Successful Treatment of Anogenital Wart with a Topical Vitamin D₃ Derivative in an Infant

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Key Words
Treatment · Topical vitamin D₃ derivative · Anogenital wart · Infant

Abstract
Anogenital warts are an infectious disorder of the anogenital lesion caused by one or more human papilloma viruses. Verruca is commonly treated with freezing with liquid nitrogen, laser therapy or application of imiquimod. Such ablative treatment may cause pain and scars on the anogenital lesion. We herein report an infant case of anogenital wart which was successfully treated with a topical vitamin D₃ derivative. Topical application of a vitamin D₃ derivative may be an alternative therapy for anogenital warts in infants.

Introduction
Anogenital warts are an infectious, proliferating disorder of the anogenital lesion caused by one or more human papilloma viruses (HPVs). In the United States, anogenital warts are treated with patient-applied chemical treatment of imiquimod and podofilox, physician-applied chemical treatment of podophyllin resin and trichloroacetic acid, and ablative treatment of cryotherapy with liquid nitrogen and laser therapy [1]. Recently, treatment with topical vitamin D₃ derivatives has been reported to be effective for HPV-infected verruca [2–6]. Here, we report an infant case with an anogenital wart on the anus, which was successfully treated with calcipotriene ointment, a vitamin D₃ derivative.

Case Report
A 1-year- and 1-month-old male presented with an anogenital wart on the anus without suspicious episodes of infection (fig. 1). The parents had no experience with anogenital warts. The wart did not
invasive into the rectum and colon. After obtaining informed consent from the parents, we treated the wart with a topical vitamin D3 derivative of calcipotriene ointment with simple application to the affected lesion twice a day. An initial response of partial regression was observed 2 months later. The apparent regression was achieved 3 months later. Complete regression was confirmed 4 months later (fig. 2). The anogenital wart did not recur for 6 months after complete regression.

Discussion

Anogenital warts are uncommon in children. Skin biopsy and identifying the type of HPV are required to diagnose precisely. Unfortunately, we could not take biopsies from the affected lesion. Therefore, our diagnosis was only based on the clinical appearance. Anogenital warts in children have been reported to be associated with both mucosotropic (HPV6 and 11) and cutaneotropic types (HPV2) of the virus [7]. Recent investigation of HPV typing in nonabused preschool children showed that 3 (1.8%) of 211 children had clinically detectable anogenital warts and that 7 samples from 5 children were HPV-positive (HPV6 and/or 16), detected by polymerase chain reaction [8]. As our patient had anogenital wart only on the mucocutaneous lesion, we surmise that our case was a nonabuse case of anogenital wart caused by mucosotropic HPV.

Verruca is usually treated with freezing with liquid nitrogen, laser therapy or application of imiquimod. Such ablative treatment may cause pain and scars. Especially, scarring may entail dysfunction of the anus and genital lesion. Topical imiquimod and podofilox were not available in Japan at that time. We medicated the patient with a therapy for the anogenital wart with a topical vitamin D3 derivative. Our case was successfully treated with simple application of calcipotriene ointment to the lesion. Using diapers for the infant patient may bring the occlusive condition.

Previously, the effect of vitamin D3 derivatives on verruca was speculated to be derived from its potential to regulate epidermal cell proliferation and differentiation and to modulate cytokine production [2, 3]. An important observation was reported which suggested that toll-like receptor (TLR) activation of human macrophages upregulated expression of vitamin D receptor and vitamin D-1-hydroxylase genes, leading to induction of the antimicrobial peptide [9]. This suggests an association of TLRs and vitamin D-mediated innate immunity [9]. Treatment with imiquimod for anogenital warts in an infant was shown to be highly effective [10]. Imiquimod induces the secretion of proinflammatory cytokines and the reaction of antitumor and antiviral cellular innate immunity through TLR 7- and 8-signaling cascade. We surmised that imiquimod and vitamin D3 derivatives, to some extent, share the same antiviral efficacy.

Previously, Egawa reported the effectiveness of a topical vitamin D3 derivative for condylomata acuminata on the corona and glans in a 74-year-old man with simple application twice a day for 4 months [6]. The infected duration of anogenital warts in adults varies from a few weeks to many years [11]. It took 4 months for the treatment of the anogenital wart in our infant patient. The possibility of a potent placebo effect was not excluded. A prospective placebo-controlled study is required to evaluate the actual efficacy.

We reported an infant having anogenital wart successfully treated with a vitamin D3 derivative without developing pain, scar or dysfunction. We propose that topical application of a vitamin D3 derivative may be an alternative therapy for anogenital warts in infants.
**Fig. 1.** Anogenital wart on the anus before treatment.

![Anogenital wart before treatment](image1)

**Fig. 2.** Complete healing of the anogenital wart 4 months after starting treatment with topical application of a vitamin D₃ derivative.

![Complete healing after treatment](image2)
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