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Editorial

Human papillomavirus (HPV) infections in urology

El urólogo ante la infección del virus del papiloma humano

The sexually transmitted disease (STD) most commonly treated today by urologists is that caused by the human papillomavirus (HPV). This is currently a serious problem in young people. Infection by the HPV is the infection most commonly associated to cancer. Among the population aged 14-49 years, 1% has clinically detectable genital lesions, 2% subclinical lesions that may be identified by peniscopy or colposcopy after acetic acid application, and 7% inapparent lesions, which may be detected by DNA testing. If an extension test with the polymerase chain reaction (PCR) is used, these figures multiply by two^{1,2}. Contagion occurs by sexual contact only, with an incidence up to 70%. This infection is more common in males with a very high sexual activity, and even more in promiscuous males. There is a 50% chance of transmission of the disease by a single sexual contact. Location of genital condyloma in the areas most commonly traumatized during intercourse allows for ensuring that the virus is transmitted by entering through small fissures. Circumcision protects against STDs because keratinization occurs in the glans and wet areas such as the coronal sulcus are eliminated. Condoms also protect against HPV infection, except in scrotum, basis of penis, perineum, and pubis. The incubation period of HPV is from 6 weeks to 8 months. It should be reminded that (genital) condyloma acuminatum in children must always lead to suspect sexual abuse. When condyloma occurs in mucosa (wet), it appears as a pedunculated, wide-based, fleshy pink, soft, crest-like, exuberant, frequently overinfected, macerated hyperplastic lesion with a foul odor. In foreskin, scrotal, pubic, and perineal (dry) skin, condyloma is more similar in appearance to a common wart.

A study in 463 heterosexual males infected by HPV found the virus by DNA testing in the foreskin in 49% of subjects, in the coronal sulcus in 35%, in scrotum in 32%, in urethra in 10.1%, and in semen in 5%³. The most common agents causing genital condyloma are HPV strains 6 and 11, having a low risk. HPV 16-18 involves a high risk and is associated to premalignant and malignant genital lesions. HPV is identified in the penis in 70%-100% of cases of intraepithelial neoplasm, in verrucous carcinoma in 80%-100%, and in invasive cancer

in only 30%-40% of cases⁴. HPV is found in approximately 70% of cervical cancers, and in only 30%-40% of penile and vulvar cancers. In a review of 30 studies published in May 2009, Backes⁵ reported that HPV 16-18 had been detected by DNA biopsy in almost a half of the 1266 penile carcinomas found (47,9%).

Genital condyloma is diagnosed by visual inspection. Homosexual patients should be asked about the type of sexual activity and anal and perineal areas should be inspected. Both sexual partners should also be closely monitored, particularly if one of them is infected. Peniscopy after application for five minutes of gauze with 3%-5% acetic acid helps diagnose HPV lesions, which stain white and are magnified (useful for flat lesions). HPV DNA testing using smears, cytology, or biopsy of genital mucosa is another, more expensive diagnostic procedure. This may be used in high-risk patients such as partners of infected women. HPV DNA testing in 99 male partners of infected women was recently reported¹. The test was positive in 93 of them (93.9%). DNA biopsy may be performed to detect HPV in some selected cases. All males affected by HPV should undergo eversion of urethral meatus and should be asked about urethral bleeding, dysuria, or a blood-stained or yellowish discharge after intercourse. Urethra becomes infected in 3%-5% of patients with HPV, and 80% of such infections occur in the Morgagni's fossa⁶. Fluoroscopic urethrocystoscopy after instillation of 5-aminolevulinic acid has been reported to be used for diagnosis and treatment of intraurethral condylomata⁷. A flexible cystoscope greatly facilitates examination of a urethra potentially infected by HPV. The vaccine against papillomavirus infection is indicated as prevention of HPV in females aged 6-26 years, and decreases incidence of disease. Vaccination decreases cervical cancer rate by 70%-80%. The vaccine is cost-effective in females. It is no indicated y males, except for some selected cases. A study conducted in the Kenya area found that 50% of men aged 18-24 years had HPV infection, and therefore recommended vaccination of young males in this region⁸. Treatments for HPV infection do not provide a definitive cure for this viral infection, and they all are long, poorly effective, and with a high recurrence rate. Despite fatigue and recurrence, patients

should be monitored regularly, even if no condyloma is seen. Condyloma acuminatum may be treated by surgery or medical management. Genital condylomas are traditionally treated with topical podophyllin, electrocoagulation, cryotherapy, YAG laser, and surgery. Treatment also depends partly on the resources available at the health care center. Treatment with immunomodulators is currently considered as the first-choice therapy. Topical application of imiquimod to the involved area three times weekly for two to three months is particularly effective. According to several series of cases reported, imiquimod achieves a 75% cure rate (with cure define as total disappearance of condylomas), and results are usually seen between the first and fourth weeks. In this treatment with imiquimod, response, size, or location in the penis are not relevant prognostic factors⁹. In patients in whom the glans is covered by foreskin, circumcision may be indicated as treatment and to prevent recurrence. Treatment of condyloma in the Morgagni's fossa may require meatotomy. In such cases, treatment with 5-fluorouracil with intraurethral lidocaine cream in several sessions provides good results¹⁰. The usual recurrence rate after treatment of intraurethral condylomas is approximately 35%. A Phase I/II study reported treatment of intraurethral condyloma in males with the HPV vaccine, which appears to induce condyloma regression in men by stimulating the immune system against papillomavirus¹¹.

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