Venereal Warts in Children

Kelly A. Sinclair, MD,* Charles R. Woods, MD, MS,† Sara H. Sinal, MD§

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Objectives

After completing this article, readers should be able to:

1. Describe the natural history and epidemiology of anogenital human papillomavirus infection.
2. Discuss diagnosis and treatment options for children who have anogenital warts.
3. Recognize when anogenital warts are suggestive of child sexual abuse and what steps are needed to manage this clinical problem.

Introduction

More than 24 million cases of human papillomavirus (HPV) infection occur in adults in the United States, with an estimated 1 million new cases developing each year. The number of outpatient visits for adults who have venereal warts (condyloma acuminata) increased fivefold from 1966 to 1981. (1) HPV infections in children may present as common skin warts, anogenital warts (AGW), oral and laryngeal papillomas, and subclinical infections. The increased incidence of AGW in children has paralleled that of adults.

AGW in children present a unique diagnostic challenge: Is the HPV infection a result of child sexual abuse (CSA), which requires reporting to Child Protective Services (CPS), or acquired through an otherwise innocuous mechanism? Practitioners must balance "missing" a case of CSA if they do not report to CPS against reporting to CPS and having parents or other caregivers potentially suffer false accusation and its potential ramifications, which may include losing custody of children.

In the past, simply identifying AGW in a young child was considered indicative of CSA by some experts. However, there is no defined national standard beyond the limited guidance provided in the 2005 American Academy of Pediatrics (AAP) Policy Statement, which states that AGW are suspicious for CSA if not perinatally acquired and the rare vertical, nonsexual means of infection have been excluded. (2) Guidance in determining perinatal acquisition or nonsexual transmission is not provided. This review examines the pathophysiology of HPV causing AGW in children and adolescents, diagnostic challenges, treatment options, and a clinical pathway for the evaluation of young children who have AGW when CSA is of concern.

Epidemiology and Transmission

HPV are double-stranded DNA viruses that belong to the family of *Papillomaviridae*. More than 200 HPV serotypes have been identified, but only 85 have been more thoroughly characterized. Skin warts caused by types 1, 2, 3, 4, 7, and 10 may occur in as many as 10% to 20% of all children, with the peak incidence between ages 12 and 16 years. Types 6 and 11 are responsible for up to 75% to 90% of genital infections and are the most common types found in oral lesions. HPV 16 and 18 also are common causes of genital tract infection and cause about two thirds of cervical cancers and many vulvar, penile, and anal cancers as well as oral cancers of epithelial origin.

HPV infections in humans fall into two general categories: cutaneous and mucosal. There is no host preference based on age, sex, or race. HPV may be present in normal-appearing cells and remain latent for months to

Abbreviations

AAP:	American Academy of Pediatrics
AGW:	anogenital warts
CPS:	Child Protective Services
CSA:	child sexual abuse
FDA:	Food and Drug Administration
HPV:	human papillomavirus
PPV:	positive predictive value
STI:	sexually transmitted infection

*Emergency Medical Services, The Children's Mercy Hospital and Clinics, Kansas City, MO.
†Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY.
§Department of Pediatrics, Wake Forest University Health Sciences, Winston-Salem, NC.

years before generating visible lesions. Multiple factors have been shown to change susceptibility and progression of disease after infection: nutrition, endogenous and exogenous hormones, tobacco use, parity, and immune status. Immunocompetent children and adolescents usually can clear HPV infection within a 2-year period by a cell-mediated immune response. Persistence of infection, including latency, appears to increase from adolescence to adulthood.

In adolescents and adults, transmission of HPV types causing AGW is primarily sexual. HPV is likely the most common sexually transmitted infection (STI), affecting up to 80% of adults. Intercourse with an infected partner results in transmission of disease in two thirds of exposures. Condoms are not as effective in preventing sexual transmission of HPV as they are in preventing transmission of other STIs. Most adolescents who become infected with HPV do so within 2 years of first sexual intercourse. Infection in adolescents is more commonly subclinical or transient than in adults, but HPV infection in sexually active adolescents can lead to cervical cancer. In female adolescents, perianal infection may result from autoinoculation from secretions caused by primary cervicovaginal infection or from anal intercourse. In male adolescents, anal intercourse is the primary cause of perianal lesions.

The prevalence of anogenital HPV infection in children and adolescents is unknown but parallels that of adults. The average age of presentation of AGW in children is 2.8 to 5.6 years. (3)(4)(5)(6) AGW in young girls are seen in the vulvar, perianal, hymenal, vaginal, and urethral areas, regardless of method of transmission. Young boys have perianal lesions; penile lesions are rare. In adolescent boys, penile lesions are more common than perianal lesions. AGW, like other STIs such as trichomoniasis, often are asymptomatic in males.

HPV serotypes that cause AGW in young children may be transmitted by perinatal exposure, heteroinoculation, autoinoculation, and indirect fomite transmission, in addition to sexual abuse. Children may autoinoculate themselves, usually from a wart on the hand to another location on the body, including the genital area. Nonsexual transmission via sharing underwear, bath towels, and swimsuits as well as bidet use has been reported. Transmission to young children from family members or other caregivers during diapering or routine care has also been described.

Lesions from an affected child and those found on caregivers or others having contact with the child may be assessed for concordance of serotype or genotype. However, documented concordance or discordance does not definitively distinguish among the possible mechanisms of acquisition of infection. Such testing is expensive and generally not recommended. Serotyping the child's lesion is not considered helpful because AGW in children are often caused by cutaneous types (up to 40% in some studies). HPV serotypes 6 and 11, most commonly considered the sexually transmitted serotypes of HPV, occasionally cause cutaneous warts in children.

Three recent large case series have shown that most young children who have AGW have no physical or forensic evidence of CSA, with rates of CSA ranging from 3% to 10%. (5)(6)(7) CSA as the means of HPV infection in children does increase with age. In a 2005 study of 74 children who had AGW in North Carolina, among those 4 to 8 years old and 8 years and older, AGW was 2.9 times and 12.1 times, respectively, more likely to have been due to CSA than in children younger than 4 years. (5) For children younger than 4 years, when a forensic history and thorough physical examination raised no concerns, the positive predictive value (PPV) of HPV infection alone was 21% for girls and 16% for boys and girls combined. For boys and girls 4 to 8 years of age and those older than 8 years, the PPVs were 36% and 70%, respectively. In a 2006 Canadian study of 72 children who had AGW, CSA was suspected or confirmed in 26% of those 2 to 6 years old and in 85% of those more than 6 years old. (6) In a 2007 study of 131 6-month-old to 9-year-old children in Kentucky referred to a pediatric gynecologist for AGW, (7) 50% had a maternal history of AGW or cervical dysplasia. Among 81 patients who had siblings, 49% of siblings also had AGW. After full legal system investigations, only three of 131 cases (2%) were "ruled to be suspicious for abuse." Perinatal transmission was considered the most likely mode of transmission for most of these children.

Diagnosis

AGW is diagnosed primarily by clinical appearance (Figs. 1 and 2). The warts start as a small, flesh-colored papule in the perianal area in males or females and subsequently grow on the hymen, in the vestibule or vulvar areas, or around the urethra in females or less commonly on the penile shaft in males. Over a period of months or sometimes very rapidly, these lesions develop into clusters of skin-colored flat warts or somewhat pedunculated larger cauliflower or berrylike keratinized masses, similar to skin warts. Warts on the skin of the penis, scrotum, labia, and perianal areas tend to be flatter, shiny, and less verrucous. In most cases, internal (speculum) examination is not performed, but when surgical treatment is undertaken for extensive warts, warts are

Figure 1. Findings in an 18-month-old girl evaluated for anogenital warts, likely from perinatal transmission.

often found in the vagina and rectum as well. In adolescents, smooth, flat warts are seen more commonly on the cervix when there is clinically identifiable infection. Outside of the cervix, the vulva is the most commonly affected site in adolescent females, and nearly 25% of affected women also have perianal lesions.

If the clinician is unsure if the lesion is a wart, which is more likely to be a concern in single lesions, a biopsy is indicated. Brushing the lesion with a Papanicolaou brush and sending the specimen for HPV testing has been recommended when the diagnosis is in doubt. We have not found this technique to be very helpful because the test result often is negative. A negative test result could be true (the lesion is not due to HPV) or false due to inadequate sampling or limitations of the assay. In our experience, molluscum contagiosum is the condition most easily confused with AGW. Molluscum typically presents as shiny papules with central umbilication, and most lesions measure 1 to 2 mm. Giant molluscum lesions have been reported in the anogenital area in children and are more easily confused with HPV. Condyloma lata lesions, which are seen in secondary syphilis, tend to be flatter and smoother. Syphilis serologies should be positive in these cases, and a brushing for dark-field testing should show spirochetes. In adolescents, vulvar papillomatosis can be confused with AGW, and these lesions are not associated with HPV infection. Hymenal remnants may also be confused with condyloma acuminatum. Other conditions in the differential diagnosis are epidermal verrucous nevus, Bowenoid papulosis, pseudoverrucous papules and nodules, neurofibromas, Langerhans histiocytosis, and malignant growths.

Figure 2. Anogenital warts are visible in the vestibule and on the hymen of a 9-year-old girl who was a victim of incest.

Treatment

Seventy-five percent of AGW resolve spontaneously within months to a few years in children who have healthy immune systems. (8) Those persisting for more than 2 years are less likely to resolve spontaneously or with treatment. (9) Many clinicians now prefer watchful waiting over immediate treatment. Treatment may be desired in long-lasting cases or when warts are causing symptoms such as pain with defecation, itching, or bleeding. There are no United States Food and Drug Administration (FDA)-approved treatments for AGW in children 12 years of age and younger. Treatments can be divided into nonsurgical and surgical. No approach has been shown to be universally successful, and recurrence is common after any treatment. Some children may require a combination of therapies. Because recurrence is common, once a child has had AGW, the appearance of new lesions after spontaneous resolution or treatment does not necessarily indicate a new exposure. This fact is particularly important when the source of infection is believed to be CSA.

Nonsurgical approaches include those that cause nonspecific tissue destruction and immunomodulators. (8) Podophyllin is available as a resin (10% to 25%) that is applied to the warts by the clinician every 1 to 2 weeks until the warts resolve. The resin should be washed off after 4 hours to minimize burning. Many parents and children find this treatment unpleasant. A similar but less potent drug is podofilox, available as a 0.5% gel or solution, which is applied to the wart once or twice daily, several days per week, by the caretaker at home, as tolerated. Podofilox is not approved for use in children younger than 12 years of age, although one study of 17 children suggests that podofilox is likely to be safe and effective in children and can be applied by the caretaker

at home with clearance rates of 88%. (10) Imiquimod, an immunomodulator, has been used for treatment of AGW. It is not approved for treatment in children younger than 12 years of age, but case series show clearance rates approaching 75% in children. The 5% cream is applied to the AGW and kept on overnight three times per week, with improvement expected in weeks to months. (10) Local irritation and pruritus can occur.

Surgical approaches include cryotherapy with liquid nitrogen, electrodesiccation, and pulsed dye laser. Surgical excision is also an option for treating a limited number of AGW. Clearance rates with these methods in adults range from 27% to 100%, but recurrence rates are approximately 25%. In our experience, surgical approaches are reserved for children who have extensive, symptomatic AGW. Because most affected children are younger than 4 years, general anesthesia is usually required. Postoperative pain and scarring can occur.

Prevention

Two vaccines for HPV are currently available in the United States for administration to females between ages 9 and 26 years. They have been shown to be highly effective in prevention of precancerous cervical lesions for at least 5 years after vaccination. Vaccination does not affect existing infection. Therefore, vaccination is most effective when administered to females before first sexual intercourse. The quadrivalent vaccine protects against HPV 16, 18, 11, and 6. The bivalent vaccine protects against HPV 16 and 18. The Advisory Committee on Immunization Practices recommends vaccination of 11- to 12-year-old girls with a three-dose schedule of 0, 2, and 6 months. (11) Vaccination also is recommended for females 13 to 26 years of age, and the series may be started as young as 9 years of age. Quadrivalent HPV vaccine is now approved by the FDA for males and may be administered to 9- to 26-year-old males to reduce their likelihood of acquiring genital warts. (See cdc.gov/hpv for additional information.)

The Issue of CSA

Specific age cutoffs, typically 24 months or older at the time of diagnosis of AGW, have been suggested in the past as a primary criterion for reporting the child to CPS for potential CSA. The variability of the incubation period from HPV infection to the development of visible AGW, the potential for small lesions from perinatally acquired infection to go unnoticed for weeks to months (or years), and the possibility of "innocent" postnatal acquisition of AGW make it difficult to justify a specific age cutoff as a sole criterion for reporting children younger than 4 years of age as suspicious for CSA. How then to proceed in the midst of this unfortunate clinical uncertainty?

Areas of Consensus

There is general agreement that the evaluation of a child who has AGW for possible CSA should include the following:

1. Primary caregivers (usually parents) should be interviewed for history regarding 1) cutaneous or AGW for themselves and other family members and 2) abnormal Papanicolaou smears or surgeries for cervical cancer in the biologic mother (although oncogenic HPV serotypes usually do not cause AGW in children, they may coexist with nononcogenic types). In addition, caregivers should be asked whether they suspect sexual abuse or if a sexual offender has had access to the child.

2. An interview with the child regarding CSA should be performed if the child is old enough to be interviewed, usually 3 to 4 years of age. The interview must be performed by a person trained in interviewing children and who is familiar with acceptable interview techniques for determining the likelihood of CSA. In a recent study of 987 children ages 2 to 17 years who had been sexually abused, 73% fully disclosed the abuse, 12% partially disclosed, 10% did not disclose, and 5% denied abuse. (12) Fifty percent of children ages 2 to 6 years of age disclosed. Factors associated with disclosure were age (older children more likely), sex (girls more likely), disclosure before the interview (results in much higher disclosure rate during the interview itself), a positive relationship between caregiver and child, and age of onset of CSA (the earlier the onset of abuse, the more likely the disclosure).

3. An inventory should be taken of frequently seen signs, symptoms, and behaviors that occur in children who have been sexually abused. Among the common behaviors are nightmares, advanced sexual knowledge for age, and acting out sexually with peers. Twenty-eight percent of sexually abused children exhibit sexual behavior problems, but in children who demonstrate intrusive or aggressive sexual behavior, only 48% have been sexually abused. (13) Normal sexual behaviors must be differentiated from repetitive, intrusive, or abusive sexual behaviors.

4. A thorough physical examination should be performed, looking for any evidence of physical or sexual abuse. This evaluation should include a careful and magnified examination of the genital and anal areas, evaluating for signs of acute trauma such as petechiae or bruising to the hymen and anal tears as well as signs of chronic trauma such as absent hymen tissue at the posterior

hymenal rim or scarring in the anogenital area. The majority of examinations in abused children yield no results of note.

5. Screening for other STIs should be performed. The 2005 AAP recommendations include testing for gonorrhea, *Chlamydia* infection, *Trichomonas* infection, human immunodeficiency virus infection, hepatitis B and C, and syphilis, depending on the circumstance of the CSA, age of the child, and time since sexual contact. (2)

6. Referral to a child abuse specialist is appropriate if the primary care practitioner or specialists involved do not feel comfortable or adequately trained to perform any parts of the previously noted evaluation.

Lack of Consensus

In 2007, we surveyed members of The Ray Helfer Society (an honorary society of physicians with a mission to provide leadership in prevention, diagnosis, and treatment of child abuse), most of whom are child abuse specialists, regarding their views on management of young children who develop AGW. Of 195 members who could be reached by email, 65 (33%) responded. There was significant disagreement as to whether children who have AGW should be reported to CPS regardless of whether further evaluation (interview of parent and child, behavioral inventory, genital/anal examination for trauma, and cultures for other STIs) suggested CSA. Given the scenario of a 4-year-old child who has AGW and whose comprehensive evaluation suggested no other evidence of CSA, 36% agreed and 44% disagreed with reporting to CPS. In response to an item regarding whether CSA was *unlikely* to be the source of AGW in a 3-year-old child, 45% agreed, 18% disagreed, and 37% were unsure. This variation, even among a small subset of child abuse specialists responding to the survey, is indicative of the lack of certainty regarding whether CSA is a common cause of AGW in young children. In addition to confusing clinicians, this ambiguity is a problematic reality for CPS workers who have the responsibility to investigate the cases when reported as suspected abuse. CPS may refuse to accept such cases for investigation because a physician cannot say whether AGW represents CSA, and CPS workers may already have significant case loads involving situations that have more definitive evidence.

Suggested Clinical Approach for Reporting to CPS

First, it is important for the practitioner to be aware of the reporting laws in his or her state and be sure that a decision not to report is acceptable under the law. In addition, if a practitioner does not have access to a skilled interviewer or is unable for some other reason to obtain a comprehensive evaluation, a decision to report may be the default option.

Table 1. Findings in a Child Who Has Anogenital Warts That Require a Report to Child Protective Services

- Parents suspect abuse
- Child discloses abuse
- Child's behaviors suggest abuse
- Physical examination suggests abuse
- Finding of a sexually transmitted infection in addition to HPV
- Any child older than 48 months of age

Exceptions include adolescents who report consensual sexual activity with an appropriate-age peer, and severely immunosuppressed children who have multiple warts at other sites with no other findings of abuse.
HPV=human papillomavirus

Table 1 outlines instances when reporting to CPS is necessary. For a child who is younger than 4 years of age when AGW are first seen and the entire evaluation (history, behavioral inventory, physical examination, and STI screening studies) yields negative results, including no concerns regarding household or other locations of child care, a report to CPS is not mandatory because perinatal or "innocent" postnatal acquisition is highly likely in this context.

Because of increased risk of CSA with age, when AGW are first seen in a child 4 years and older, we routinely make a CPS report because the physical examination can be negative for any other evidence of CSA and children do not always disclose their abuse, even to skilled forensic interviewers. Some clinicians may choose routine reporting of children too young to be reliably interviewed to CPS to elicit a home visit and bring to light any CPS record of previous concerns potentially unknown to the clinician. In these cases, the clinician accepts as unavoidable the stress a CPS investigation will bring to a potentially innocent family.

For a patient who is pubertal, the possibility of consensual sexual activity must be explored. If consensual activity occurred with a peer of appropriate age, no report is needed. If the partner is of inappropriate age (especially if meeting the definition of statutory rape by state law) or if the patient says sexual activity was not consensual, a report should be made. If no report is made, careful follow-up by the primary care physician

Table 2. Follow-up Screening for Sexual Abuse in Children Who Have Anogenital Warts Not Reported as Suspected Child Sexual Abuse

History

- New caretaker concerns about abuse
- New disclosure by the child
- Symptoms of anal/genital trauma or infection (vaginal discharge, vaginal/anal bleeding, or pain)
- Behaviors (nonspecific but often seen in CSA cases)
  - –Unusual fears
  - –Sleep disturbances
  - –Change in school performance
  - –Anger and acting out
- Behaviors (more specific for CSA)
  - –Sexual knowledge unusual for age of child
  - –Acting out sexual acts with peers
  - –Inappropriate exposure or excessive touching of genitalia of self or others

Examination Findings

- Trauma to genital/anal area
- Trauma to skin in area of breasts, such as bite marks
- Trauma to the mouth or pharynx, such as bruising of tongue or palate

Laboratory Testing

- Confirmed sexually transmitted infection

CSA=child sexual abuse

is indicated to observe for any future signs of CSA (Table 2).

When the report is made, the CPS workers should be told that HPV infection causing AGW may be a result of CSA, but other sources of infection cannot be totally eliminated. However, the case being reported is considered at high risk for CSA because of the age of the child or the presence of other positive factors (eg, disclosure by the child, suspicion on the part of the parent, sexualized behaviors, abnormal physical findings, or another STI). If CSA is suspected by a nonfamily member or caretaker, a report to law enforcement would take the place of reporting to CPS. In the case of young children, this is an uncommon scenario.

Parents need to be informed that state law requires reporting of suspected abuse and although other causes of HPV infection are possible, based on high risk factors, a CPS report must be made. Parents also should be told that CPS will be made aware of the scientific limitations in the area of AGW.

Summary

- HPV is widely prevalent and acquired from a variety of sources and a variety of routes.
- The average age for presentation of AGW in prepubertal children is 3.75 to 4 years. (3)(4)(5)(6)
- AGW in children younger than 4 years of age are typically acquired from nonsexual transmission. (5)(6)(7)
- CSA must be considered in any child who has AGW; the older the child, the more likely the AGW has resulted from sexual abuse. However, thorough evaluation is necessary before determining if reporting to CPS is necessary.
- Adolescents generally acquire AGW through sexual activity that is usually but not always consensual. Adolescents are now encouraged to be immunized against specific types of HPV to prevent cervical cancer.
- AGW can be treated, but it is unclear whether lesions resolve more rapidly with treatment. (8)(9) Most AGW in young children and adolescents do not need to be treated because they resolve spontaneously.
- AGW recurrence is common after treatment. In a child who has been a victim of CSA, recurrence does not necessarily mean the child has been reabused. (9)

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PIR Quiz

Quiz also available online at http://pedsinreview.aappublications.org.

16. You find perivulvar warts in a 2-year-old girl. She has a thin vaginal discharge, but the remainder of her examination findings are normal. History reveals she has difficulty sleeping. Of the following, the strongest argument that this finding should be reported to CPS is:

    A. Age of the child.
    B. Frequent nightmares.
    C. Location of the warts.
    D. Sex of the child.
    E. *Trichomonas vaginalis* in the wet prep.

17. You find perivulvar warts in a 7-year-old girl. Aside from a thin vaginal discharge, the remainder of her examination findings are normal. Wet prep and culture of the discharge yield no evidence for STI. History reveals occasional sleepwalking. Of the following, the strongest argument that this finding should be reported to CPS is:

    A. Age of the child.
    B. Her denial of abuse.
    C. Her sleep disturbance.
    D. Presence of discharge.
    E. Sex of the child.

18. A 17-year-old girl has had asymptomatic vulvar warts for 3 years for which she never has received treatment. These warts:

    A. Are likely to resolve without treatment.
    B. Are very unlikely to recur after treatment.
    C. May be transmitted despite condom use.
    D. Most likely reflect nonsexual contact.
    E. Require treatment.

19. When administered as recommended, currently available HPV vaccines:

    A. Are not useful for preventing HPV infections in males.
    B. Conceal CSA.
    C. Mitigate pre-existing HPV infections.
    D. Prevent anogenital infection by all HPV serotypes.
    E. Prevent the development of precancerous cervical lesions.

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