MANAGEMENT OF ANOGENITAL HPV IN CHILDHOOD

KEY POINTS

- The prevalence of asymptomatic HPV infection in children is unknown.
- Anogenital warts in children may be acquired via sexual transmission, requiring specialist referral and multidisciplinary assessment.
- Other routes of transmission include vertical transmission from the mother, particularly in younger children, or self-inoculation.
- Although there is no cut-off age that delineates vertical from horizontal transmission, it is reasonable to suggest that horizontal, vertical or perinatal transmission becomes increasingly unlikely in children over the age of 4 years.
- Diagnosis is clinical and biopsy is rarely indicated. Virological typing and serology are of no value for forensic purposes.
- Anogenital warts in children need to be distinguished from other raised lesions, including molluscum contagiosum or condyloma lata (syphilis).
- Spontaneous clearance is common and treatment should be reserved for those with significant symptoms.
- Juvenile-onset recurrent laryngeal papillomatosis can result from vertical transmission and children can present with respiratory symptoms; there is a small malignant potential.
- There is insufficient evidence to determine the significance of oral warts in relation to child sexual abuse at the current time.
- Cervical screening in those with a cervix who have had a history of sexual contact/abuse or exposure to HPV in childhood should commence at the age recommended by the National Cervical Screening Programme.

Epidemiology

HPV is the most common viral infection of the adult and adolescent female genital tract.[1-4] Although there was an increase in case reports of anogenital warts in children in the 1980s and 1990s,[5-7] serological studies suggest the population prevalence in children

remains low.[8] The prevalence of asymptomatic HPV infection of the anogenital region in children is unknown.

Clinical presentation

Children usually present because a caregiver has noted the lesions, although some present with pain or bleeding on defaecation, or secondary infection. Classical cauliflower-like condyloma acuminata do occur in children, but anogenital warts have multiple appearances.[9,10] There is very little data on the prevalence of infection of the cervix or vagina in children who present with peri-anal or vulval warts.[11]

The incubation period in children is unknown. There is a high likelihood of spontaneous regression over time.[12] HPV may be particularly troublesome in children on immuno-suppressive therapy, and the possibility of immune deficiency (including HIV) should be considered in any child who has particularly refractory lesions.[13,14]

Molecular diagnosis

In determining the source of infection, virology adds little to the history and clinical examination.[15] There is little, if any, value in typing for forensic purposes.

Molecular diagnosis relies on the detection of HPV DNA. The use of polymerase chain reaction (PCR) is highly sensitive, but there is always a risk of contamination. Many HPV types have been described, but no specific type is consistently associated with a particular clinical appearance.[16] Infection with multiple HPV types is common,[17] and it is technically impossible to be sure that all types from a given individual have been isolated. HPV DNA can be found in apparently normal tissue surrounding clinical lesions[12] and in vaginal washings from individuals with no detectable lesions.[18,19] In adolescents and adults, HPV types 1–4 and 7 are found almost exclusively in skin warts (non anogenital).[16] In children, however, there is a significant prevalence of HPV types 1–3 in anogenital warts.[20,21] Laryngeal papillomas are usually, but not always, associated with HPV types 6 or 11.[22,23]

Neoplasia

Malignancy has been reported in children with laryngeal papillomatosis.[24] The risk of late malignancy in children with anogenital infection is not known. There are case reports of vulval dysplasia and carcinoma in young adolescents who had vulval warts from infancy[25,26] and of Bowenoid papulosis (intraepithelial neoplasia) in childhood.[27,28] There is no data that early screening in this group improves outcome. Cervical screening in those with a cervix who have had a history of sexual contact/abuse or exposure to HPV

in childhood should commence at the age recommended by the National Cervical Screening Programme (i.e. not earlier).

Methods of transmission

In adults, anogenital HPV is a sexually transmitted infection. Sexual transmission clearly occurs in children, but other forms of transmission also occur.

Vertical transmission

This topic is discussed in detail in the "Pregnancy and Breastfeeding" document. Overall, although possible, the risk of HPV transfer from mothers to their offspring appears low.[29,30] Furthermore, the possibility of sexual transmission should also be considered because several cases have been described in which there was known sexual abuse from a perpetrator who had ano-genital warts.[31,32] On the basis of the evidence to date, it is reasonable to conclude that most vertical transmission will manifest itself in young children and that child sexual abuse may not be the cause of HPV in many cases.

The maximum "latent period" of infection acquired at birth is unknown. Many studies have shown a high rate of "undetermined" modes of transmission in children, particularly in those presenting with anogenital warts before the age of 4 years.[35] It can be difficult in toddlers to be sure exactly when the first lesion appeared, and it is thought that many infections in those presenting before the age of 4 years, were acquired at birth.

It is reasonable to suggest that horizontal, vertical or perinatal transmission becomes increasingly unlikely in children over the age of 4 years.

Sexual transmission

It was not until 1971 that it was recognised that anogenital warts in children might be sexually transmitted. The true incidence of sexually transmitted HPV in children is unknown. From 1971 to 1993, 300 cases of childhood anogenital warts were published, of which 29% were sexually transmitted. The proportion of reported sexual abuse in these cases varied from 0–100%, which may have reflected differences in the populations studied and/or study methodology.[9] A multicentre study found that the prevalence of HPV in children referred for possible sexual abuse was 13.7% compared with 1.3% in a control group.[36]

Accumulating evidence suggests that, in children, the presence of warts in the anogenital region in isolation is not necessarily an indicator of childhood sexual abuse.[33,37-45] American Academy of Pediatrics (AAP) guidance states that "genital warts (human

papillomavirus) can be sexually transmitted in children, but these infections are not diagnostic of abuse by themselves".[46]

Other means of transmission

Dermatological literature suggests that children may acquire anogenital warts by infection from cutaneous warts on their own hands (auto-inoculation) or on the hands of adults (hetero-inoculation). Arguments for this hypothesis are the prevalence of HPV 2 in anogenital warts in childhood, and a number of suggestive case reports and case series.[5,20,47] A Spanish longitudinal study of women enrolled during pregnancy found that the mother's HPV status at the 6-week post-partum visit was a stronger determinant of HPV infection in the child than maternal HPV status in pregnancy, and suggested that horizontal mother-to-child transmission during the first few months of life might be more important than vertical transmission.[48] Other authors have also raised the possibility of fomite transmission.[43]

Conclusion

It must be recognised that there are other methods of HPV transmission in children other than sexual transmission, especially in children aged below 4 years. However, sexual contact must always be considered in the differential diagnosis, and a comprehensive multidisciplinary assessment may be required if there are any other factors that cause concern, even in young children.

Assessment

The age at which the lesions first appeared needs to be established, along with lesion-associated symptoms. All means of transmission should be considered: vertical (maternal infection including cervical smears; symptoms of respiratory infection); innocent inoculation (other warts in the child or young person; warts in other relatives or caregivers); sexual transmission (adolescent sexual activity; disclosure of sexual abuse; behaviour changes; risk factors for sexual abuse, such as contact with a known sexual offender or a family history of sexual abuse).

It is important to examine the whole body (including the conjunctivae, mouth and throat) for warts. The genitalia and anus should be examined with a light source and some kind of magnification, such as an auroscope. In females, the labia should be parted and the vulva inspected carefully. In males, do not forget to examine the corona and frenum of the penis (if the foreskin is readily retractile). Remember that not everything that presents as a wart is HPV. The most common alternative diagnosis is molluscum contagiosum, but condyloma lata (syphilis) has been mistaken for genital warts in a

child,[49] and almost any kind of papular rash may present in the anogenital region. The diagnosis can usually be made clinically if the child is seen by an experienced clinician, and biopsy is seldom indicated.

If a child under 4 years of age presents with anogenital warts, assessment for sexual abuse is probably not indicated in most cases unless there are factors that raise concern in addition to the warts themselves. In older children who present with anogenital warts, a referral for a multidisciplinary assessment for possible sexual abuse is also recommended, irrespective of whether other concerns have been identified.

The 2021 BASHH guidelines recommend that sexual abuse must be considered in any child presenting with anogenital warts.[35] The diagnosis of anogenital warts in a child under 13 years of age dictates a referral to (or at the least a consultation with) a paediatrician with expertise in this area. Children over the age of 13 need to be considered on a case-by-case basis.

If in doubt - irrespective of the age of the child/young person - consult with a paediatrician with expertise in this area. If you do refer, leave other investigations for sexual abuse to the referring clinician. A full assessment for possible sexual abuse will include examination by a doctor trained in the medical assessment of sexual abuse, screening for other sexually transmitted infections (STIs), and consideration of referral to the statutory authorities for further investigation. Even then, the result may be inconclusive.[50]

More extensive medical investigations (such as laryngoscopy, proctoscopy, cystoscopy or vaginoscopy) might be indicated on rare occasions if there were oral lesions or respiratory symptoms in a young child, or if lesions appeared to extend into the anus, urethra or vagina.

Treatment

Anogenital warts will usually regress spontaneously. Infection may be multi-focal, and HPV DNA is almost certainly present in adjacent ‘normal’ tissue. At present, there is no evidence that treatment in childhood will reduce the (unproven) risk of later neoplasia. Treatment ”can be difficult, prolonged and only marginally efficacious”[1] and recurrence is common. For all these reasons, active treatment is not usually recommended. Treatment should be reserved for those with significant symptoms.

There are many forms of treatment,[43,51,52] but in young children with extensive lesions, laser or diathermy under general anaesthetic is probably the best option. In these cases, a referral to the appropriate surgical service is recommended. Several case reports attest

to the safety and efficacy of imiquimod cream in children.[53] However, there are no randomised controlled trials of therapy in childhood. The most common therapy for juvenile-onset respiratory papillomatosis is laryngoscopy and surgical debulking with laser, sometimes in conjunction with adjuvant antiviral agents.[54]

Follow-up

The child should be followed to ensure that the lesions regress, with subsequent follow-up after 3–6 months to ensure that lesions have not recurred. In cases of vertical transmission, it is important to ensure that the mother receives appropriate follow-up of her own infection. If the treated individual is a sexually active adolescent, screening for other STIs should be performed and sexual health advice should be provided. In sexual abuse cases, the child should be followed by the relevant services/agencies to ensure that appropriate steps have been taken to ensure their ongoing safety, and to provide support and counselling.

There are currently no evidence-based recommendations to guide long-term follow-up. It is reasonable to be concerned that children and adolescents with anogenital HPV infection may be at increased long-term risk of malignancy. Therefore, it would be reasonable to recommend early consultation for individuals of either sex who have anogenital or urethral symptoms. Routine cervical screening should follow the National Cervical Screening Guidelines.[55]

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