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Disseminated molluscum contagiosum in a HIV-positive child. Improvement after therapy with 5% imiquimod.

Martin Theiler, Werner Kempf, Katrin Kerl, Lars E. French, Günther F.L. Hofbauer

Department of Dermatology, University Hospital, Zurich, Switzerland.

Corresponding author:

Günther Hofbauer, MD

Department of Dermatology

University Hospital

CH-8091 Zurich

Switzerland

E-mail: *hofbauer@usz.ch*

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Abstract

Background: Molluscum contagiosum (MC) is a frequent and usually benign cutaneous infection with molluscum contagiosum virus (MCV), affecting mainly children and young sexually active adults. With the emergence of HIV/AIDS, a new patient group at risk has been identified with often extensive skin involvement and recalcitrant disease.

Main observations: We report a case of a girl with connatal HIV-infection, suffering from extensive, disseminated MC. Due to multi-resistance, an effective antiretroviral therapy could not be established for years, rendering an effective treatment of MC by established treatment options virtually impossible. An off-label use of imiquimod showed a marked improvement of lesion counts in this patient, whereas a complete clearance could only be achieved once effective antiretroviral therapy was introduced.

Conclusions: We believe that imiquimod may represent a valuable treatment option for molluscum contagiosum especially in the context of marked immunosuppression, where sensitive areas like the face and neck are often involved and scarring must be avoided. (*J Dermatol Case Rep.* 2011; 5(2): 19-23.)

Introduction

Molluscum contagiosum (MC) are very common cutaneous warts caused by molluscum contagiosum virus (MCV), a double-stranded DNA virus of the poxvirus family. The typical clinical presentation consists of small, umbilicated, skin-coloured, pearly papules with predilection of the trunk, axillae, antecubital and popliteal fossae and genital area. Incidence first peaks in pre-school children.[1] A second incidence peak occurs in young adults, where the condition is generally considered a sexually transmitted infection. HIV-positive patients were identified as a risk group in the 1980's with incidence rates of up to 18% in infected individuals.[2-4] An inverse correlation between the number of molluscum lesions and CD4-cell-counts could be demonstrated, identifying MC as a marker for pronounced immune dysfunction in this patient group.[3] Immunosuppressed patients often show extensive disease with frequent involvement of face, neck and genital area and atypical clinical presentation.[5] In advanced stages of immunosuppression, giant or verrucous forms of MC may occur.[6,7]

In immunocompetent individuals, lesions usually clear spontaneously within several months or years, whereas in immunosuppressed patients, the disease tends to take a more chronic course and often is unresponsive to various treatments. Many different therapeutic options for MC have been described, which can be divided into destructive, cytotoxic, antiviral and immune-modifying modalities.[8,9] Lately, particular interest has been paid to the topical immune modulator imiquimod, a member of the imidazoquinoline family. Imiquimod stimulates TLR7 and TLR8, inducing an antiviral local immune response.[10] Several trials showed good clinical response of molluscum lesions to treatment with imiquimod, although mainly in immunocompetent patients.[9,11-15] Limited data on the use of imiquimod in adult HIV-positive individuals is available,[16-19] mainly on the basis of case reports or small case series.

Here, we report a case of extensive MC in a girl with connatal HIV-infection who showed improvement of her lesions with topical imiquimod. Complete clearance of all lesions could only be achieved once highly active antiretroviral therapy was established.

Case report

An 11-year-old girl with connatal HIV-infection presented to our out-patient clinic for immunosuppressed patients with extensive, confluent, umbilicated papules on all extremities and the trunk. Lesions had first appeared several months before presentation. A clinical diagnosis of extensive giant MC was confirmed by histology (Fig. 1). At the time, the patient was on antiretroviral therapy, but due to multi-resistance, the viral-load was high at 183927 copies/mL, and CD4-cell counts were at 160/µL, consistent with a marked suppression of cellular immunity. Atopy was present based on personal history and skin tests, which constitutes a risk factor for extensive MC disease.[20]

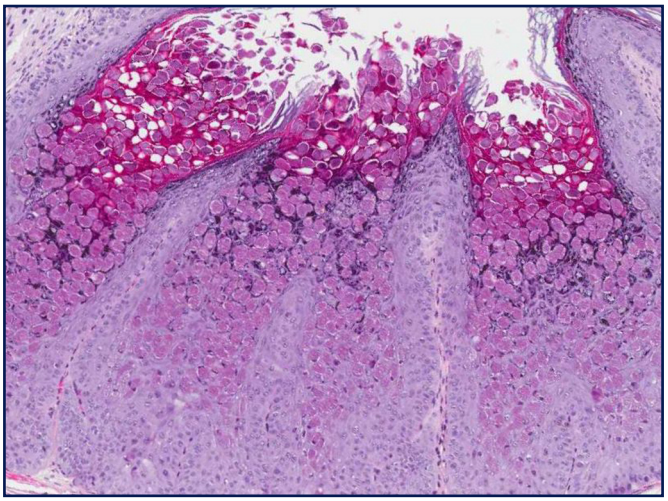


Figure 1

Histology of MC in our patient showed lobulated, endophytic hyperplasia of the epidermis and typical intracytoplasmic viral inclusions.

Surgical removal of several lesions had been performed before, resulting in significant scarring. The patient at the time declined further cryotherapy or curettage. Because of the widespread disease, we prescribed off-label imiquimod 5%-cream on the right leg. The left side was treated with salicylic acid 5% in petrolatum only. Application of imiquimod three times weekly showed no significant improvement after 3 months. We therefore stepped up the treatment to 5 weekly applications under occlusion on the right leg. Eight weeks with 5 applications weekly under occlusion showed a remarkable improvement of the treated area (Fig. 2). Treatment was therefore continued. Apart from mild erythema, there were no relevant side effects observed or reported by the patient. After 7 months of treatment, an approximately 50% improvement compared to the untreated regions could be documented, while irritation with progressive extent of the lesions was seen in the area treated with salicylic acid 5% in petrolatum (Fig. 2).

With the emergence of new anti-retroviral agents, highly active anti-retroviral therapy (HAART) could be established 4 years later. With CD4-cell counts returning to normal levels, clearance of almost all remaining mollusca was achieved. Remaining lesions were removed surgically with significant scarring as a result. On continued and effective HAART, the patient has remained free of mollusca contagiosa since 20 months.

Discussion

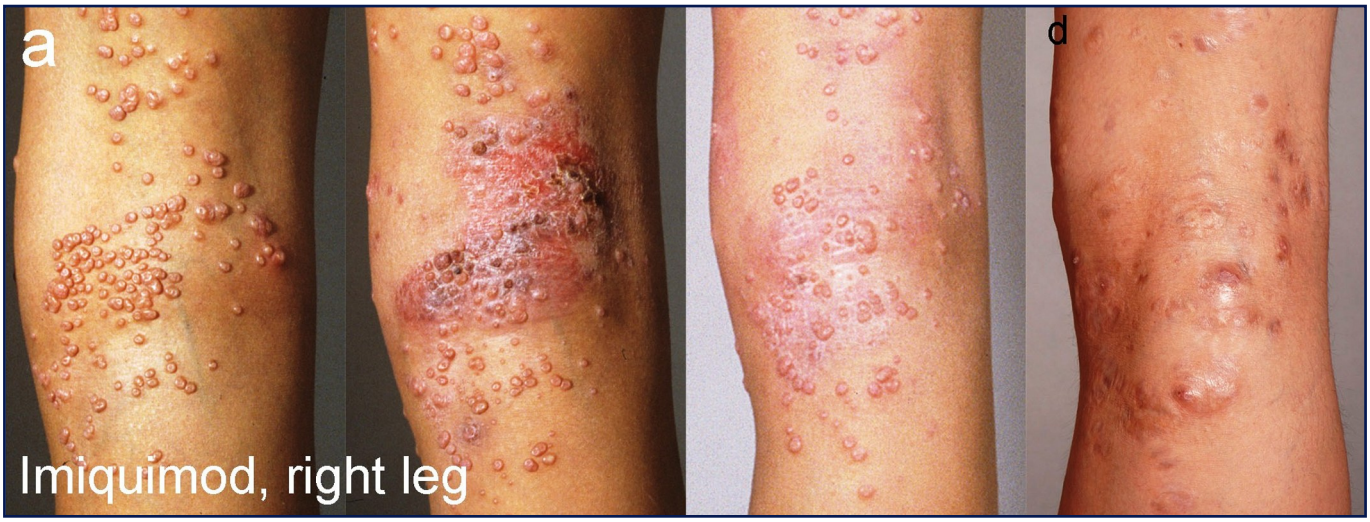
MC usually resolve spontaneously after several months to years in immunocompetent individuals. Lesions may spread, however, until they eventually resolve. Outcomes are less favorable in immunosuppressed individuals.[4] Therefore, treatment is generally advised to prevent sexual transmission, autoinoculation and potential scarring and is often requested by the affected patients.[21]

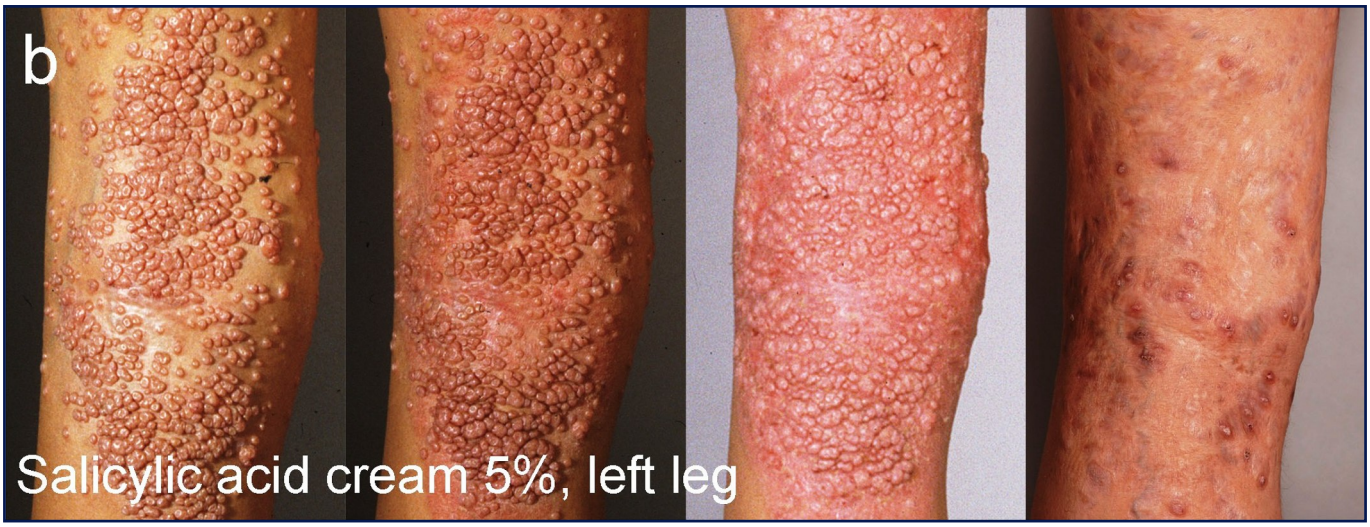
MCV has different mechanisms of evading host immune responses. It produces chemokines which result in inhibition of monocyte function and leukocyte migration into the site of infection.[8] Correspondingly, a reduced number of Langerhans cells, the main antigen presenting cells of the epidermis, could be demonstrated in areas of molluscum lesions both in immunocompetent and immunodeficient individuals.[22] Further, MCV encodes for a major histocompatibility complex (MHC) I-like heavy chain homolog that lacks important parts for peptide binding and presentation and might therefore interfere with presentation of MCV antigens on the surface of infected cells.[23] Additionally, MCV produces a caspase 8 inhibitor, resulting in decreased apoptosis secondary to death-receptor signals like FAS and thus prolonged survival of infected cells.[24]

Imiquimod, a member of the imidazoquinoline family, has potent antiviral and antiproliferative properties. It induces the production of a wide range of proinflammatory and antiviral cytokines like interferon-α, IL-12, TNF-α and interferon-γ[10,25] followed by the activation of innate and Th1-weighted acquired immunity. An activation of Langerhans cells with upregulated antigen presentation and increased migration to the draining lymph nodes could be shown.[26] Moreover, imiquimod seems to directly induce apoptosis independent of death-receptors via the mitochondrial pathway.[27]

These observations provide a good rationale for the use of imiquimod in viral infection. Indeed, a strong antiviral efficacy has been demonstrated in numerous trials on condylomata acuminata (HPV),[28] but there is increasing evidence from open as well as double-blind, controlled trials for good clinical results in infections with MCV,[9,11-15] also in comparison to other established treatment options.[9,13] Furthermore, imiquimod led to successful outcome of MCV in immunocompromised patients, although primarily reported as single cases.[16-19,29] Compared with many destructive therapies, imiquimod is atraumatic, usually non-scarring and therefore well suited for use in children. A recent safety study on imiquimod showed good tolerability in this patient group.[30]

We could observe a good clinical response to treatment with imiquimod in our patient as compared to the opposing leg treated only with salicylic acid 5% in petrolatum. Complete clearance, however, was not achieved. Occlusive treatment resulted in increased efficacy probably due to the improved penetration of the drug. Complete cure was reached after establishment of a highly active antiretroviral therapy and





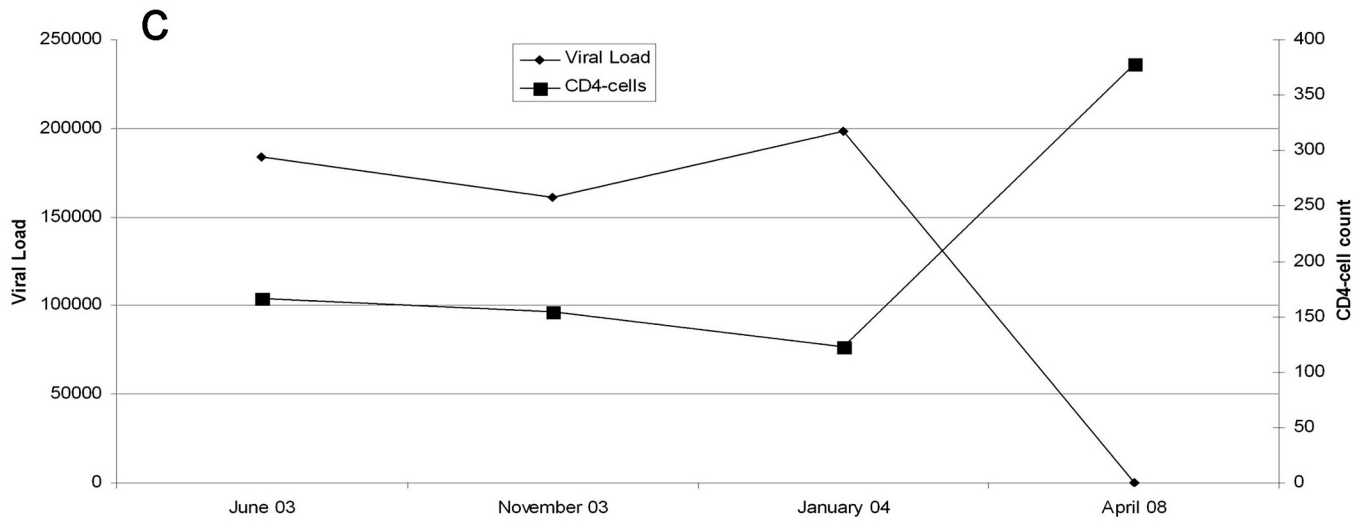


Figure 2

Clinical course of MC with (a) imiquimod, (b) salicylic acid 5% in petrolatum over time. Panel (c) shows CD4 count and HIV viral copy number.

surgical treatment of the remaining lesions, which resulted in significant scarring. Healing of the lesions under HAART has been described and is somewhat intuitive,[31,32] although a risk of a deterioration in the context of the immune reconstitution inflammatory syndrome has been reported.[33]

Conclusion

Reconstitution of normal immunologic function where possible remains the mainstay of therapy for MC in immunocompromised patients. Nevertheless, we think that imiquimod seems a valuable therapeutic option in immunosuppressed patients with recalcitrant MC infection of the skin, where extensive disease frequently affects sensitive areas like the face and neck and therefore scarring must be avoided.

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