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Urethral condylomas in men: experience in 123 patients without previous treatment

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Abstract

The most common sexually transmitted infection is infection by human papillomavirus. There are more than 100 types of human papillomavirus, and over 30 of them involve the genital area. Urethral involvement is uncommon and usually limited to the distal 3 cm of the meatus. There are various treatments for urethral condylomas; as a rule, they are limited by a difficult approach, by recurrences, and by potential complications, the most significant of which is urethral stenosis. The purpose of the treatments is to remove the warts and induce lesion-free periods. Such treatments do not eliminate the infection nor do they prevent continued transmission of the virus. We retrospectively evaluated 123 patients diagnosed and treated for condylomas in the genital area at our Institution between April 2009 and April 2012. The patients' mean age was 28.7 years (range 19–51). Of the 123 patients included, 48 (39%) had a history of previous STIs, most frequently gonococcal urethritis. Three of them had a urethral malformation in the shape of hypospadias, and other three reported a previous urologic manipulation (catheterisation). Meatal/urethral condylomas are rare, cryotherapy is simple, easy to apply, and has a very low risk of complications in patients with externally accessible warts.

Keywords

Meatal/urethral condyloma, cryotherapy, 5% fluorouracil gel, conservative treatment

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Introduction

The most common sexually transmitted infection (STI) is infection by human papillomavirus (HPV).[1] There are more than 100 types of HPV, and over 30 of them involve the genital area. It is thought that approximately 80% of sexually active people will be infected with HPV at some time during their life.[2]

Most genital infections are asymptomatic, not recognisable, or subclinical, and generally are self-limited. HPV infection is more frequent than visible genital warts.[3] Genital warts are commonly associated with serotypes 6 and 11, whereas other high-grade serotypes such as 16, 18, 31, 33, and 35 are associated with intraepithelial neoplasias[4] (of the cervix, penis, anus, and vulva). Urethral involvement is uncommon and little recognised, and usually limited to the distal 3 cm of the meatus. There are various treatments for urethral condylomas; as a rule, they are limited by a difficult approach, by recurrences, and by potential complications, the most significant of which is urethral stenosis.[5] The purpose of the treatments is to remove the warts and induce lesion-free periods. Such treatments do not eliminate the infection nor do they prevent continued transmission of the virus. This work describes our experience in the management of patients with urethral condylomas.

Objectives

To examine clinical presentation and effectiveness of cryotherapy in a group of men who presented meatal and urethral condylomas.

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Materials and methods

One thousand and seventy-seven men presented at our institution between April 2009 and April 2012 because of condylomas in the genital area. The patients came to us either through referral from our Centre's emergency service or via direct referral by other specialists.

Of these 1077 patients, 135 (12.5%) presented with urethral lesions, 123 had received no prior treatment, while 12 had been treated (six with electrocoagulation and six with topical applications of trichloroacetic acid) and for this reason were excluded from the trial.

All patients received the usual serum screening: HIV, syphilis, and HBV (except three who were known to be HIV+). Starting at the time of diagnosis, the patients were controlled regularly every 7 to 15 days, depending on the treatment prescribed. Following lesion disappearance, controls were performed after 30 days, and if the lesion-free status persisted, urethroscopy was scheduled at 6 months.

Diagnostic method

1. Urethroscopy prior to initiation of treatment in men presenting with voiding difficulties as an initial symptom. There were only four such cases; in all of them the presence of warts was verified beyond the navicular fossa (three at the distal penile urethra, and one affecting the whole of the urethra).
2. Direct view by means of meatal eversion (Figure 1).
3. Use of otoscope through the urethral meatus, including application of 5% acetic acid for more accurate lesion viewing in case of doubt.

Neither virus typing nor histology analysis according to the STI guidelines was performed.[6]

Figure 1. Meatal eversion in case of meatal condyloma.

Statistical analysis

Descriptive analyses were expressed as mean ± standard deviations and percentage for continuous and categorical data, respectively. The comparisons between and patients characteristics and number of cryotherapy sessions were performed using the Chi square test (Fischer's exact test with observed frequencies <5) for categorical variables whereas continuous variables were tested using Pearson test. A multivariate linear regression backward stepwise model was performed to identify variables related to number of sessions, including the remaining variables with a significant univariate association ($p < 0.2$). All statistical analyses were performed using a statistical software package (SPSS version 17.0, IBM, Chicago, IL, USA). p Value <0.05 was considered to be statistically significant.

Results

The patients' mean age was 28.7 years (range 19–51 years). Of the 123 patients included, 48 (39%) had a history of previous STIs, most frequently gonococcal urethritis (Table 1). Three of them had a urethral malformation in the shape of hypospadias, and other three reported a previous urologic manipulation (catheterisation).

Reason for consultation

Seventy-two patients (58.5%) consulted because of an exophytic formation in the meatus, 33 (26.8%) because of condylomas in the genital area, 12 (9.7%) because of dysuria, three (2.4%) because of urethrorrhagia, and three (2.4%) because of stinging upon voiding (Table 2).

Toxic habits

Sixty patients (48.78%) were smokers: 18 smoked an average of five cigarettes daily, 30 smoked an average

Table 1. Patients with previous STD (12 patients with more than one STD).

Urethritis	18
Genitals Condilomas[a]	15
Genitals Herpes	12
HIV+[b]	9
Molluscum C	6

[a]Other locations different from actual ones and more than 3 years from last episode.
[b]All in ART, con CD4 counts between entre 260 and 740, with undetectable viral loads 30,000c.

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Table 2. Clinic Manifestations (n = 123).

Exophytic on meatus	72 (58.5%)
Penis condilomas	33 (26.8%)
Voiding problems	12 (9.7%)
Urethrorrhagia	3 (2.4%)
"Burning" while voiding	3 (2.4%)

of 10 cigarettes daily, and 12 smoked more than 30 cigarettes daily.

Sexual behaviour

Of the patients, 114 (92%) had intercourse with women only, six (4.8%) with men only, and three (2.4%) with men and women indiscriminately. At the time of diagnosis, 102 patients had no stable partner, and this group had a mean of three sexual partners during the 6 months prior to consultation. All of the patients reported using condoms for intercourse with penetration, while none reported using them for oral sex.

Duration of progression

The duration of progression was variable, from less than 1 month to 18 months. Progression was defined as the time between the first manifestation of genital warts (by the patient) and the first consult with the specialist.

Treatments performed

The primary treatment performed was cryotherapy. Thirty-three patients (26%) received more than one treatment (Table 3). The access route to condylomas was a simple meatus eversion; in no case did a meatotomy prove necessary.

Serology studies

All serology studies were negative.

Number of sessions necessary to eradicate clinically evident lesions

Regardless of the treatment applied, the mean number of sessions per patient required to eradicate clinically evident lesions was 2.2, with a range of 1–5. Of the 123 patients treated for genital warts, 34 needed one session to eradicate completely genital warts, 45 needed two sessions, 28 needed three sessions, 10 needed four sessions and, finally, six needed five sessions. The mean number of cryotherapy sessions was two for nonsmokers and three for smokers ($p = 0.049$). But in multivariate analysis tobacco consumption was not related with number of sessions.

Table 3. Treatments applied at all locations.

• **Contact cryotherapy** (2 sessions 10 to 15 sec each wart, each 14 days)	78
• **Cryotherapy + electrocoagulation (external lesions)** (each 14 days)	15
• **Cryotherapy + podophyllin resin 25% (external lesions)** (apply, let dry for 1 min, wash after 2–4 hours, each 14 days)	18
• **5-Fluoroacil** (2 g of gel with 5% fluorouracil with urethral applicator, leave inside urethra about 30 min, weekly)	12

Thirty-three of the patients with urethral condylomas (26.8%) had concomitant penile warts. The diagnosis of urethral lesions among these patients was fortuitous, occurring during the course of their physical examination. These patients required a greater number of therapy sessions.

Recurrence

Since 26% of the patients received more than one treatment, it was not possible to evaluate recurrences as a function of the therapy applied.

Controls

Control urethroscopies were performed between 6 and 12 months following the last visit. All of them were negative with respect to exophytic lesions.

Discussion

Urethral condyloma is a rare clinical manifestation of HPV, occurring in just 5% of cases.[7,8] It is more frequent among young, sexually active men. Among patients in the present study, the incidence of urethral condyloma was clearly higher, at 12.5%.

Clinical presentation

Some studies[9] have reported that most patients with urethral lesions present clinical manifestations such as stinging when voiding, urethrorrhagia, and dysuria. Only 18 (15%) patients in our series presented with these symptoms. In these cases, the primary reason for consultation was dysuria.

Thirty-three (26.8%) patients were not aware of having urethral meatus lesions. Ninety (73.2%) patients had visible lesions only in the meatus, and no other apparent lesion in the genital area; these findings are similar to those of other reference series.[10]

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Diagnostic methods

The use of endoscopic explorations in the course of initial visits is controversial. Some authors systematically explore the urethra early during the diagnostic visit.[11–13] We are not partial to performing these tests early, and this attitude is in agreement with other authors' routine.[14–16] HPV infection is transmitted through contact, and there is a low probability of finding condylomas beyond the first 3 cm of urethra. The danger of endoscopic exploration is the potential for self-inoculation into more proximal areas of the urethra; if there are no symptoms of obstruction, it is convenient to eliminate the visible lesions first.

Extensive urethral lesions may benefit from immunosuppression.[16] Six of the nine HIV-positive patients, with a greater viral burden and a lower CD4 count, presented with a more extensive involvement of the urethra, as was made obvious by endoscopy. On the other hand, the three patients with meatal malformation (hypospadias) also had involvement of the outer third of the urethra.

The association of HPV 16 and 18 infections with neoplastic lesions of the cervix, penis, anus, and vulva is well-known.[17–19] Genital condylomas are usually produced by different serotypes, 6 and 11. Consequently, it is considered wise neither to obtain specimens for pathologic analysis nor to perform virus typing in a routine fashion, as recommended by the most important guidelines.[20]

Treatments

A number of treatments have been described for meatal/urethral condylomas.[21–23] The most widely used is electrocoagulation excision, but consideration should be given to its potential to elicit fibrosis, which causes one of the most feared complications: stenosis. Some authors advice CO_2 laser vaporisation, as this method may reduce side-effects.

Our treatment of choice for obvious meatal lesions is cryotherapy, which has a high success rate accompanied by a lower risk of complications. Access for performance of cryotherapy is straightforward: meatal eversion permits access to the warts, which are usually located within the first few centimetres, and requires no anesthesia.

In our 12 patients with urethral involvement, the selected treatment was 5% fluorouracil gel instillation. In each patient an endoscopic examination performed between 6 and 12 months later disclosed no lesions. None of the patients presented with complications. Consequently, we believe that 5% fluorouracil gel instillation is the treatment of choice in cases of urethral involvement.

The probability of recurrence makes it advisable to examine patients regularly for approximately 1 year.

Conclusions

Meatal/urethral condylomas are rare. However, their incidence is higher when they are routinely and actively investigated as careful analysis ultimately permits their diagnosis. We do not recommend endoscopic manipulation if there are no obstructive symptoms. A relationship appears to be confirmed between more extensive involvement and immunologic status. Previous urologic manipulations and meatal malformations suggest the possibility that the lesions may be more extensive. Cryotherapy is simple, easy to apply, and has a very low risk of complications in patients with externally accessible warts. Five percent fluorouracil gel instillation is recommended as an excellent initial therapeutic option in cases of urethral dissemination.

Declaration of conflicting interests

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References

1. Douglas J and Moreland A. Genital human papillomavirus infections. In: Morse Sa, Ballard RC, Holmes K, et al. (eds) *Atlas of sexually transmitted diseases and AIDS*. Third edition. Edinbourgh: Mosby, 2003, pp.261–278.
2. De Villiers EM, Fauquet C, Broker TR, et al. Classification of papilloma viruses. *Virology* 2004; 324: 17–27.
3. Center for Disease Control and Prevention. Sexually transmitted diseases. treatment guidelines 2006. *MMWR* 2006; 88–98.
4. Winer RL and Koutsky LA. Genital human papillomavirus infection. In: Holmes K, Sparling PF, Stamm WE, et al. (eds) *Sexually transmitted diseases*. New York: McGraw Hill, 2008, pp.489–508.
5. Graversen PH, Bagi P and Rosenkilde P. Laser treatment of recurrent urethral condylomata acuminate in men. *Scand J Urol Nephrol* 1990; 24: 163–166.
6. Von Krogh G, Lacey CJ, Gross G, et al. European course on HPV associated pathology: guidelines for primary care physicians for the diagnosis and management of anogenital warts. *Sex Transm Infect* 2000; 76: 162–168.
7. Debenedicts TJ, Marmar JL and Pradiss D. Intraurethral condyloma acuminata: Management and review of the literature. *J Urol* 1977; 118: 767–769.

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8. Kleiman H and Lancaster Y. Condylomata acuminata of the bladder. *J Urol* 1962; 88: 52–55.
9. Nogueira JL. Tumores de la uretra masculina y femenina. In: Jiménez Cruz JF. and y Rioja Sanz LA (eds) *Tratado de urología*. Barcelona: Poros editores, 1990, p.1239.
10. Huguet J, Errando C, Regalado R, et al. Condilomas uretrales en el varón: experiencia en 48 casos. *Arch Esp De Urol* 1996; 49: 675–680.
11. Zabbo A. Condylomata acuminata. In: Seidmon EJ and Hanno PM (eds) *Current urologic therapy*. Philadelphia: Saunders, 1994, pp.417–420.
12. Kaplinsky RS, Pranikoff K, Chassan S, et al. Indication for urethoscopy in male patients with penile condylomata. *J Urol* 1995; 153: 1120–1121.
13. Pollack HM, DeBenedictis TJ, Marmal JL, et al. Urethrographic manifestations of venereal warts (condyloma acuminate). *Radiology* 1978; 126: 643–646.
14. Masse S, Tosi-Kruse A, Carmel M, et al. Condyloma acuminatum of the bladder. *Urology* 1981; 17: 381–382.
15. Sarkar F, Miles B, Plieth D, et al. Detection of human papillomavirus in squamous neoplasia of the penis. *Prostate* 1993; 22: 171–180.
16. Beutner KR, Richwald GA, Wiley DJ, et al. External genital warts: report of the American Medical Association Consensus Conference. *Clin Infect Dis* 1998; 27: 796–806.
17. Culp OS and Kaplan IW. Condylomata acuminata: two hundred cases treated with podophillin. *Ann Surg* 1944; 120: 251–256.
18. Sabaneg ES Jr and Thomson IM. Fulguration of urthral condylomata:modified technic using visual urethrotome. *Urology* 1991; 37: 172.
19. Milam DF, Joseph A and Smith J. Urologic laser surgery. In: Gillenwater J, Grayhack JT, Howards S, et al. (eds) *Adult and pediatric urology*. Third ed. Saint Louis: Mosby, 1996, pp.369–393.
20. Gammon DC, Reed KA, Patel M, et al. Intraurethral fluorouracil and lidocaine for intraurethral condyloma acuminate. *Am J Health-Syst Pharm* 2008; 65: 1830–1833.
21. Dretler SP and Klein LA. The eradication of intraurethral condyloma acuminata with 5% 5-fluorouracil cream. *J Urol* 1975; 113: 195–198.
22. Ge CG, Jiang J, Jiang Q, et al. Holmium:YAG laser ablation combined intraurethral fluorouracil perfusion as treatment option for intraurethral *Condyloma acuminata* in men. *Minerva Urol Nefrol* 2014; 66: 77–81.
23. Huang J, Zeng Q, Zuo C, et al. The combination of CO_2 laser vaporation and photodynamic therapy in treatment of condylomata acuminata. *Photodiagnosis Photodyn Ther* 2014; 11: 130–133.

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