

Discordance of Human Genotype of Papilloma Virus in Mother and Toddler with Condyloma Acuminata

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Abstract: Condyloma acuminata (CA) is a Human Papilloma Virus (HPV) infection that is rarely found in children. Transmission can be through vaginal contact, sexual abuse, auto or heteroinoculation or fomites. Polymerase Chain Reaction (PCR) examination is the gold standard for determining the cause of HPV genotype. This case report aimed to trace CA transmission to toddlers (ages <3 years). A female toddler has warts around the anus with a history of vaginal delivery and no sign of sexual abuse. The mother has warts on the genitals and between the fingers in pregnancy. The CA diagnosis was based on toddler's physical examination, acetowhite tests, and perianal biopsies. The endocervical smear from the mother was in accordance with the CA and the wart biopsy from the mother's fingers appropriate for verruca vulgaris. PCR has examined 39 HPV genotypes in the mother and the child. In the child showed HPV genotype 11, from mother's cervical swab sample showed HPV genotype 87 and indeterminate result from the mother's fingers. The discordance of HPV genotypes in the mother and the child is likely due to heteroinoculation transmission from the family who took care the child, or still possible from the mother but not detected on PCR examination because it only can examine 39 types of HPV. Identification with whole PCR is needed to ensure the source of transmission.

1 INTRODUCTION

Condyloma acuminata (CA) or genital warts are infections of the Human Papilloma Virus (HPV) which are rarely found in children. Until now, more than 200 HPV genotypes have been identified using the PCR method. (Ghedira et al., 2016; Chen et al., 2018, Sohrabi et al., 2017) More than 90% of cases of perianal and anal CA in adults and children are caused by HPV groups with low risk of neoplastic namely HPV 6 or 11, but there is also evidence that HPV 1, 2, 4, 7, 27, 57, 60 and 63 are the causes Sohrabi et al., 2017. Genotypes of HPV types 16, 18, 31, and 33 are HPV groups with a tendency to become intraepithelial neoplasia and invasive squamous cell carcinoma. (Lacour et al., 2012) Whereas, in HPV 87 there is still little literature to discuss. This type of HPV is associated with a tendency to occur in HIV patients. (Menzo et al., 2001) CA transmission can be through contact

during vaginal delivery, sexual abuse, auto or heteroinoculation, or through fomites. (Lacour et al., 2012; Menzo et al., 2001; Tract et al., 2005) Predilection of lesions in girls with CA is in the vulva, perianal, vagina, and urethral regions whereas in boys lesions are most often present in perianal and rarely occur in the penis. (Boxman et al., 1999) Polymerase Chain Reaction (PCR) examination is the gold standard in determining causative HPV genotypes. (Sonnex et al., 2014)

Although common in adulthood, CA in children is an unusual condition. In several studies reported the dominance of female sex in children age with CA with an average age ranging from 2.8 to 5.6 years. The prevalence of CA from epidemiological data that occurs in Indonesia is around 5-19%, while the prevalence in infants and children is less than 4.3%. (Jenison et al., 2000) The incidence of CA in adulthood in Dr. Sardjito Hospital for the past five years was 605 cases while the toddlers (under three

years old) were only 1 case. This paper reports one case of CA in toddlers who came to the Dermatology and Venereology clinic of Dr. Sardjito Hospital with complaints of warts on the perianal. The purpose of this case report is to trace the transmission possibilities.

2 CASE

A 15 months old girl came to the Dermatology and Venereology clinic of Dr. Sardjito Hospital with the chief complaint of warts appearing around the anal. From heteroanamnesis and alloanamnesis found that warts appeared since a few weeks ago, shaped rough bumps, skin color, size less than 0.5 cm. It did not feel itchy, painful, and there was no interference with bowel movements. They said she never been treated before. The patient was an only child, born with appropriate gestational age, vaginal delivery, with a head presentation. There were no airway disorders, hoarseness, stridor, or eye disorders. Every day the patient lived and was cared for by her mother and grandmother, mother had the habit of using towels alternately with her children to clean their genitals after urinating and no history of sexual abuse. Her parents were divorced, and her father did not live at home.

A mother who was three months pregnant had been diagnosed by dermatology, and

venereology specialist had genital warts in her vagina and had been treated. The size of the wart decreased but did not fall out until postpartum, and the patient never attends follow up again. The mother also had a wart with a diameter of 0.5 cm between the index finger of her right hand.

Physical examination of children showed right general conditions with vital signs within normal limits, and there were no signs of sexual abuse or enlarged lymph nodes. The perianal examination was revealed a verrucous papule, skin color, multiple with a size of 0.2 cm-0.5 cm (**Figure 1A**). The acetowhite test showed positive results, and on histopathological examination, with Hematoxylin-Eosin (HE) staining showed results in the epidermis showed mild hyperkeratosis, parakeratosis, partial hypergranulosis, spongiosis, irregular acanthosis, parabasal hyperplasia, and little lymphocyte acrositosis. Among them were keratinocytes with cytoplasm halo perinuclear and the nucleus was slightly enlarged (coilocytosis). In the dermis, there was quite a lot of lymphocytic and periadnexal infiltration. There was no malignant sign. Conclusion of perianal histopathology was in accordance with CA (**Figure 1B**). PCR examination was performed for 39 types of HPV. Children and mother's HPV DNA was obtained from the extraction of CA tissue in paraffin blocks. PCR examination in perianal CA specimens of children showed HPV 11 genotype (**Figure 2A**).

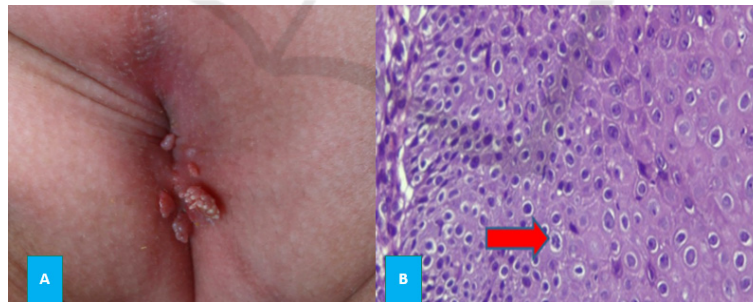


Figure 1: **A:** Perianal condyloma acuminata on the child; **1B:** Histopathological examination with Hematoxylin-Eosin (HE) staining revealed keratinocyte with halo perinuclear cytoplasm and the nucleus a bit enlarged or coilocytosis (arrow)

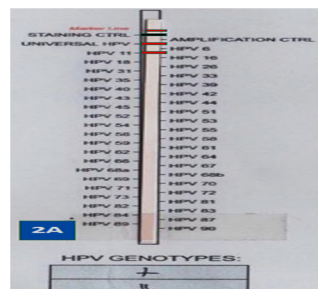


Figure 2: A. PCR CA of the child perianal resulted in HPV genotype 11

The physical examination of the mother when she came to the Dr.Sardjito Hospital showed no vaginal CA, and on in speculum examination (**Figure 3A**) the cervix appeared to be calm and no discharge nor verrucous papules were found, but found a skin-colored verrucous papule, a solitary size of about 0.5cm in right manus interdigit II (**Figure 3B**).

Histopathological examination of verruca skin tissue specimens with HE staining showed that the epidermis appears hyperkeratotic, acanthosis, papillomatosis, partly with hypergranulosis. Among them were keratinocytes with cytoplasm halo perinuclear and the nucleus was slightly enlarged (coilocytosis). The dermis looks puffy with small perivascular lymphocytes. There was no malignant

sign. Conclusions on histopathological biopsies were in accordance with verruca vulgaris. (**Figure 3C**).

Histopathological examination of cervical swabs appeared ectocervical cells in the form of many intermediate cells and few parabasal cells. We obtained a few endocervical epithelial cells and not finding displaced metaplasia or malignant epithelial cells. The background was erythrocytes, many polymorphonuclear leukocytes, and few lymphocytes. The conclusion to the Pap smear was Papanicolaou Class I (non-peculiar inflammation, *Bethesda system: Negative for Intraepithelial Lesion or Malignancy*). PCR examination with cervical swab showed HPV genotype 87 (**Figure 4A**), whereas, with skin material, the lesions of verrucae vulgaris on the fingers were undetermined (**Figure 4B**).

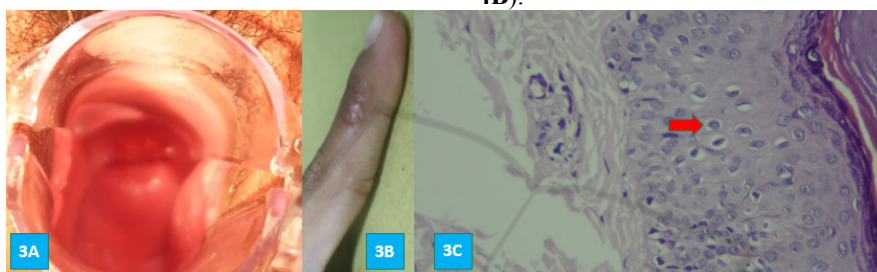


Figure 3: **A:** Inspecto examination to mother cervix showed calm cervix no discharge found nor verrucous papule. **3B:** Verrucous vulgaris on interdigit of mother hand. **3C:** Histopathological examination with Hematoxylin Eosin (HE) of verrucous vulgaris on the finger showed coilocyte (red arrow).

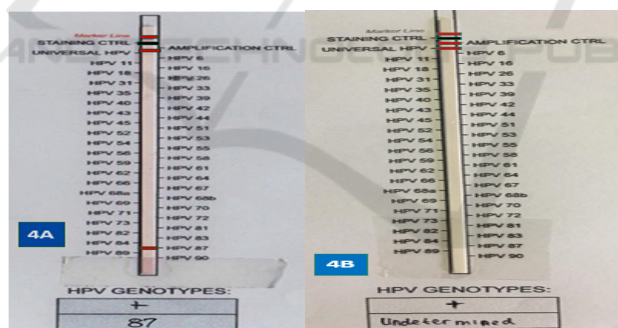


Figure 4: **A.** PCR of mother cervix showed HPV genotype 87. **4B.** PCR interdigit II manus dextra of the mother showed undetermined.

Patients are advised to be referred to an ENT specialist and ophthalmology specialist to track the presence or absence of laryngeal papillomatosis and eye keratitis. Until this case report is made, it has not been tracked due to limited costs.

3 DISCUSSION

Condylomaacuminata often referred to as chicken combs or genital warts, is one of the sexually

transmitted infections caused by HPV. *Human Papilloma Virus* is included in the *papovaviridae* family, the genus *polyomavirus*. The clinical manifestations of HPV infection in the genitals can be classic symptoms, such as prominent cauliflower, small smooth papules like flesh or hyperpigmented papules that combine to form keratotic plaques or papules or like verruca vulgaris The CA diagnosis in perianal children, in this case, is confirmed by the suitability of clinical features, histopathology and the discovery of HPV genotype 11 on PCR examination. In the mother, it can be concluded that

it has an asymptomatic CA on the cervix because there is no lesion clinically, but on histopathological examination and PCR examination shows HPV infection genotype 87; while the diagnosis of verruca vulgaris on the mother's finger is also matched with the clinical and histopathological features.

Condyloma acuminata in children can occur due to transmission through vaginal delivery, sexual abuse, auto or heteroinoculation, and fomites. In cases, suspected transmission occurs during vaginal delivery because CA lesions in children appear at the age of 15 months while the mother emerges vaginal CA at 3 months gestation, with an incubation calculation of about 12 months. The literature shows that HPV incubation ranges from 1-12 months.(Chen et al.,2018,Sohrabi et al.,2017) However, vaginal transmission is still questionable because it turns out that the HPV genotype in children is different from the HPV genotype in mothers. Suspicion of transmission due to sexual violence can be excluded because neither from alloanamnesis nor physical examination shows signs of sexual abuse. Suspicion of transmission through autoinoculation can be excluded because the patient does not have a CA at locations other than perianal. Suspicion of heteroinoculation transmission through the mother's finger when cleaning the patient's anus, or through fomites due to the habit of using towels alternately with the patient to clean the genitals or perianal is indisputable because on PCR examination the warts on the fingers are undetermined or HPV is present but not in accordance of 39 types of HPV examined. Veruca vulgaris is a benign proliferation of the skin and epidermal mucosa caused by HPV. The most common type of HPV is types 1, 3, 27, and 57. Whereas based on predilection, most often occur, especially in places that often experience trauma such as fingers, hands, and knees. HPV in the hands and feet is usually typed 1, 2, 4, 27, 57 and 19. Transmission of the perianal CA in children can be through the caregiver's fingers to genitalia. (Menzo et al.,2001). Based on several studies, the transmission of CA through fomites often occurs through surgical equipment, gloves with less sterilization, floor, toilet seat or through alternating towels.(Lacour et al.,2012)

PCR examination is the gold standard in determining HPV genotypes. The use of ultrasensitive examination methods with real-time PCR can detect \geq four dominant genotypes in 25% of CA cases(Sonnex et al.,2014;Jenison et al,2000;Hawkins et al.,2013)

PCR examination in this case used Ampliquality Express type HPV with 99% instrument sensitivity and 98.6% specificity that detected 39 types of HPV genotypes, namely: 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 67, 68a, 68b, 70, 71, 72, 73, 81, 82, 83, 84, 87, 89, and 90.⁶ The detection of vaginal transmission from mother to child can actually be done if the mother comes when there is still a vaginal CA. However, when she came to follow up, her vaginal CA was gone, so the sample was only taken from the mother's cervical swab. The presence of laryngeal papillomatosis and eye keratitis as a result of HPV transmission during vaginal delivery cannot be detected because the patient refuses to be referred.

The limitations of the PCR method with cervical swab specimens were only detected by some of the most dominant types of HPV because of the natural competition between HPV genotypes of CA. The types of specimens taken from the cervix also often do not accurately describe the cause of the HPV genotype, because some HPV genotypes are only found in the basal cervical tissue. Skills and techniques really determine the taking of test specimens. Whereas, different results can be found in HPV infections in the skin, where coinfection caused by more than ten genotypes can be detected even in deficient amounts.

4 CONCLUSION

One case of perianal CA on toddlers aged 15 months with mothers suffering from asymptomatic CA in the cervix and veruca vulgaris in the fingers is reported, but there is no match for HPV genotypes between the child and the mother. Thus, transmission in children cannot be determined. HPV genotype examination is needed with the whole PCR method both in mother and child and screening to the family who care for the child to identify the transmission source.

REFERENCES

- Boxman ILA, Hogewoning A, Mulder LHC, Nico JAN, Bavinck B, Schegget JANTER. 1999. Detection of Human Papillomavirus Types 6 and 11 in Pubic and Perianal Hair from Patients with Genital Warts. *J Clin Microbiol.*;37(7):2270-3.
- Chen Z, Zhou J. 2018. Distribution of human papillomavirus genotypes and its relationship to clinicopathology in invasive cervical carcinoma in

- Zhejiang Province , China. *J cancer Res therapeutics*.;780-4.
- Ghedira R, Mahfoudh W, Hadhri S, Gabbouj S, Bouanene I, Khairi H, et al. 2016. Human papillomavirus genotypes and HPV- 16 variants distribution among Tunisian women with normal cytology and squamous intraepithelial lesions. *Infect Agent Cancer [Internet]*.;11:1-10. Available from: <http://dx.doi.org/10.1186/s13027-016-0109-2>
- Hawkin Mg,Winder DM,Ball SLR. Vaughan K, Sonnex C, Stanley MA, et al. 2013. Detection of specific HPV subtypes responsible for the pathogenesis of condylomata acuminata. *Virol J [Internet]*;10(1):1. Available from: *Virology Journal*
- Jenison SA, Yu X, Valentine JM, Koutsky LA, Christiansen AE, Beckmann AM, et al. 2000. Evidence of Prevalent Genital-Type Human Papillomavirus Infections in Adults and Children. *J Infect Dis*.;162:60-9.
- Menzo S, Monchetti A, Trozzi C, Ciavattini A, Carloni G, Varaldo PE, et al. 2001. Identification of Six Putative Novel Human Papillomaviruses (HPV) and Characterization
- Sohrabi A, Hajia M, Jamali F, Kharazi F.2017.Is incidence of multiple HPV genotypes rising in genital infections *J Infect Public Health [Internet]*.;xxx:4-7. Available from: <http://dx.doi.org/10.1016/j.jiph.2016.10.006> of Candidate HPV Type 87.;75(23):11913-9.
- Sonnex C, Strauss S, Gray JJ. 2014.Detection of human papillomavirus DNA on the fingers of patients with genital warts. *bmj*;75:317-9
- Tract R, Papillomavirus H, Transmission P, Abuse TS. 2005. Anogenital and Respiratory Tract Human Papillomavirus Infections Among Children: Age, Gender, and Potential Transmission Through Sexual Abuse. *Pediatrics*.;116(4):815-25.