Extensive Chemical Burns in a Child from Misuse of Cantharidin: A Case Report

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ABSTRACT

Molluscum contagiosum (MC) is typically a benign and self-limited viral infection affecting the skin. When treatment of MC is requested, application of cantharidin in a physician's office is generally a safe, effective and commonly used treatment option for MC. Its misuse, however, can result in rare but significant adverse outcomes. This case report details an unfortunate incident of a child who developed a severe chemical burn as a result of misuse of Cantharidin 1% – Podophyllin – Salicylic Acid (Canthacur-PS) for the treatment of MC. Furthermore, it highlights the importance of physician familiarity with the poxvirus infection, the indications to treat MC in immunocompetent children, and the various treatment options, including the safe administration and potential complications of cantharidin. In children, cantharidin can easily and safely be applied to lesions in a non-traumatic and controlled manner in the physician's office. Caregiver education on the post-treatment management and early signs of potential complications may also prevent similar adverse outcomes from cantharidin misuse.

RÉSUMÉ

Le molluscum contagiosum (MC) est une infection virale généralement bénigne et spontanément résolutive affectant la peau. L'application de cantharidine dans un cabinet de médecin est une option thérapeutique sécuritaire, efficace et couramment utilisée pour traiter le MC. Toutefois, son mauvais usage peut entraîner des effets indésirables rares, mais importants. Cette étude de cas décrit l'incident malheureux d'un enfant ayant développé une brûlure chimique sévère en réponse à un mauvais usage de Canthacur-PS, qui contient de la cantharidine 1 %, de la podophylline et de l'acide salicylique, pour le traitement du MC. En outre, elle met en évidence l'importance pour les médecins de bien connaître cette infection au poxvirus, les indications de traitement du MC chez les enfants immunocompétents, et les options de traitement disponibles, incluant l'administration sécuritaire et les complications possibles de la cantharidine. Chez les enfants, la cantharidine peut facilement être appliquée aux lésions de manière sécuritaire, contrôlée et non traumatique dans un cabinet de médecin. La formation des soignants sur la prise en charge post-traitement et les signes précurseurs de complications possibles à la suite d'un mauvais usage de la cantharidine pourrait également aider à prévenir des effets indésirables similaires.

Molluscum contagiosum (MC) is a common childhood mucocutaneous viral infection characterized by small, discrete, dome-shaped, umbilicated papule(s) [1]. It is caused by the MC virus, in the Poxviridae Molluscipox genus. The epidermis is commonly inoculated at sites of impaired skin barrier function from direct minor trauma, such as from scratching or shaving [2]. The disease predominantly affects immunocompetent children, but can be more extensive in the setting of immunosuppression. In adults, it is often sexually transmitted and immunocompromised individuals are more susceptible, most notably in the setting of human immunodeficiency virus infection. Reported prevalence of the disease varies widely across the literature. It is estimated that MC virus affects approximately 4.6% of children in the United States and its incidence has been rising since the 1960s [1].

In immunocompetent children, MC is benign and self-resolves within a few months to years without active treatment. At times, the lesions can be widespread, distressing to the patient- particularly when present on the face- and may be associated with a molluscum dermatitis, potentially exacerbating underlying atopic dermatitis. Following an inflammatory host immune response to virally infected lesions, patients can also develop an id reaction-like eruption of erythematous, pruritic papules on the extensors. Such symptomatic scenarios often warrant active treatment despite the benign and self-limiting nature of the poxvirus infection. When deciding on a treatment plan, patient preference along with the risks and benefits of each treatment option must be considered [1]. Treatment of MC is usually well tolerated and can effectively alleviate symptoms, limit spread, clear the infection, improve cosmetic appearance, reduce patient distress, prevent secondary bacterial infections, and help control underlying atopic dermatitis [3].

There are many different treatment options for MC, including

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physical and ablative methods such as curettage, manual expression, cryotherapy, chemovesicants, keratolytics, immune modulators, and antiviral drugs [**Table 1**] [1]. In the pediatric population, cantharidin is a quick, non-traumatic, and effective option in the office setting [2]. When applied properly, it produces a moderately controlled but delayed blistering reaction, resulting in mild erythema, blistering and pain which self-resolves within a few days [2,4,5].

Herein, we report a rare adverse outcome of a severe chemical burn in a child as a result of inappropriate treatment of MC with Cantharidin 1% – Podophyllin – Salicylic Acid (Canthacur-PS). Awareness of the MC infection and the proper use of cantharidin can facilitate safe and effective treatment. Moreover, it can prevent similar adverse outcomes from the inappropriate use of cantharidin.

CASE PRESENTATION

A 5-year-old healthy female presented to the Emergency Department at the Children's Hospital of Eastern Ontario with extensive painful chemical burns on the abdomen and upper thigh. The patient had erroneously been prescribed cantharidin 1% – podophyllin – salicylic acid (Canthacur-PS®) for home-administration. The medication was liberally applied to MC and surrounding areas of normal skin. A second application was repeated within 24 hours. Subsequently, she developed several bullae on the abdomen and thigh that evolved into large erosions, including areas of full-thickness ulcers. The total affected area covered approximately 10% of the total body surface area. Regions of full thickness involvement were eventually excised and closed by a plastic surgeon [**Figure 1**]. Ultimately, the patient was left with extensive scarring over her abdomen and right thigh following application

Table 1: Treatment ladder for childhood molluscum contagiosum [10].

Therapeutic Option	Mechanism	Example (s)
No active treatment	In immunocompetent patients, lesions do resolve spontaneously due to body's host immune response. Associated risk of spreading, pruritus and/or dermatitis, especially in the setting of underlying atopic dermatitis.	
Physical therapy	Physical or ablative destruction of molluscum contagiosum.	Curettage Cryotherapy Electrodesiccation Manual extraction CO2 ablative laser Pulsed dye laser
Chemical agent	Chemically destroys or acts as an irritant to stimulate an immunologic response.-	Phenol Trichloroacetic acid Cantharidin Podophyllotoxin Salicylic acid gel Benzoyl peroxide Retinoic acid Potassium hydroxide
Immune modulator	Enhances immune function and stimlates the clearance of the poxvirus.	Imiquimod Cimetidine Candida antigen Diphencyprone
Antiviral agent	Direct antiviral effect as a nitric oxide donor.	Cidofovir (in HIV patients)

Note: Adapted from [1].

Figure 1: Right lower abdomen and upper thigh post-surgical resection of full thickness chemical burns from misuse of Cantha-cur-PS® for MC.

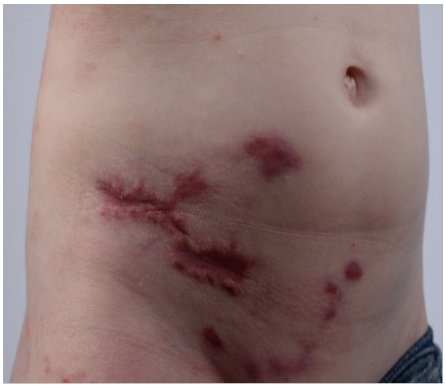

Figure 2: Right lower abdomen and upper thigh after a couple months with residual scarring.

of cantharidin 1% – podophyllin – salicylic acid for MC [**Figure 2**].

DISCUSSION

MC virus infection is very common amongst young children and easily spreads throughout the pediatric population [2]. It is a frequent reason to visit the family physician, pediatrician or dermatologist. In general, it is benign and self-limiting. Treatment is not always necessary but may be pursued in some cases for symptomatic relief, cosmesis, to limit spread, or to improve underlying eczema [3]. There are different options available for treatment of MC and the most appropriate therapeutic approach may vary depending on the clinical situation.

A recent trial comparing four recognized treatments of MC in a pediatric population (salicylic and lactic acid film, curettage, cantharidin, and imiquimod) found that curettage was the most effective treatment, with 80.6% of patients requiring only one visit to achieve clinical clearance. However, curettage can be challenging to perform in children as it requires the use of anesthesia and instrumentation, necessitating a process which is emotionally distressing for many children. In the study, cantharidin was found to be the second most effective treatment option in terms of overall patient and parent satisfaction [6]. In addition to its efficacy, cantharidin is a favourable option in children due to its quick, painless and controlled application in the office setting. Overall parental and physician satisfaction range from 60 to 90% with cantharidin in the Pediatric and Dermatology literature [4,7,8].

Cantharidin is a potent topical vesicant, derived from the "blister beetle," Lytta vesicatoria. The beetle-derived protein phosphatase inhibitor penetrates the epidermis, producing acantholysis and an intraepidermal blister [3,8]. When applied by an experienced physician, this controlled blistering reaction typically clears the infection safely, effectively, and without scarring [2,4,5]. However, adverse effects have been reported to range anywhere from 6-46 % [4]. These most commonly include pain, irritation, and inflammation from the blister [4]. The Food and Drug Administration also lists second- and third-degree burns and other extremely rare risks when cantharidin is applied with fatally high doses, ingested, or inhaled. Highly unlikely but reported risks include systemic toxicity, seizures, kidney damage, hypotension, hematuria, and cardiac abnormalities [9].

To our knowledge, there have been two case reports in the literature describing chemical burns secondary to cantharidin [10,11]. One additional case resulting in toxic shock syndrome from cantharidin has also been reported [12]. In general, cantharidin 0.7% is a safe treatment option for MC, but here we report a rare incident in which cantharidin 1% – podophyllin – salicylic acid was misused, resulting in full thickness chemical burns which could have been prevented. It emphasizes the importance that prescribing physicians should fully understand the product use before selecting it. Awareness of this rare complication, and other risks of cantharidin in treating MC, may foster safe use of the medication and prevent similar adverse events. In this case, three identifiable events may have prevented this serious adverse outcome.

First, the patient was prescribed Canthacur-PS® instead of plain Canthacur®. Cantharidin 0.7%, which is marketed in Canada as Canthacur® by Paladin Labs Inc., or CANTHARONE® by Dormer Laboratories Inc., is the standard of care when treating MC with cantharidin. Canthacur-PS® however, or similarly CANTHARONE® PLUS with podophyllin 2%, contains a higher concentration of cantharidin 1%, in addition to podophyllin 5% and salicylic acid 30%. The risk of excessive blistering, scarring and chemical cellulitis is higher with cantharidin 1% – podophyllin – salicylic acid than with cantharidin alone [7,8]. The risk was further increased with generous and repeated application to unaffected skin and

prolonged contact. Subsequently, Canthacur-PS® was dispensed at a pharmacy for self-administration against product monograph recommendations. Finally, the patient's guardian(s) failed to receive education on product use.

Under Health Canada regulation, the Natural Health Product monograph states it is designed strictly for physician application and under no circumstance should cantharidin 0.7% or cantharidin 1% – podophyllin – salicylic acid be dispensed or prescribed for patient administration [11]. At the first visit, the physician should assess sensitivity by treating only a few MC lesions, using a pointed wooden stick to apply a very small amount of solution to individual lesions. The solution should be left to dry uncovered and washed off within 4 to 6 hours with soap and water, or sooner if the patient develops discomfort. The treatment can be repeated in one to two weeks to more lesions using a similar protocol, once the inflammation has subsided [11].

In summary, this case highlights the importance of physician familiarity with cantharidin when selecting it as an active treatment for the common MC virus infection. Cantharidin 0.7% should be recognized as distinct from cantharidin 1% – podophyllin – salicylic acid and the latter should not be used to treat MC. Application to lesions should be restricted to the physician's office. And finally, all patients and their guardians should be told about the post-treatment management, potential side effects, and risks. Awareness of this serious adverse event and appropriate precautions can prevent future adverse outcomes, including chemical burns and scarring associated with the misuse of cantharidin.

KEY LEARNING POINTS

- Molluscum contagiosum is typically a benign and self-limited viral infection affecting the skin which does not always require active treatment, most notably in asymptomatic immunocompetent children.
- It presents as small, umbilicated, firm papules that can spread, become itchy, irritated and symptomatic for patients.
- Cantharidin can be a safe and effective treatment for MC but misuse can result in adverse reactions, including severe chemical burns.
- Cantharidin application should only be performed in a physician's office.
- Prescription and usage of Canthacur® and Canthecur-PS® should be clearly differentiated.

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