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Genital Warts

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Abstract

Anogenital warts are the most prevalent sexually transmitted viral infections in the United States of America. Symptomatic warts can be seen in nearly 1% of the population aged 15 to 49 years. Genital warts are highly contagious through sexual contact. AGWs can be diagnosed by careful visual inspection. Several methods have been described for the treatment of warts; however, all have their own limitations and are not always successful. Warts often recur even after being completely removed. The treatments of warts can be divided into 2 broad categories, ie, surgical and nonsurgical methods. The patient himself/herself can apply the nonsurgical methods, or a physician can perform it. Podophyllotoxin is a good medical substance. Imiquimod can act as an immune response modifier and stimulate locally produced cytokine. Topical treatments of warts increase local production of interferon and decrease viral load of HPV. The surgical methods for genital warts include curettage, electrosurgery, and application of a scalpel under general or local anesthesia. Scattered keratinized lesions can be removed by electrosurgery. Patients with multiple or large warts of any location should be referred for surgical treatment under general anesthesia.

Keywords: Wart, Genital, Medical Treatment, Surgical Treatment

1. Introduction

Anogenital warts are the most prevalent sexually transmitted viral infections in the United States of America. Although both sexes (males and females) can be affected by genital warts, the available data indicates that 67% of patients are female (1).

Symptomatic warts can be seen in about 1% of the population aged 15 to 49 years. These warts (AGWs) are created by HPV (short for human papillomavirus), particularly Genotypes 4 and 11. Condylomata acuminata and condyloma are its synonym terms. These warts are considered among the most important factors for referring to a physician. Injecting the tetravalent Gardasil vaccine is among effective factors against HPV 6, 11, 16, and 18 and can dramatically alter the epidemiology of this disease (2).

2. Transmission Method

Genital warts are highly contagious through sexual contact and their transmission rate is nearly 65%. After transmission of the virus, the HPV incubation period ranges from 3 weeks to 8 months; however, most warts appear 2 to 3 months after an HPV infection (2, 3).

3. HPV Types

Nearly 40 genotypes of HPV, which can infect the genital tract, have been identified. HPV genotypes are classified into 2 groups of low-risk and high-risk. The low-risk HPV genotypes, such as genotypes 6, 11, 42, 43, and 44, may cause genital warts and sometimes cause low-grade dysplasia (4-6). The high-risk HPV genotypes, like genotypes 16, 18, 31, 33, 35, 39, and 45, are able to cause high grade dysplasia (CIN 2, 3) and are invasive squamous cell carcinomas in the cervix, vulva, vagina, and anus (rectum) (6, 7).

4. Detection Method

In female patients, 90% of anogenital warts are in the form of raised pink, gray, or brown lesions that can be seen in cauliflower-shaped clusters or in the shape of interlocking papules and a large plaque. Warts may be observed in the mons pubis, vulva, vagina, cervix, perineum, urethra, perianal area, anal canal, and inner thighs. These warts are often asymptomatic; however, they may cause itching, bleeding, and pain.

5. Differential Diagnosis

Differential diagnosis of AGWs in children and adolescents includes molluscum contagiosum, fibroepithelial polyps, vulvar papillomatosis, condylomata lata (secondary syphilis), and rarely intraepithelial dysplasia (Bowenoid papulosis and SCC in situ), invasive SCC, and adenocarcinoma (8).

6. Diagnosis

AGWs can be diagnosed by careful visual inspection. Applying 3% to 5% acetic acid or HPV-DNA test are not usually recommended (9). Performing an anoscopy or examining the anal canal with a speculum may be required to thoroughly check warts inside the anal canal, the vagina, or the cervix. A biopsy may also be necessary in the event that a wart seems abnormal, has an abnormal color, or is resistant to the treatment, or in people with weakened immune systems (10).

7. Warts in Pregnancy

During pregnancy, especially between 12th and 14th weeks of pregnancy, genital warts may grow fast. These warts may sometimes become very large particularly when new warts develop during pregnancy. Compared to nonpregnant women, these warts get larger in pregnant women (11, 12). Pregnancy increases activities of HPV, resulting from decreased cellular immunity and increased blood flow and number of vessels in the genital area that occur due to pregnancy. Furthermore, the mentioned warts are fragile during pregnancy and usually cause itching and bleeding (12). In some cases, warts may exceptionally enlarge and block the birth canal. In such cases in which a patient may suffer from excessive bleeding or labor dystocia, performing a Cesarean section is suggested (12).

HPV can be transmitted from a mother to her fetus during labor (13). This may cause lesions in the conjunctival, oral, and/or anogenital area in the neonatal period (14). Prenatal transmission of the virus, Types 6 and 11, rarely causes juvenile laryngeal papilomatosis (JLP). In such cases, the possibility of performing a Cesarean section should be discussed with the mother who has warts at the time of delivery (15).

Although epidemiological studies do not indicate that performing Cesarean section has any protective effects, Cesarean sections are usually recommended in the case of premature rupture of membranes or high viral load. Another risk factor in cases of genital warts is bacterial infection caused by entrapment of bacteria which may cause chorioamnionitis and fetal infection like when premature rupture of membranes occurs (16). Recently, several studies mentioned that preterm delivery and placental disorders occur as a result of HPV viral oncogenes (17).

8. Management of Genital Warts

1) In pregnant women: both surgical and nonsurgical methods can be applied for the treatment of warts during pregnancy. The surgical treatment methods which act through destructing tissues and can be applied during pregnancy include electrocautery, removing the tissue with scissors or a knife, cryotherapy, and using CO_2 laser. These methods are preferred to the nonsurgical methods. Among the nonsurgical treatment methods, the use of trichloroacetic acid (TCA) can be mentioned. This is a safe method which can be applied by a physician to treat small lesions during pregnancy; however, it is not very effective (16-18).

2) In nonpregnant women: several methods have been described for the treatment of warts; however, all of these methods have their own limitations and are not always successful. Warts often recur even after being completely removed. The treatments of warts can be divided into 2 broad categories, ie, surgical and nonsurgical methods. The nonsurgical methods can be applied by either a patient himself/herself or a physician.

8.1. Self-Treatment

Podophyllotoxin is a good medical substance derived from podophyllin, which is available in the form a pure standard product. This medical substance is approved to be safer and more efficient than podophyllin. In the USA, podophyllotoxin is available in the form of creams or solutions that can be applied by patients themselves. The use of podophyllotoxin cream is appropriate for the treatment of anogenital warts in female patients. This medical cream should be used twice a day, 3 times a week, followed by a 4-day rest period. These cycles should be repeated weekly for 4 weeks. Large wart areas (10 cm or more) should not be treated at once because when these areas become necrotic, they cause pain (12, 19).

The toll-like receptor agonist imiquimod can act as an immune response modifier and stimulate locally produced cytokine. Topical treatments of warts increase local production of interferon and decrease viral load of HPV. Imiquimod has 2 types. The 5% imiquimod (marketed as Aldara) is available in Iran and is used for external warts and its application is not recommended during pregnancy. Imiquimod can be used for vaginal lesions, and washing hands before and after applying it is suggested.

At bedtime, a patient should apply this cream to the clean and dry skin in the location of the lesion, rub it until the cream disappears, and leave the cream on the area for 6 to 10 hours. Afterwards, the area should be washed off with water and mild soap. Because this cream undermines the protective effects of condoms and diaphragms, the patient should not have sexual intercourse until the cream is on the skin.

Aldara should be used 3 times a week for up to 16 weeks. Mild local inflammatory reactions including erythema, bumps, sores, rashes, and blisters may be seen as

signs of using this cream. Lesions are completely removed in 40% to 50% of women; however, in 30% of cases, lesions recur after 12 weeks (12, 20, 21).

8.2. Clinical-Based Therapies

A) 90% to 99% trichloroacetic acid (TCA) is a solution used for small and separate lesions. It should be applied directly and sparingly to each wart. The treated area should be washed twice a day. The area is checked in the seventh day of the treatment. TCA is a destructive and caustic substance that should be applied by experienced professionals.

B) Cryotherapy is used for a wide range of lesions. It can be applied in closed systems by using nitrous oxide or spraying liquid nitrogen directly. This treatment is usually applied weekly.

C) Surgical methods used to treat genital warts include curettage, electrosurgery, and application of a scalpel under general or local anesthesia. Scattered keratinized lesions can be removed by electro surgery. Patients with multiple or large warts of any location should be referred for surgical treatment under general anesthesia.

Vaginal lesions can be treated by cryosurgery, podophyllin, or TCA (22). For small lesions of external genitalia (lesions $\geq$ 5), imiquimod or podophyllotoxin are recommended for initial treatment in females. Imiquimod is often suggested because of simulating the immune system and the observed effects it has against dysplasia; however, it is very expensive.

Sinecatechins is among other treatment methods which can be applied by patients themselves. This is an expensive treatment method. Whenever a patient does not respond to a treatment method after 3 weeks, or the lesion has not been completely removed 6 to 12 weeks after initiating the treatment, it is better to choose another treatment method or perform cryotherapy.

TCA or cryotherapy is recommended to treat small vaginal lesions. TCA, bichloroacetic acid (BCA), and interferon are only drugs used to treat vaginal warts; however, many patients cannot tolerate intra lesional interferon injections (22-24).

In the case of large lesions ($> 20\ cm^2$) or bulky lesions, because medical treatments need a long period of time and are often incomplete and hard to bear, surgery is recommended as an initial treatment.

Because laser is a controlled-depth treatment, destructing tissues by laser is very useful for vaginal warts. Given its few damaging effects and because it is technically easy to perform as it can be controlled better than electrocautery, the mentioned method is useful for treating large lesions.

Recurrent lesions are usually treated through reapplying the method that led to the initial removal of the lesion. Reapplying the previously used method is very likely to be successful.

To treat resistant lesions, a surgical method or an intra lesional injection of interferon or TCA are recommended. It is suggested that an excisional biopsy be performed to histologic evaluation and rule out malignancy in resistant lesions. Performing a biopsy, before initiating a treatment, is also recommended for postmenopausal women (25-32).

9. Follow-Up Care after Treatment

Using sitz bath, mild analgesics, and soft covers can ease discomfort and pain in patients. Sexual activities may be initiated whenever a patient feels comfortable; however, this usually takes a few weeks (33).

There are no standard methods to monitor and track these patients after the treatment is terminated. Women with genital and anal warts should be screened for cervical cancer based on the guidelines (21).

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