Human Papillomavirus (HPV) Infection is common in adolescents and can present with genital warts, precancerous lesions or cervical cancer many decades after acquiring the infection. Genital warts are the most common presentation in adolescents and are usually diagnosed clinically. Screening programs with pap smears and liquid-based cytology are the main tools for the early detection of HPV-associated precancerous lesions. DNA testing is available for HPV typing. Treatment of genital warts can include observation alone or destructive therapy. Treatment of HPV-related precancerous lesions, such as low-grade squamous intraepithelial lesions, should be close monitoring and follow-up. Treatment of cervical cancer is usually inefficient; therefore we should focus on the prevention of the condition by the administration of human papillomavirus vaccines before the initiation of sexual activity.

Overview

Human papillomavirus (HPV) infection is the most common sexually transmitted infection. This viral agent has been associated with genital warts, low-grade in-situ
dysplasia and cervical cancer. HPVs are divided into:

- Low risk subtypes which are 6 and 11, both of which are causative agents for genital warts.
- High risk subtypes which include HPV 16 and 18. They are associated with cervical cancer, which is rarely seen in adolescents.

**Epidemiology of Human Papillomavirus Infection in Adolescents**

HPV infections are estimated to occur in 5.5 million cases per year. Currently, 20 million Americans are estimated to be infected with the viral agent. Up to 75% of sexually active males and females will acquire HPV during their lifetime.

Sexually transmitted infections including HPV are way **more common in adolescents compared to adults**. This has been attributed to the sexual behavior of adolescents in addition to the immaturity of the genital tract. A recent study has shown that 50% of HPV-negative adolescents acquired the infection within three years. Because of these alarming figures, it has been suggested that HPV vaccination should be administered to presexually active children and adolescents.

The main risk factors for HPV infection are a **greater number of sexual partners and sexual activity at a younger age**. Young adolescents usually have columnar and metaplastic cells lining the ectocervix. These immature cells are more likely to acquire HPV compared to the squamous epithelium that is found in adults.

The main mode of transmission of HPV is skin-to-skin contact. Sexual activity is associated with abrasions or tears to the squamous and mucosal epithelium. These small injuries make it easier for the viral agent to enter and infect the epithelium. HPV can be also transmitted with fingerplay or other forms of foreplay that involve skin-to-skin contact without intercourse. In addition to sexual contact HPV can also be spread via oral or anal sex. HPV can be also transmitted with fingerplay or other forms of foreplay that involve skin-to-skin contact without intercourse.

The main risk factors for HPV-associated cervical cancer are the presence of a high-risk HPV type or impaired immune status of the host. **Cigarette smoking, alcohol consumption, multiparity and co-infection with chlamydia trachomatis or herpes simplex virus** are other risk factors for invasive HPV-associated cervical cancer in adolescents.

Prevention of HPV infections is based on sex education, the use of condoms and vaccination against HPV. These methods have shown good results and are believed to be sufficient to lower the risk of invasive cervical cancer in the future generations once they become established in the healthcare system.

**Risk Factors**

The main risk factors for HPV-associated cervical cancer are:

1. The presence of a high-risk HPV type or impaired immune status of the host.
2. Cigarette smoking.
3. Alcohol consumption.
4. Multiparity
Clinical Presentation of Human Papillomavirus Infection in Adolescents

The clinical presentation of HPV infection can be classified into genital warts, precancerous lesions and cancerous lesions. The exact presentation is based on the type of acquired HPV and not the duration of the disease. Low-risk HPV types, for instance, have been associated with genital warts and low-grade genital abnormalities but not with cervical cancer.

The incubation period of HPV infection is variable. HPV-related genital warts usually appear within months after acquiring the virus, whereas, HPV-associated cervical cancer usually develops decades after acquiring the virus.

Most cases of HPV infection are, in fact, asymptomatic. Additionally, low-risk HPV types are very likely to be cleared out within 30 months of acquiring the infection.

Cervical Dysplasia

Adolescents with cervical dysplasia are usually identified by screening. Low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesions (HSIL) are the two main types of cervical dysplasia that can be caused by HPV infection. These lesions most commonly regress in adolescents without any intervention. Follow-up cytology examination is all that is needed when LSIL is diagnosed. Colposcopy should not be performed in a typical case of LSIL in an adolescent.

Genital Warts

Most adolescents who seek medical attention because of HPV infection do so because of the development of genital warts, a.k.a condylomata acuminata. The lesions are exophytic cauliflower-like growths that are seen on the penis, vulva, vagina and cervix. Perianal and intra-anal genital warts can be also seen.

Low-risk HPV are usually associated with genital warts and the potential for malignant transformation is very low. Recurrent genital warts after treatment are common. Other warts associated with HPV include:

- Common warts which are rough, raised bumps that are found on the hands, fingers, and elbows.
- Plantar warts which are hard growths on the feet, mostly on the heels.
- Flat warts that generally affect children and young adults. They are raised lesions with flat tops.

Cervical Cancer

Cervical cancer usually happens due to the progression of LSIL. Up to 96% of LSILs in adolescents will regress. Therefore, most cases of cervical cancer that happen many decades after acquiring the infection are due to either a high-risk HPV type that persists and does not get cleared by the immune system or due to impaired immunity in the host.
Diagnostic Workup for Human Papillomavirus Infection in Adolescents

The diagnosis of genital warts is based on history taking and clinical examination findings. No further testing is required except for viral DNA testing for HPV typing. Sexually active adolescents should also receive a pap smear and viral DNA testing from cervical secretions or from the cervical epithelium to exclude precancerous or cancerous lesions.

Cytological examination in case of cervical dysplasia usually reveals basal cell proliferation, nuclear enlargement, koilocytosis and abnormal mitotic figures. These findings are in fact a spectrum that correlates with the degree of cervical dysplasia, i.e., LSIL versus HSIL.

When LSIL or HSIL is diagnosed, viral DNA testing with a polymerase chain reaction assay is indicated for typing. Patients who are found to be infected with high-risk HPV types that are known to persist should receive a colposcopy with cervical biopsy. The histologic examination can help in excluding HSIL or cervical cancer.

Screening programs for HPV are started three years after the first sexual activity. Pap smears are usually repeated on a yearly basis, and when three consecutive pap smears are deemed as normal, screening can be switched to liquid based cytology every two years.

Treatment of Human Papillomavirus Infection in Adolescents

Genital warts can be treated with destructive therapies:

- Chemical compounds such as podophyllin, imiquimod and podofilox.
- Cryotherapy which is a method that uses liquid nitrogen to freeze abnormal areas.
- Laser therapy which is the use of light beams to remove abnormal tissue.
- Electrocautery which is the use of electrical current to remove the pathological tissue.
- Surgical removal of the abnormal tissue has also been used.

Patients who are found to have LSIL on their pap smear or liquid-based cytology should be offered a repeat cytology test after six months. A viral DNA test should be performed after 12 months to determine the virus type and the likelihood of persistence. If LSIL persists or progresses to HSIL, then therapies to eliminate early disease include:

- Ablative therapies such as cryotherapy and laser ablation are used.
- Excessive therapies such as loop electrosurgical excision procedure (LEEP) or conization therapy should be offered.
- Adolescents who receive one of these treatments should know that they are associated with an increased risk of preterm delivery in the future.

In the unfortunate event of development of cervical cancer then treatment is based on the stage of the disease and entails:

- Chemotherapy using cisplatin therapy.
- Radiotherapy that may be via external beam or brachytherapy.
Surgical procedures such as radical hysterectomy, debulking and total pelvic exenteration.

The treatment of cervical cancer is inefficient and costly. Therefore, the focus should be on the prevention of cervical cancer. A bivalent vaccine against HPV types 16 and 18 and a quadrivalent vaccine against HPV 6, 11, 16 and 18 are available. These vaccines should be given to all girls before the initiation of sexual activity.

References


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