RECURRENT VULVAR CONDILOMA TREATMENT IN INFANT: A CASE REPORT

Tratamento de condiloma vulvar recorrente em lactente: um relato de caso

Denise Gasparetti Drumond¹, Gabriel Duque Pannain¹, Tarlline Ribeiro Sirilo¹, Miralva Aurora Galvão Carvalho¹, Samuel Drumond Esperança², Homero Gonçalves Junior¹

ABSTRACT

Introduction: Anogenital warts are one of the major clinical manifestations of the Human Papillomavirus (HPV). Case reports in children have grown in the last decades; however, there are still difficulties in determining the virus epidemiology and the best therapy for this age group. Objective: To report a case of recurrent vulvar condyloma in a sexually abused infant who presented complete resolution of the lesions after the use of topical imiquimod. Methods: Data research and medical record review were performed in addition to a qualitative study consisted of a wide literature appreciation on the subject. Results: After undergoing extensive therapy, the patient was successfully treated using topical imiquimod. Conclusion: Observation of this particular case suggests that imiquimod may be a safe and effective therapeutic alternative for the treatment of condyloma in the pediatric population. However, theoretical foundations for such conduct are scarce. Thus, the need for further studies on the subject is reinforced.

Keywords: Condylomata acuminata; Papillomaviridae; vulvar diseases; imiquimod.

RESUMO

Introdução: As verrugas anogenitais constituem uma das principais manifestações clínicas da infecção pelo vírus do Papiloma Humano (HPV). Relatos de casos em crianças têm crescido nas últimas décadas; contudo, ainda há dificuldades em determinar a epidemiologia do vírus e definir a melhor terapêutica para essa faixa etária. Objetivo: Relatar um caso de condiloma vulvar recorrente em uma lactente abusada sexualmente que apresentou resolução completa das lesões após o uso de imiquimode tópico. Métodos: Foi realizado levantamento de dados e revisão de prontuário, além de estudo qualitativo composto por apreciação ampla da literatura acerca do tema em questão. Resultados: Depois de ser submetido à extensa terapêutica, a paciente foi tratada com sucesso utilizando imiquimode tópico. Conclusão: A observação desse caso específico sugere que o imiquimode pode ser uma alternativa terapêutica segura e eficaz para o tratamento de condiloma na população pediátrica. Entretanto, embasamentos teóricos para tal conduta são escassos. Assim, reforça-se a necessidade do desenvolvimento de mais estudos sobre a temática.

Palavras-chave: Condiloma acuminado; HPV; doenças da vulva; imiquimode.

INTRODUCTION

Anogenital warts are one of the main clinical manifestations of Human Papillomavirus (HPV) infection^(1,2). According to the medical literature, cases reported in pediatric age have grown in recent decades^(2,3). However, determining the epidemiology of the virus and defining the best therapy for the lesions in this age group is still a major dilemma in Pediatrics^(4,5).

Studies indicate that the period between the initial infection and the emergence of clinical manifestations of the virus vary from three weeks to eight months, except in children, as the period is still unknown⁽²⁾. In adulthood, the virus is transmitted primarily via sexual intercourse, while the main forms of HPV transmission in children, in addition to sexual transmission (either oral-genital, genital-genital, genital-anal contact or digital manipulation of the children's intimate parts), include vertical transmission, self-inoculation and direct or indirect personal contact with contaminated objects or surfaces^(4,6-9).

The prevalence of HPV in sexually abused children varies from 5 to 33%, and around 16% in children without suspicion of abuse⁽⁵⁾.

The incidence of sexual abuse is difficult to estimate, mainly because a large percentage of these cases goes unnoticed⁽⁸⁾. In addition, this condition is associated with high rates of adverse outcomes, with physical and psychological consequences for the child⁽⁸⁾. In regard to the implications of a sexual abuse investigation, other forms of contagion should always be considered before transmission is defined as occurred by sexual abuse⁽⁷⁾.

Several treatment options are available for genital warts, but few of them are adequate for children⁽¹⁰⁾. The selected therapy should then be individualized, considering mainly the child's tolerability⁽⁷⁾.

According to the above mentioned, registering a case of recurrent vulvar condyloma in infant is proposed, in order to illustrate the difficulties found for its therapeutic approach.

CASE REPORT

The case report was approved by the local Ethics and Research Committee with Opinion No. 3.370.374.

A nine-month-old child admitted to the University Hospital of Universidade Federal de Juiz de Fora (UFJF) with vulvar condylomatosis (**Figure 1**), already under the care of the Tutelary Council, was referred to the surgery center for lesion excision. Cauterization of the lesions with an electric scalpel was the primary option. The child was discharged three days after the procedure with recommendation of local care. After approximately 45 days of cauterization,

¹Department of Surgery, Medicine School, Universidade Federal de Juiz de Fora – Juiz de Fora (MG), Brazil.

²Medical Sciences and Health School, Medicine School, Universidade Federal de Juiz de Fora – Juiz de Fora (MG), Brazil.

the patient returned to the outpatient clinic with recurrence of the lesions (Figure 2).

After resurgence of the condylomatous lesions, weekly cauterizations with 70% trichloroacetic acid were elected as treatment. The procedure was performed for two months, but there was still recurrence of the symptoms (**Figure 3**).

Due to the systematic recurrence of the lesions, the treatment with *Thuya occidentallis* was chosen. After 30 days of application of a creamy formulation of *Thuya Occidentalis* (three times a week), the condylomatous lesions disappeared. However, the lesions reappeared after two months. Then, using Imiquimod for three weeks (three times a week) in a residual condyloma, a definite improvement of the lesions was finally observed (**Figure 4**).

DISCUSSION

The way infants acquire condyloma should be a priority in medical care. It is important to determine whether there is any evidence of sexual abuse and try to establish the origin of the virus. Faced with situations such as the suspicion of sexual abuse reported in this work, it is also essential that care is provided by a multidisciplinary team, ensuring a complete medical and social assessment^(7,11).

Suspicion of abuse should be raised regarding the following facts: the explanations about the lesion are vague or absent, there are different versions of the fact, and when the story is inconsistent with the physical findings^(12,13). In this context, the case reported here



Figure 1 – Multiple vegetative lesions conflowing in the perineal and perianal region, and perilesional erythema present in the first care, prior to any treatment.



Figure 2 – Recurrence of vegetative lesions 45 days after resection with electric scalpel.



Figure 3 – Papular lesions, in lower volume, relapsed in the perineal and perianal region after treatment with 70% trichloroacetic acid.

DRUMOND et al.

was submitted to a multidisciplinary team, communicated to the Child Protection Council, and after the sexual abuse by the father was confirmed, the Tutelary Council carried on with the legal-assistance measures.

Regarding the treatment of anogenital lesions in pediatric age, it is known that studies with this approach are still limited, with no consensus regarding the best method to be used. Thus, the therapeutic choice should be individualized and defined according to the experience of the service, since each therapeutic option presents its advantages and disadvantages, and there is no medication considered superior and capable of eliminating HPV so far⁽⁷⁾.

Treatments may be topical (destructive by chemical, physical, immunomodulator or excisional agents) or systemic⁽¹⁴⁾. Conventional treatment consists of the lesion chemical destruction through topical application of podophylin, 5-fluorouracil, trichloroacetic acid and podophyllotoxin. Physical destruction methods include cryotherapy, laser, electrocauterization, and surgical excision⁽¹⁵⁾.

Topical treatments, such as imiquimod 5% cream and podophylin 20%, are options that should be considered, whenever possible, as they are less traumatic and have fewer sequelae. However, studies are conflicting and there is no consensus asserting that such methods are effective and free from adverse effects in patients under 12 years of age. At the time the patient was attended at our service, there were scarce studies that verified the safety of Imiquimod 5% in infants, and its use was disregarded at first^(7,16,17).

Another therapeutic method used is the high-frequency surgery, used mainly in those cases with numerous lesions, a situation whose topical treatment with chemical agents could be toxic due to the quantity required. This procedure was elected first in this study



Figure 4 – After the treatment with Imiquimode.

since this was the case of the patient reported. It consists of applying a high frequency current to excise the affected site. The technique is relatively simple and quite cost-effective, since it is performed with local anesthesia and without the need for a surgery center⁽¹⁸⁾.

As the treatment for high-frequency surgery did not show the expected effect, it was thought to use trichloroacetic acid, given the importance of its destructive therapeutic effect that causes the hydrolysis of cellular proteins, leading to apoptosis, without systemic toxicity (unlike other topical methods). Other effects consist mainly of local symptoms, such as pain at the site of application, burning, and hyperpigmentation^(19,20). It is important to stand out, however, that the patient, despite demonstrating discomfort during the application of the acid, did not evolve with alteration of perilesional skin staining.

In refractory cases to standard treatments, as the one of this study, the use of phytotherapy may be an alternative. *Thuja occidentalis* is a phytotherapeutic option described in the literature. In folk medicine, the extract has been used to treat repetition bronchitis, enuresis, cystitis, psoriasis, uterine carcinomas, amenorrhea, and rheumatologic symptoms. *T. occidentalis* can be used orally or by topical application. It is known to cause significant increase of some inflammatory mediators in order to activate a local inflammatory response, showing a possible antiviral activity. However, further studies are needed to clarify their exact action mechanism⁽²¹⁻²⁴⁾.

Finally, due to the difficulty of complete resolution of the lesions based on this bibliography, the infant was submitted to imiquimode therapy. Imiquimod is a local application synthetic immunomodulating agent that acts on the innate and cellular immune system mediated by interferon alfa and tumor necrosis factor-alpha (IFN- α). Recent studies have shown that the imiquimod treatment in the child population shows good results, especially in lesions located in mucous membranes, where absorption is enhanced. The resolution of the lesions is usually obtained in 72 to 84% of the cases, and local recurrence rates range from 5 to 19%.

One of the main treatment advantages is the fact that it can be carried out at home and painless, as pain is a frequent symptom in destructive methods. Topical treatment is well tolerated, having as its main side effect contact dermatitis, occurring mainly in places of skin occlusion⁽¹⁷⁾. Although erythema is often reported in the literature, no important adverse effect occurred during the approach of the case presented in this report, and this was the definitive therapy for the resolution of recurrent lesions.

CONCLUSION

The observation of this specific case suggests that imiquimod may be a safe and effective therapeutic alternative for the treatment of condyloma in the pediatric population. However, data regarding treatment in this age group are scarce, which hinders the conduct of refractory cases to those known to be safe and described by the literature. Thus, the importance of developing more studies on the theme is reinforced. Moreover, although vertical transmission is the main form of transmission, sexual abuse should always be considered, since only the diagnostic suspicion from the health professional, as happened in this reported experience, is able to facilitate the investigation and conduct of the case.

Participation of each author

All authors contributed equally.

Funding

The authors declare there was no financing of any kind for this research

Conflict of interests

The authors declare no conflict of interests.

REFERENCES

- Marcoux D, Nadeau K, McCuaig C, Powell J, Oligny LL. Pediatric anogenital warts: a 7-year review of children referred to a tertiary-care hospital in Montreal, Canada. Pediatr Dermatol. 2006;23(3):199-207. https://doi.org/10.1111/j.1525-1470.2006.00218.x
- Rodrigues LRE, Portugal V, Rodrigues N, Nápoles S, Casanova C. Verrugas Anogenitais na Criança: A importância da Abordagem Multidisciplinar. Acta Med Port. 2011;24(2):367-70.
- Culton DA, Morrell DS, Burkhart CN. The management of condyloma acuminata in the pediatric population. Pediatr Ann. 2009;38(7):368-72. https://doi.org/10.3928/00904481-20090622-05
- Sinclair KA, Woods CR, Kirse DJ, Sinal SH. Anogenital and respiratory tract human papillomavirus infections among children: age, gender, and potential transmission through sexual abuse. Pediatrics. 2005;116(4):815-25. https://doi.org/10.1542/peds.2005-0652
- Unger ER, Fajman NN, Maloney EM, Onyekwuluje J, Swan DC, Howard L, et al. Anogenital human papillomavirus in sexually abused and nonabused children: a multicenter study. Pediatrics. 2011;128(3):e658-65. https://doi.org/10.1542/peds.2010-2247
- Costa-Silva M, Fernandes I, Rodrigues AG, Lisboa C. Anogenital warts in pediatric population. Ann Br Dermatol. 2017;92(5):675-81. http://dx.doi. org/10.1590/abd1806-4841.201756411
- Veasey JV, Dall'Antonia M, Miguel BAF, Mayor SAS, Campaner AB, Manzione TS. Condilomas anogenitais em crianças: análise descritiva de 20 casos. Surg Cosmet Dermatol. 2017;9(2):130-3. http://www.doi. org/10.5935/scd1984-8773.201792993
- Rizvi AA, Kanwar AJ, Goel S. Condyloma acuminata in a 3-year-old female: Sexual abuse or not? Indian J Pediatr Dermatol. 2016;17(3):221-2. http://doi.org/10.4103/2319-7250.179498
- Syrjänen S, Puranen M. Human papillomavirus infections in children: the potential role of maternal transmission. Crit Rev Oral Biol Med. 2000;11(2):259-74. https://doi.org/10.1177/10454411000110020801
- Thornsberry L, English III J. Evidence-based treatment and prevention of external genital warts in female pediatric and adolescent patients. J Pediatr Adolesc Gynecol. 2012;25(2):150-4. https://doi.org/10.1016/j. jpag.2011.10.004
- Percinoto ACC, Danelon M, Crivelini MM, Cunha RF, Percinoto C. Condyloma acuminata in the tongue and palate of a sexually abused child: a case report. BMC Res Notes. 2014;7:467. https://dx.doi. org/10.1186%2F1756-0500-7-467
- Hettler J, Greenes DS. Can the initial history predict whether a child with a head injury has been abused? Pediatrics. 2003;111(3):602-7. https://doi. org/10.1542/peds.111.3.602

- Swerdlin A, Berkowitz C, Craft N. Cutaneous signs of child abuse.
 J Am Acad Dermatol. 2007;57(3):371-92. https://doi.org/10.1016/j.jaad.2007.06.001
- Moresi JM, Herbert CR, Cohen BA. Treatment of anogenital warts in children with topical 0. 05% podofilox gel and 5% imiquimod cream. Pediatr Dermatol. 2001;18(5):448-50. https://doi.org/10.1046/j.1525-1470.2001.1980a.x
- Brás F, Sardinha R, Pacheco A. Modalidades terapêuticas no tratamento dos condilomas acuminados. Acta Obstet Ginecol Port. 2015;9(5):383-92.
- Forcier M, Musacchio N. An overview of human papillomavirus infection for the dermatologist: disease, diagnosis, management, and prevention. Dermatol Ther. 2010;23(5):458-76. https://doi.org/10.1111/j.1529-8019.2010.01350.x
- Brandt H, Patriota R, Belda Junior W, Fernandes J, Criado P. Tratamento do papiloma vírus humano na infância com creme de imiquimode a 5%. An Bras Dermatol. 2009;84(5):549-53. http://dx.doi.org/10.1590/S0365-05962010000400020
- Perlman SE, Lubianca JN, Kahn JA. Characteristics of a group of adolescents undergoing loop electrical excision procedure (LEEP). J Pediatr Adolesc Gynecol. 2003;16(1):15-20. https://doi.org/10.1016/ s1083-3188(02)00209-7
- Pezeshkpoor F, Banihashemi M, Yazdanpanah M, Yousefzadeh H, Sharghi M, Hoseinzadeh H. Comparative study of topical 80% trichloroacetic acid with 35% trichloroacetic acid in the treatment of the common wart. J Drugs Dermatol. 2012;11(11):e66-9.
- Jayaprasad S, Subramaniyan R, Devgan S. Comparative evaluation of topical 10% potassium hydroxide and 30% trichloroacetic acid in the treatment of plane warts. Indian J Dermatol. 2016;61(6):634-9. https:// doi.org/10.4103/0019-5154.193670
- Bodinet C, Lindequist U, Teuscher E, Freudenstein J. Effect of an orally applied herbal immunomodulator on cytokine induction and antibody response in normal and immunosuppressed mice. Phytomedicine. 2002;9(7):606-13. https://doi.org/10.1078/094471102321616418
- Bodinet C, Freudenstein J. Effects of an orally applied aqueous-ethanolic extract of a mixture of Thujae occidentalis herba, Baptisiae tinctoriae radix, Echinaceae purpureae radix and Echinaceae pallidae radix on antibody response against sheep red blood cells in mice. Planta Med. 1999;65(8):695-9. https://doi.org/10.1055/s-1999-14044
- 23. Gohla SH, Haubeck H-D, Schrum S, Soltau H, Neth RD. Activation of CD4-positive T cells by polysaccharide fractions isolated from the Cupressaceae Thuja occidentalis L. (Arborvitae). In: Neth R, Gallo RC, Greaves MF, Gaedicke G, Gohla S, Mannweiler K, et al., editors. Modern Trends in Human Leukemia VIII. Berlin: Springer; 1989. p. 268-72.
- Torres A, Vargas Y, Uribe D, Carrasco C, Torres C, Rocha R, et al. Proapoptotic and anti-angiogenic properties of the α/β-thujone fraction from Thuja occidentalis on glioblastoma cells. J Neuro Oncol. 2016;128(1):9-19. https://doi.org/10.1007/s11060-016-2076-2

Address for correspondence: GABRIEL DUQUE PANNAIN

Rua Itamar Soares de Oliveira, 211, apt. 202 – Cascatinha Juiz de Fora (MG), Brazil

CEP: 36033-260

E-mail: gabrielduquep@gmail.com

Received on: 06.11.2019 Approved on: 09.30.2019