Anogenital giant condyloma in an infant with liver transplantation

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Abstract

Human papillomavirus (HPV) types 6 and 11 were detected in a 3-year-old girl with extensive anogenital condylomata. Although sexual abuse must be considered, non-sexual transmission is evident in at least 57% of children with anogenital warts. Perinatal transmission may occur in approximately 24.5% of infants born to HPV-positive mothers. We present an immunosuppressed child with giant condylomata and discuss transmission, work up, and treatment.

Keywords: condyloma, human papillomavirus, imiquimod, liver transplantation, tacrolimus

Introduction

Anogenital condyloma acuminatum is a common sexually transmitted disease among females and males [1]. The causal role of human papillomaviruses (HPV) in anogenital condyloma formation has been firmly established biologically and epidemiologically [2]. The immune system effectively repels the majority of HPV infections and is associated with cutaneous cell-mediated immune responses. However, approximately 10% of individuals develop a persistent infection [1]. Human papillomaviruses are classified into high- or low-risk types depending upon the oncogenic potential. Low-risk types 6 and 11 are isolated in approximately 90% of genital wart cases [2]. A number of treatment options are available for anogenital warts [3], including topical ointments, cryotherapy, laser vaporization, electrosurgery, and surgical excision. However, there is no treatment for pediatric patients approved by the Food and Drug Administration. Herein, we present a pediatric patient with rapidly increasing anogenital condyloma after liver transplantation. Combination therapy with topical imiquimod and CO_2 laser therapy was effective and contributed to improve the patient's quality of life.

Case Synopsis

A three-year-old girl was evaluated in our clinic with enlarging, papules and nodules of two-months' duration. There was a decrease in quality of life because of dysuria. She had a medical history of Alagille syndrome and received liver transplantation at the age of eight months. Oral tacrolimus had been given since the operation and continued at a maintenance dose. Physical examination revealed cauliflower-like lesions consisting of multiple, dark brownish papules and nodules aggregated on the anogenital region (**Figure 1**). There were no other surrounding lesions suspicious of warts.

The histology of a skin biopsy taken from the labia majora revealed a thick, outward epidermal proliferation (**Figure 2**). On high-power magnification, there were no atypical nuclei or koilocytes in the epidermis. Immunohistochemistry using anti-HPV polyclonal antibody staining (Dako Japan, Japan) showed a negative finding in the epidermis. We performed a genetic analysis of the biopsied lesional skin using TaKaRa PCR Human

Figure 1. *Multiple, dark brownish papules and nodules were observed on the external anogenital area.*

Papillomavirus Typing kit (Takara Bio Inc., Japan). Genomic DNA was extracted from a paraffin-embedded tissue section. The presence of HPV DNA including types 6 and 11 was detected and confirmed by PCR using the primer pairs provided in the set and agarose gel electrophoresis (**Figure 3**, lane 1, 228 bp). The PCR product digested by AfaI was divided into two DNA fragments (**Figure 3**, lane 2, 132 and 96 bp), which indicated the presence of HPV type 6 DNA. HPV DNA testing was not performed in her parents because they had no obvious HPV-associated skin or mucous lesions. Laboratory tests showed increased white blood cell counts (11400/μL), AST (37IU/L), LDH (295IU/L), ALP (711IU/L), and total bile acid (34.9μmol/L), and syphilis tests were negative. Because the patient was intolerant to cryotherapy, treatment with imiquimod 5% cream was initiated (3 times weekly). At the end of 16 weeks of therapy, some lesions were still present. Residual condylomata were treated with CO_2 laser ablation and completely disappeared without scar formation.

Discussion

Herein, we report a pediatric child with rapidly progressive anogenital giant condylomata. Giant condyloma exhibits extensive growth of cauliflower-like lesions on the genital and/or perianal region, which in children, occurs less frequently than in adults. Not only immunosuppressed children with human immunodeficiency virus infection [4], but also healthy children may develop rapidly progressive anogenital giant condyloma [5]. The present case underwent liver transplantation and oral tacrolimus was administered. A similar case was reported in a male renal transplant recipient on tacrolimus, who developed urethral condyloma acuminata [6]. In addition, the incidence of anogenital HPV infection is increased by 17-fold in immunosuppressed renal transplant patients [7]. Post-transplant immunosuppression may promote the development of anogenital condylomata. In organ transplant patients, rates of HPV infection increase with increased severity and duration of immunosuppression, because the reduced cytotoxic T-lymphocyte reactivity to HPV oncoproteins leads to impaired ability to clear HPV [8].

Generally, the proposed mechanism for perinatal and genital transmission includes vertical transmission, autoinoculation, sexual transmission, and indirect transmission through contaminated objects and surfaces. Childhood sexual abuse must also be considered in all children presenting with anogenital giant condyloma, although it occurs in higher frequency in older children [9]. In 57% of children with anogenital warts, HPV infection results from non-sexual transmission [10]. Although the parents of our patient had no complaints associated with HPV infection, we considered both perinatal transmission and indirect contact with contaminated

Figure 2. *A skin biopsy specimen from the labia majora showed a thick, outward proliferation with no atypical nuclei or koilocytes in the epidermis. H&E, 40×.*

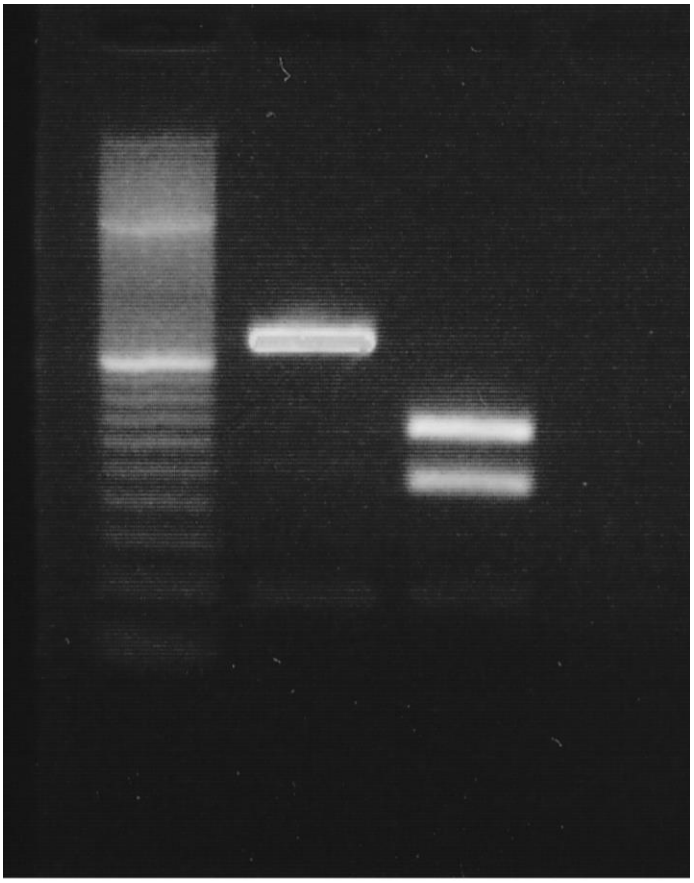

Figure 3. *Presence of human papillomavirus (HPV) DNA was determined by PCR and restriction enzyme analysis using a TaKaRa PCR Human Papillomavirus Typing kit (Takara Bio Inc., Japan). Genomic DNA was extracted from paraffin-embedded tissue section. The presence of benign HPV DNA including types 6 and 11 was detected by PCR and agarose gel electrophoresis (lane 1, 228 bp). The PCR product digested by AfaI was divided into two DNA fragments (lane 2, 132 and 96 bp), which indicate the presence of HPV type 6 DNA.*

fomites. Perinatal HPV transmission through the birth canal is reported in 24.5% of children delivered by HPV-positive mothers [11]. Juvenile onset recurrent respiratory papillomatosis, which is mostly caused by HPV types 6 or 11, is perinatally acquired from an HPV-infected mother. It is known to develop at 2-3 years of life [12]. Because HPV-associated lesions could clinically appear later, there is a possibility that latently infe cted HPV, transmitted through the birth canal, is involved in development of the genital condyloma.

Anogenital condylomata are commonly associated with HPV types 6 and 11. In the present case, HPV type 6 DNA was detected in the lesional skin by analysis of PCR products. Shimizu et al. reported an adult case of pigmented condyloma acuminatum related to HPV type 6 in the genital region, resembling seborrheic keratosis [13]. On the other hand, an adult case of seborrheic keratosis of the vulva clinically mimicking a genital wart was reported [14]. Differentiation between condyloma and seborrheic keratosis in the genital area is sometimes difficult; in these cases, HPV typing is useful for diagnosing the disease.

Although pediatric genital warts may resolve spontaneously, the treatment of extensive perianal genital warts in children can be challenging. It has been reported that imiquimod 5% cream is an effective treatment option for children with extensive and rapidly progressive perianal warts. In our case, topical imiquimod cream was partially effective; however, some lesions remained despite applying the cream for 16 weeks. The reason may relate to the large size and administration of immunosuppressant may have reduced the therapeutic effects of imiquimod. Carbon dioxide laser therapy in combination with photodynamic therapy is also effective in treating genital condylomata and preventing recurrence [15]. A combination of various treatment strategies for treatment of recalcitrant giant condyloma is needed especially in immune-compromised patients.

Conclusion

We present a 3-year-old girl with giant anogenital condylomata arising after liver transplantation. In an immunosuppressed state, condylomata tend to grow rapidly and be less responsive to conventional treatments. In our case, combination therapy with imiquimod 5% cream and CO_2 laser ablation was effective. Her giant condylomata completely resolved without scar formation. For recalcitrant giant condyloma, combination therapy is generally required.

Potential conflicts of interest

The authors declare no conflicts of interest.

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