

Molluscum Contagiosum

A Review for Healthcare Providers

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ABSTRACT: Molluscum contagiosum (MC) is a common dermatology condition affecting the worldwide population. MC is caused by the MC virus, a member of the *Poxviridae* family. The virus predominantly affects children, sexually active adolescents and young adults, individuals involved in contact sports, and immunocompromised individuals. The condition is self-limited and will eventually clear spontaneously without treatment. Many individuals do elect treatment, and management strategies are discussed along with potential side effects. Selected treatment outcomes printed in a recent Cochrane systematic review are summarized.

Key words: Molluscum Contagiosum

Molluscum contagiosum (MC) is a viral condition that arises from the *Poxviridae* family, which also includes smallpox, vaccinia, cowpox, monkeypox, tanapox, orf, and milker's nodules (Mancini et al., 2018). Genomic sequencing of the *Molluscipoxvirus* (MCV) genus has identified four MCV types felt to emerge from a common ancestor, with MCV1 and MCV2 as the most common (Zorec et al., 2018). Recent studies have discovered five genotypes each of MCV1 and MCV2, with MCV2 more likely to be identified in immunosuppressed individuals (Zorec et al., 2018). MCV is associated with interference of the host T-cell response, which ultimately inhibits the individual's ability to quickly eradicate the virus (Zorec et al., 2018). MC is transmitted by direct skin-to-skin contact and autoinoculation and rarely via fomites such as shared towels, with an incubation period of 2–6 weeks from infection to clinical signs (Meza-Romero, Navarete-Deshante, & Downey, 2019).

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EPIDEMIOLOGY OF MC

Viral skin conditions are listed within the top 50 worldwide diseases, making them a considerable public burden (Karimkhani et al., 2017). Since the eradication of smallpox, MC is the most frequently encountered of the pox viruses in humans (Mancini et al., 2018). MC commonly occurs in pediatric, sexually active adolescents and young adults and in immunocompromised populations (Meza-Romero et al., 2019). In addition, MC may be common in contact sports participants, predominantly wrestling, as the integrity of the skin is often compromised by friction against the wrestling mat (Peterson, Nash, & Anderson, 2019). The condition is rarely encountered in infants less than 1 year old because of inherent maternal immunity. However, MC can occur in neonates if the mother has genital lesions during the time of delivery (Meza-Romero et al., 2019).

CLINICAL SIGNS OF MC

MC lesions are firm, smooth, waxy papules or nodules with a central umbilication that are pink to whitish colored. The center contains a soft cheesy-like substance termed the "molluscum body." Lesions can be located anywhere upon the body but tend to be more common in skin folds of the neck, axillae, extremities, buttocks, and genital areas (Figure 1). MC lesions may appear on most skin surfaces but do not appear on palms of hands and soles of feet. Sizes may range from a few millimeters to over 1 centimeter with large, disfiguring lesions occurring in immunocompromised patients, specifically those individuals with HIV/AIDS (Mancini et al., 2018). Individuals with loss of an intact skin barrier in conditions such as atopic dermatitis are more prone to develop MC (Mancini et al., 2018). MC is considered a self-limited condition with the individual's immune system clearing the virus in several months. However, lesions may last for several years as clearance is dependent on the competency of the immune system (Meza-Romero et al., 2019).

OTHER CUTANEOUS LESIONS ASSOCIATED WITH MC

Occasionally, other cutaneous lesions may be associated with MC, which appear quite different from the classic lesion. An exuberant immune system response is often



FIGURE 1. Typical umbilicated molluscum papules.

heralded by increased erythema and surrounding edema of the MC lesions indicating the beginning of the end (BOTE) sign (Meza-Romero et al., 2019). Although the BOTE sign can be distressing to the individual, this is a favorable sign as the MC is resolving and should not be treated with topical steroids or anti-infective medications. Another possible cutaneous reaction is an inflammatory response consisting of papules that favors the elbow and knees, resembling Gianotti-Crosti (Mancini et al., 2018; Figure 2). This is an id reaction, or autoeczematization, characterized by eruptions of lesions distant from a primary dermatosis. They are most associated with allergic contact dermatitis but may occur in infections such as MC, fungal, and scabies (Haddock, Cheng, & Barrio, 2017). The id reaction does not need to be treated unless it is symptomatic for pruritus.

DIFFERENTIAL DIAGNOSIS

Diagnosis of MC is a relatively easy clinical decision. However, there are other lesions that may be confused with MC. The differential diagnosis may include basal cell carcinoma, juvenile xanthogranuloma, condyloma acuminata, verruca, adnexal tumors, milia, and papular granuloma annulare (Mancini et al., 2018). The BOTE sign and id reactions may also potentially impede diagnosis. A biopsy should be considered if the diagnosis is not clear. Histological examination will show molluscum bodies (intracytoplasmic inclusion bodies) within the keratinocytes of the epidermis for a conclusive diagnosis (Mancini et al., 2018).

Treatment Modalities

Upon diagnosis of MC, the decision must be made to treat or not to treat as this is a self-limited condition. The American Academy of Pediatrics' (2015) parent guide advises against treatment for limited and isolated lesions because most interventions have a degree of discomfort and a limited potential to scar. Thus, the healthcare provider should have a frank discussion with the patient or parents of the

pediatric patient on the risks and benefits of treating MC, while also including information on potential spread of the virus through autoinoculation and to other individuals. The decision to treat is based on several factors, including alleviation of discomfort, cosmetic reasons, social stigma issues, limiting the spread to other areas of the body or spread to other individuals, prevention of scarring and secondary infections, and prevention of trauma to the lesions by self-manipulation (van der Wouden et al., 2017).

Treatment modalities can be divided into the following categories: destruction/mechanical, chemical, immunological, and antiviral. Occasionally, there is overlap between the categories such as the inflammation that can accompany destruction/mechanical and chemical treatments may also help to stimulate the innate immune system to target the virus. Destructive/mechanical treatments include curettage and liquid nitrogen. Curettage is scraping of the lesion with a curetting device or a punch biopsy tool. The curette is centered over the lesion at a 30° angle to the lesion and used with a quick scrape removing the lesion while stabilizing the skin, keeping it taut. The punch biopsy device is also used at a 30° angle, but the lesion is approached from the side and scraped forward while keeping the skin taut (Meza-Romero et al., 2019). Curettage is very useful for a small number of lesions but can be painful and does leave an open area of the skin, which can lead to potential



FIGURE 2. Id reaction in a child treated for molluscum contagiosum.

scarring and bacterial access (Meza-Romero et al., 2019). An alternate method of destruction is to nick the top of the MC lesion with a sterile needle or number 11 blade followed by compressing the lesion to remove the molluscum body.

Liquid nitrogen may be sprayed directly on the lesions or applied with a cotton-tipped applicator dipped in liquid nitrogen applied directly to the lesion. The number of freeze-thaw cycles may be dependent on the size of the lesion and patient tolerance of the procedure but is generally limited to one to two cycles (Meza-Romero et al., 2019). Liquid nitrogen can be very painful and has the potential to result in hyperpigmented or hypopigmented areas. The pigment changes are rarely permanent but may last months and be distressing to the patient and parents of pediatric patients. Numerous treatments with liquid nitrogen may be needed to eradicate the lesions.

Pulse-dye lasers have also been utilized as destructive methods to treat MC. The energy of the laser may destroy or at least create enough irritation to stimulate the immune system to clear the lesion. The side effects of laser may include initial discomfort, and in most cases, scarring does not occur. Settings are dependent on the size of the lesion (Griffith, Yazdani Abyaneh, Falto-Aizpurua, & Nouri, 2014). Pulse-dye laser treatment has been successfully used in immunocompromised individuals (Fisher et al., 2019). Consideration should be given to the use of a topical anesthetic of 5% lidocaine and/or 5% tetracaine applied 1 hour before treatment for individuals who are extremely anxious about destruction techniques or those individuals with low pain tolerance (Noska, 2015).

Chemical therapies disrupt the keratinocytes of the epidermis and include acid application to the lesions. Many types of acids have been utilized in treatment of MC including salicylic, lactic, glycolic, and trichloroacetic. Acids are keratolytic and dissolve the keratin (Dave & Abdelmaksoud, 2018). Problems incurred with use of chemical acids include discomfort and scarring and should absolutely be avoided on the face and periocular areas (Meza-Romero et al., 2019). In addition, applications of an acid formulation should only be used on a cooperative patient to prevent disastrous complications. Topical retinoids can also be used to treat MC lesions. Topical tretinoin acts by desquamation of the keratinocytes (Coyner & Masterson, 2016; Noska, 2015). None of the chemical therapies is specifically labeled for use in treatment of MC.

The most utilized chemical therapies are cantharidin and potassium hydroxide. However, neither is specifically indicated for MC treatment. Cantharidin is derived from a blistering beetle extract that inhibits phosphodiesterase (Karimkhani et al., 2017). The solution is applied via the wooden end of a cotton-tipped applicator to each lesion. The treated lesions should remain dry for at least 2–4 hours. Often, dressings such as band aids are applied over the lesions to prevent accidental transfer of the solution to eyes and other sensitive skin areas. The expected result is a blister that may be yellowish in color, resulting in

irritation to the lesion. The advantage of cantharidin is it is usually tolerated well and is not painful unless applied to an open skin area (Guzman, Schairer, Garelik, & Coochen, 2018; Jahnke, Hwang, Griffith, & Shwayder, 2018). The disadvantage of cantharidin treatment is the size and discomfort of the resultant blisters, which can be distressing to the patient and parents (Vakharia, Chopra, Silverberg, & Silverberg, 2018). If the blister is causing intense discomfort, it may be opened to release the accumulated fluid. Numerous treatments of cantharidin every 2–4 weeks are often required (Coyner & Masterson, 2016).

Potassium hydroxide is an alkaline compound that dissolves keratin. It is used in a 5%–20% solution with various regimens of application including two times daily, once daily, and every other day. It is generally well tolerated, with localized side effects of a burning sensation (Giner-Soriano et al., 2019; Teixidó et al., 2018).

Immunological treatments include imiquimod, cimetidine, diphencyprone, and candidin. These agents all act by stimulating the individual's own immune response. None of the immunological treatments is specifically indicated for MC treatment. Imiquimod 5% acts upon toll-like receptor 7, which should activate the innate immune response (DiBiagio, Pyle, & Green, 2018). There are various regimens associated with imiquimod such as applications daily, two times weekly, and three times weekly. The application site must become erythematous and irritated to launch the immune response.

Cimetidine is given orally with a standard dose of 25–40 mg/kg per day. It is an H₂ receptor agonist and may stimulate hypersensitive responses. Cimetidine is given daily until resolution of the lesions or until side effects of stomach irritation occur (Meza-Romero et al., 2019).

Diphencyprone is a chemical that, when applied to a sensitized individual, causes an allergic reaction. The individual is sensitized to the chemical by placing a small amount of 1% or 2% diphencyprone on the inner, upper arm covered with an occlusive dressing. Most individuals will develop a brisk erythematous response within 48 hours and are considered sensitized. A diluted solution, generally less than 1%, is applied to the MC lesions. Expected outcomes are erythema and, sometimes, blisters at the treated sites, which ultimately should activate the immune system to recognize and eradicate the MCV. Treatments may be applied two times weekly to weekly dependent on the individual's response (Coyner & Masterson, 2016). Diphencyprone is not commercially available and must be mixed at a compounding pharmacy.

Candidin is an extract of *Candida albicans*. It is injected intralesionally, which in most cases causes an intense immunological response (Meza-Romero et al., 2019). Candidin has reported success in immunocompromised patients (Thomas, Gillihan, & Longo, 2019). The delivery method of candidin is a distinct disadvantage because of procedural discomfort.

Podophyllotoxin cream and cidofovir are antiviral therapies occasionally used off-label for MC treatment. Podophyllotoxin cream (podofilox) is labeled for the treatment of verruca vulgaris. It is available in a 0.3% and 0.5% cream and acts by preventing the division and multiplication of viral cells until the cells eventually die. It is generally considered safe and effective but should be used in caution in pregnant women because of the presumed toxicity to the fetus (Centers for Disease Control and Prevention, 2017). Cidofovir acts by inhibiting viral replication and is commercially formulated for intravenous use to treat cytomegalovirus in the immunocompromised patient. It is compounded in a cream formulation when treating MC (Mancini et al., 2018).

CASE REPORT STUDIES

Topical sinecatechins, derived from green tea leaves, are approved for the treatment of genital condyloma acuminata. They have been utilized to treat recalcitrant MC. The mechanism of action is not known but thought to activate the immune system (Padilla et al., 2016). Ingenol mebutate topical gel, a diterpenes extract from the *Euphorbia pepylus* plant, commonly known as milkweed, has also been listed as a potential MC treatment. The mechanism of action for this medication is unknown. It is approved for the use of actinic keratosis and comes in 0.015% and 0.05% (Del Rosso, 2016). East Indian sandalwood oil product has reported success in treating MC when applied daily for 12 weeks of therapy (Haque & Coury, 2018). Intralesional 5-fluorouracil has shown potential in treating MC in an immunocompromised patient (Bhattacharjee, Kumaran, & Vinay, 2018). In addition, a patient with MC and folliculotropic mycosis fungoides was successfully treated with interferon-alpha via intralesional injections (Melchers et al., 2019). The healthcare provider must use caution in analyzing the results of case study reports as they lack clinical trials to determine effectiveness in the general population.

EFFECTIVENESS OF MC THERAPIES

A Cochrane systematic review regarding the effectiveness of MC treatments was published by van der Wouden et al. (2017). Randomized clinical studies of MC treatments published before 2016 were included in the review. Exclusion criteria were studies that included immunocompromised individuals and MC cases that were sexually transmitted. Twenty studies of topical therapies and two studies of systemic therapies were evaluated. Topical therapies included imiquimod, 10% Australian lemon myrtle tree oil, potassium hydroxide, cantharidin, phenol, salicylic acid, 70% alcohol, benzoyl peroxide cream, tretinoin, and sodium nitrate. Systemic therapies evaluated were cimetidine and homeopathic calcarea carbonica—a mineral-based therapy purported to be useful in many ailments.

Clinical studies were assessed in terms of improvement of condition, cure of condition, time taken for improvement,

recurrence, and adverse reactions of treatment. The Cochrane reviewers analyzed each study according to quality of evidence regarding the study conclusions. These results are summarized in Table 1.

The reviewers noted that physical destruction methods of curettage and liquid nitrogen were not included in any study. They concluded that no one agent studied showed superiority. In addition, they concluded that allowing MC to resolve via natural resolution was desired.

APPROACH TO THE PATIENT WITH MC

Initial assessment of the patient with MC includes a thorough clinical examination to determine location and number of lesions. History review should explore the course of the condition including outcomes of any prior treatments and associated symptoms. In addition, the healthcare provider should ascertain if there is a history of scarring with prior physical trauma, involvement in activities such as team sports necessitating rapid resolution, possibility of pregnancy in age-appropriate women, and patient immunocompetency.

The healthcare provider needs to lead discussion with the patient or parents of the pediatric patient regarding MC as a viral condition, which is self-limiting in nature. The discussion should also include available treatment options, potential side effects of the treatments, and that treatments are not labeled specifically for treatment of MC. Finally, the discussion should include that numerous treatments may be required to resolve the condition.

TABLE 1. Evidence Level Summary of Studies

Level of Evidence	Study Results
High	No studies met this evidence criteria
Moderate	Topical 5% imiquimod no more effective than vehicle
Low	Topical 5% imiquimod less effective than liquid nitrogen spray or 10% potassium hydroxide
Low	10% Australian lemon myrtle tree oil more effective than olive oil
Low	10% benzoyl peroxide cream more effective than 0.05% topical tretinoin
Low	5% sodium nitrite co-applied with 5% salicylic acid more effective than 5% salicylic acid alone
Low	Iodine plus tea tree oil more effective than either alone
Low	10% potassium hydroxide more effective than saline
Low	Calcarea carbonica more effective than placebo

Adapted from van der Wouden et al. (2017).

When treatment is desired, the choice of therapy should be a joint decision. Limited numbers of lesions may be best treated by curettage in an adult and in some cooperative younger individuals. Numerous lesions may be treated by topical therapy such as cantharidin or potassium hydroxide. Topical treatments that do not cause discomfort at the time of administration may be the best choice for young patients. Occasionally, recalcitrant cases may benefit from combination therapies (Go, Nishimura-Yagi, Miyata, & Mitsuishi, 2018).

SPECIAL CONSIDERATIONS

Pregnant patients should be treated with curettage, cryotherapy, or laser as they are safe treatment options. Teratogenic treatments such as podophyllotoxin and imiquimod should be avoided (Noska, 2015). Patients with sexually acquired MC in the genital area should have screening for other sexually transmitted infections. They should be advised to avoid shaving hair in the genital area as this may contribute to spread of the lesions.

A lesion adjacent to the eye, but not located on the lid structure, may be treated by the experienced healthcare provider. Careful patient assessment is necessary regarding the patient's ability to keep the head stable during the procedure. If the healthcare provider does not feel comfortable with the procedure or if numerous lesions are in the periocular area, the patient should be referred to an ophthalmologist for management (Noska, 2015).

Immunosuppressed patients with MC present special challenges as lesions may be widespread and large sized. Podophyllotoxin cream 0.05% (podofilox) is a recommended treatment for immunosuppressed individuals (Centers for Disease Control and Prevention, 2017). Other treatment options recommended in this group of patients include the antiviral medication cidofovir (Mancini et al., 2018) and 5-fluorouracil.

CONCLUSION

MC is a cowpox virus that potentially affect patients representing several age groups and is frequently encountered in the dermatology setting. It is a self-limiting condition that will spontaneously clear, and many experts recommend allowing natural resolution. Many options can be utilized for those individuals desiring treatment. The healthcare provider needs to be cognizant of treatment options, potential adverse effects, and effectiveness. ■

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