urethral CA is an uncommon manifestation of HPV infections (0.5–5% of cases), which develop mostly limited to the distal 3 centimeters of meatus.[5-7] Urethral CA is more common in young men who are sexually active, especially with multi-partner. An extensive lesion of urethral CA is also associated with immunocompromised, especially HIV patients with lower CD4 level, and with a history of inappropriate manipulation of the urethral lesion which could elicit an unnecessary inoculation of HPV to the surrounding normal tissue.[5] In the present case, the patient is a young homosexual man who had been sexually active with multi-partner, and with negative HIV status at the present consultation. A history of lesion self-manipulation by the patient was obtained after he bought a TCA 80% solution from an online marketplace and applied the solution at home twice without any supervision of health professionals. Afterward, an erosion was developed in navicular fossa which most likely favor the extensive lesion of CA due to unnecessary self-inoculation of HPV.

In meatal CA, the patient is usually aware about the mass appearing at his/her urethral orifice.[5] On physical examination, meatal eversion would expose a meatal "cauliflower-like" lesion and the acetowhite test helps to distinguish between CA and the normal tissue, as in the present case. However, in more proximal urethral CA, dysuria, voiding difficulty, or hematuria are the first problems that commonly bring the patient to the doctor, and the CA lesion is usually observed after urethroscopy examination. In our case, the proximal urethra might be involved. However, urethroscopy exploration was considered unwise due to occluded meatus by the CA lesion which might elicit unnecessary trauma and worsen the progression. Therefore, eradicating the visible meatal lesion first was advisable.[5]

Although up to 90% of CA cases are associated with the low-risk HPV (types 6 and 11), co-infection with the high-risk HPV and neoplasia induced by the low-risk HPV had been reported before,[1,2,8] especially in a lesion with atypical form and refractory to the standard CA treatments. In such cases, histopathological verification is necessary before treating the lesion as a simple CA.[1] In the present case, the mass was not improved after standard chemical surgery treatments (TCA and podophyllin solutions) and a new mass even developed after the application. Fortunately, histopathological examination revealed a simple CA with no malignant process occurring in the lesion.

In non-urethral CA, treatment options varied from standard topical treatments such as podophyllin solution, podophyllotoxin 0.5%, TCA solutions, or imiquimod, to surgical interventions such as cryotherapy, surgical excision, or CO_2 laser.[9] However, in urethral CA, treatment options are limited due to several concerns: the lesion is more difficult to approach and might has a higher risk of fatal complications, especially urethral stenosis.[5,10] Several treatments have been recommended for treating urethral CA.[11,12] A study of 123 male patients with urethral CA concluded that in patients with visible meatal lesion, cryotherapy offered the most benefits with a higher successful rate and minimal complications. While in urethral CA lesions located at beyond 3cm of the meatus, 5-fluorouracil (5-FU) instillation enhanced the eradication of the lesion with minimal adverse effects.[5] Moreover, a combination of topical and surgical treatment in recurrent urethral CA was also reported. The debulking effect of 5-FU prior to the surgery can help to avoid extensive surgical procedures and therefore reducing the risk of tissue fibrosis.[2] Other modalities including CO_2 laser and topical photodynamic therapy by using 5-aminolevulinicacid were also reported to have promising results.[10,13]

In the present case, common topical treatments for CA failed to eradicate the lesion. Apart from patient's self-manipulation to the lesion that might inhibit the treatment efficacy, it was also in accordance with the fact that urethral CA is more refractory to common topical treatments and, in such condition, a more intensive therapy is highly recommended. During the COVID-19 pandemic, some healthcare facilities, including ours, may limit the access to certain procedures, including cryotherapy and CO_2 lasers. Therefore, the patient was sent to the urology clinic to underwent surgical excision. Such a more intensive CA treatment is required for those who failed to show any improvements after repeated topical treatments.

Conclusion

Urethral CA is an uncommon manifestation of HPV. Histopathological examination may benefit to exclude any malignant process, especially in a lesion with atypical form and

refractory to the standard therapy. Treatment options are more limited, and an inappropriate procedure can lead to a more extensive lesion and fatal complications such as urethral stenosis. Previous studies have reported that cryotherapy is effective for a visible meatal lesion, while a more proximal wart can benefit from 5-FU instillation or in combination with surgical interventions.

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