

Treatment of Anogenital Warts in an 18-month-old Girl with 5% Imiquimod Cream

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SUMMARY Possible modes of transmission of the human papilloma virus (HPV) in children include perinatal transmission, sexual transmission, or extragenital contact. Conventional treatment options with chemical and physical destruction methods can be difficult and painful and often require general anesthesia. Imiquimod is a topically active immunomodulatory agent that has been shown to successfully treat pediatric anogenital warts. We report on a case of extensive anogenital warts in a 18-month-old girl who was successfully treated with topical 5% imiquimod cream.

KEY WORDS: anogenital warts, children, imiquimod

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INTRODUCTION

Condyloma acuminatum, i.e. genital warts, are caused by infection with the human papilloma virus (HPV), mostly by low risk HPV 6 and 11. The incidence of anogenital warts in children is unknown but is suspected to be on the rise based on the increase in adult HPV infections (1). Perinatal infection may occur transplacentally via amniotic fluid during gestation and delivery, and through direct exposure to cervical and genital lesions during birth. In addition to sexual abuse, postnatal infections can be acquired through heteroinoculation or autoinoculation from nongenital mucocutaneous HPV sources and fomite transmission (2). Several studies have demonstrated that HPV can be acquired in the neonatal period, persisting in some infants for up to 26 months (3). Surgical treatment options include cryotherapy, laser vaporisation, electrocautery, and excision. These methods are

painful, often requiring general anesthesia, with recurrences being common. Nonsurgical approaches in children include the use of podophyllotoxin and imiquimod. Although some studies demonstrate their safety and efficacy, these drugs are not approved for use in children under 12 years of age (1,4).

We report on a 18-month-old girl with extensive anogenital warts who was successfully treated with topical 5% imiquimod cream.

CASE REPORT

A healthy 18-month-old female child was referred to our Department of pediatric and adolescent gynecology, Children's Hospital Zagreb, with a 7-month history of anogenital warts. The girl was born by Caesarean section because of pelvic presentation. She

was a healthy child until the warts started to grow. She was previously unsuccessfully treated with 5-fluorouracil cream, fluorouracil and salicylic acid solution, 50% and 80% trichloroacetic acid, as well as cryotherapy in another institution. The father reported genital warts 5-months ago, when he was treated by cryotherapy. He was evaluated by our dermatologist, and had no evidence of genital warts at the time. The mother was also evaluated, but no symptoms of HPV infection were found, and she had no history of genital warts.

Physical examination of the child was normal except for the presence of multiple skin-colored, confluent verrucous papules affecting the vulva and perianal region (Figure 1). Gynecological examination showed no abnormalities. The hymen was intact, and there was no evidence of ulcerations or other signs of trauma to the vaginal or anal orifices. A biopsy of the warts was performed under local anesthesia and low risk HPV was confirmed using Digene Hybrid Capture II test. The histologic picture was typical for hyperproliferative papilloma, showing abundant koilocytosis and being compatible with condyloma.

The girl was treated with 5% imiquimod cream, applied at home to the lesions three times a week, before bedtime. After 8 to 10 hours, the cream was removed by washing the treated area with mild soap and water. The mother and child visited our hospital every 3-4 weeks and at every visit, there was evident reduction in the number and size of warts. Treatment was continued for a total of 11 weeks, during which time the lesions cleared almost completely (Figure 2).



Figure 1. Multiple skin-colored, confluent verrucous papules in the vulvar and perianal regions, prior to treatment.

At the end of the imiquimod treatment, the remains of three small papules fell down spontaneously 3 days later, and complete clearance of the lesions was achieved. Only one adverse effect was recorded, a one-day burning of the perilesional skin. No systemic adverse effects were noticed. After eighteen months of follow-up there was no evidence of recurrence.

DISCUSSION

Condylomata acuminata are anogenital warts caused by the human papilloma virus (HPV), mostly by low risk HPV 6 and 11, but types 1, 2, 16, and 18 are also found. The highest risk population for HPV infection are sexually active young people under the age of 26, especially sexually active adolescents. Condyloma in the children under the age of 3 years is commonly believed to be vertically transmitted from a virally infected genital tract or through caretakers with hand warts (3). Although genital warts in small children may be vertically transmitted, sexual abuse must always be ruled out through social history and physical examination for signs of abuse (5,6). In our case, there was no evidence of sexual abuse on clinical examination, although the girl's father had been treated for genital condyloma several months ago. In this case, the probable route of transmission is non-sexual, close contact with her father in his role as a caregiver.

Diagnosis of anogenital warts is usually made on physical examination. A biopsy and HPV detection using Digene Hybrid Capture II test can also be done to detect the viral type or if the diagnosis is question-



Figure 2. Total regression of lesions after 11 weeks of imiquimod treatment.

able, or when child abuse is suspected. In our patient, we have did both diagnostic tests which established the diagnosis of *condylomata acuminata*.

Treatment of lesions resulting from HPV should be individualized. The conventional therapy treatment includes chemical and physical destruction of the lesions. They often require the use of anesthesia, and recurrences of the lesions are common (7). Our patient was treated with most of the conventional methods, but without any result.

Imiquimod is a topically active immunomodulatory agent that induces keratinocytes to produce interferon alfa and other cytokines in order to inhibit viral replication. Imiquimod also enhances cell-mediated immunity (8). The use of imiquimod for pediatric anogenital warts has been reported to be an effective treatment (7,9-11,14). An overview of these results was presented by Masuko *et al.* (8). We have modified their table with new cases (Table 1). In these studies, duration of treatment was between 2 and 12 weeks. Duration of therapy in our case was 11 weeks, and the rest of three small papules resolved spontaneously three days after the therapy with imiquimod was finished. Complete clearance of the lesions was

achieved. Imiquimod treatment has been shown to be a successful treatment for *condylomata acuminata* in adults and long-lasting cutaneous warts and molluscum contagiosum in children. Clearance of external warts is achieved in 72% to 84% of the cases, and local recurrence rates were 5%-19% (12). In case of incomplete resolution, some authors suggest that a combination of imiquimod and destructive methods may play a role in the treatment of extensive condyloma (12).

Overall, 5% imiquimod cream is well tolerated. The most common adverse reactions include erythema, burning, itching, and tenderness, frequently limited to application sites. Less than 1% of the cream applied topically is absorbed systemically. Side effects are usually mild and well-tolerated (13). Although the treatment in our case lasted 11 weeks, only mild one-day burning was present.

CONCLUSION

Therapy with imiquimod has many advantages, such as easy, painless application at home, mild side effects, and a low recurrence rate. It is safe and tolerable in children. Disadvantages include the high price

Table 1. The use of imiquimod 5% cream for pediatric anogenital warts. Modified table from Masuko *et al.* (8).

Publication year	Authors	Faculty	Age	Sex	Area	Duration of therapy	Outcome	Side effects	No recurrence
2001	Gruber and Wilkinson	UK	2 years	Boy	Perianal	5 weeks	Cleared	Mild pruritus	15 months
2001	Moresi <i>et al.</i>	USA	<2 years (n=2) 2-5 years(n=3) >5 years(n=3)	Four boys Four girls	Perianal: eight Genital lesions: one Boy and one girl	2 months for four. 3-4 months for four	Cleared in six Remained in two	Few or none in four Itching in one Redness in one Irritation in two	6-12 months in six patients
2001	Schaen and Mercurio	USA	6 months	Girl	Perianal + vulvar	3 weeks	Cleared	None	No date
2003	Mayewski <i>et al.</i>	Poland	19 months	Boy	Perianal	8 weeks	Cleared	Local erythema	6 months
2007	Campaner <i>et al.</i>	Brazil	7 years	Girl	Perianal + vulvar	12 weeks	Add electrocautery	Local erythema, burning, and itching	6 months
2010	Masuko	Japan	28 months	Girl	Perianal + vulvar	7 weeks	Cleared	None	4 weeks
2010	Clivati Brand <i>et al.</i>	Brazil	1 year 2 years 18 months 2 years	Boy Boy Girl Girl	Perianal Perianal Perianal Perianal+ vulvar	4 weeks 3 weeks 4 weeks 3 weeks	Cleared Cleared Cleared Cleared	None Local erythema None None	6 months in all
2012	Leclair <i>et al.</i>	Canada	3 years	Girl	Perianal+ groin +glutea	6 weeks	Cleared	Minor redness	24 months
2013	Our case	Croatia	18 month	Girl	Perianal+ vulvar	11 weeks	Cleared	Mild local burning	18 months

of the cream, especially in long term application. Imiquimod could be the first line of treatment for extensive condyloma in children. Despite the excellent response to imiquimod, careful long-term follow-up is indicated because of the risk of recurrences and unknown risk of development of anogenital neoplasia.

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