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Pediatric Molluscum Contagiosum: Reflections on the Last Challenging Poxvirus Infection, Part 2

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Molluscum contagiosum (MC) is a common dermatologic infection that usually affects school-aged children, sexually active young adults, and immunocompromised individuals. It is a benign and self-limiting disease, with most cases undergoing spontaneous resolution within 6 to 9 months. However, a more severe and prolonged course is associated with immunosuppression or atopic dermatitis. Treatment is recommended because of the high rate of associated symptoms, risk for transmissibility, and cosmetic or social concerns. Therapeutic modalities are subdivided into 3 types: destructive, immunomodulatory, and antiviral. We review the advantages and disadvantages of various agents and discuss combination therapy.

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Molluscum contagiosum (MC) is a common viral infection of the skin and mucous membranes that predominantly affects school-aged children, sexually active young adults, and immunocompromised individuals. It is considered a benign and self-limiting disease, though it can have a severe and protracted course in patients with an impaired immune system or atopic dermatitis. Molluscum contagiosum is caused by the molluscum contagiosum virus (MCV), a highly contagious poxvirus. The skin eruptions spontaneously resolve within months in children

with normal immune systems but can persist for years.¹ Its prolonged course, associated symptoms, and lack of cosmesis can be bothersome to patients and may cause concern to patients and parents/guardians. Part 1 of this 2-part series reviewed the epidemiology, clinical description, and diagnosis of MC.²

A continuous debate exists about the management of this disease. Some clinicians believe it should be left alone to run its natural course, while others support the use of therapeutic measures. We often favor treating this condition, not only for cosmetic reasons but also to prevent transmission, reduce autoinoculation, and relieve associated symptoms. We review many effective therapeutic options that are currently available, which can be broadly subdivided into 3 types: destructive, immunomodulatory, and antiviral.

Treating MC

There is no general consensus on the management of MC. Traditionally the treatment of choice has been cautious neglect or watchful waiting because of the benign and self-limiting nature of this infection. However, it is now recommended that patients receive active therapeutic intervention because of the high rate of associated symptoms, risk for transmissibility, and cosmetic or social concerns. Up to 32% of patients report 1 or more symptoms associated with MC, including pruritus, inflammation, bacterial superinfection, bleeding, and pain.³ Molluscum contagiosum virus is highly contagious and can result in localized outbreaks if not properly managed. Given the high prevalence of atopic dermatitis among children (estimated to be 17.2% in the United States⁴), therapy should be initiated to prevent transmission, especially in immunosuppressed patients. Scar formation can be a concern and may be cosmetically unappealing. Affected

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children may not be allowed to attend school or participate in certain activities. In addition, they may be subject to teasing and social exclusion, which can substantially affect their quality of life. Therefore, many patients and guardians desire therapy.

Treatment selection should be individualized based on patient preference and circumstances. The clinician should take into account the child's age, the guardians' financial status, and the distance from the residence to the place of treatment. Guardians concerned about cosmesis should understand that therapy may cause pigmentary alterations and sometimes scars. Combinations of therapies also have been used with variable success. It should be noted that topical agents are not approved by the US Food and Drug Administration for the treatment of MC and are being employed on an off-label basis.

Destructive Therapy

Destructive measures are the most commonly used therapies for the treatment of MC. They can be physical or chemical and are designed to remove or destroy infected tissue. The release of viral antigens from infected keratinocytes elicits an immune response to help clear the infection. Commonly used therapies include curettage, cryotherapy, vesiculating agents, or topical irritants. Physically destructive therapy may be frightening and traumatic for children; therefore, clinicians should facilitate good patient rapport, guardian assistance, and distractive techniques. Potential adverse events inherent to ablative procedures are bleeding, pain, discomfort, and psychological or emotional distress.

Physical Destruction—Curettage is a widely used form of destructive therapy that is safe and effective.^{1,5} It produces immediate results and is associated with a low rate of scarring and secondary infection. One study found it to be most efficacious compared to 3 other commonly used forms of therapy: cantharidin, salicylic acid and lactic acid, and imiquimod.⁵ Results were based on patient-guardian satisfaction and total number of visits required for complete clearance (N=124). Eighty-six percent of patients and guardians reported a positive experience, with 81% requiring only 1 office visit. It also was associated with the lowest rate of adverse effects.⁵ Given that curettage is a physically ablative procedure, some discomfort or bleeding may be experienced. Some postinflammatory changes also may be experienced following the procedure. To minimize pain, a topical anesthetic should be applied prior to performing curettage or other physically destructive procedures. A eutectic mixture of the anesthetics lidocaine 2.5% and prilocaine 2.5% cream applied for 1 hour under an occlusive dressing has been shown to eliminate or considerably

reduce pain with negligible local reaction. However, application to a body surface area in excess of the recommended amount can result in methemoglobinemia or central nervous system toxicity. Therefore, it should be judiciously applied with strict adherence to dosage recommendations. Because of the potential toxicity, some clinicians have replaced it with topical lidocaine.⁵ If curettage remains intolerable with use of a topical anesthetic, a systemic sedative can be considered. For children with extensive disease, general anesthesia may be warranted.

Curettage may not be practical in the setting of a busy medical practice. It can be a time-consuming procedure because of techniques used to put the patient at ease and time needed for the anesthetic to become most effective. Another disadvantage is the failure of patients to acquire immunity to the virus; therefore, recurrences may occur. It is not feasible in widespread cases, particularly in infants and children. Some clinicians have not recommended curettage in children younger than 10 years.⁶ Nevertheless, if curettage is properly performed under favorable conditions and adequate anesthesia, it should be considered a first-line treatment in pediatric patients.

Other physically ablative treatments include cryotherapy, laser therapy, manual extrusion, and electrodesiccation. Cryotherapy is an inexpensive and effective form of therapy. The procedure is rapidly performed with a low rate of scar formation. However, it is associated with more discomfort than curettage and cantharidin. The 585-nm pulsed dye laser for collagen remodeling is a painless, effective, and bloodless treatment of MC. By selectively damaging aberrant blood vessels and adjacent connective tissue, it induces a cell-mediated reaction to clear the infection. Administration is easy and quick to perform, resulting in a prompt response. Most patients only require 1 treatment and have minimal side effects. It is particularly useful for treating children with a large number of papules.⁷⁻⁹ Manual extrusion by squeezing is a common treatment method.¹⁰ One study demonstrated complete resolution in 76.8% (43/56) of patients; however, 37.5% (21/56) had scar formation. In comparison to natural resolution, this rate of scarring is unacceptably high.¹¹

Chemical Destruction—Cantharidin is a painless alternative that is safe, efficacious, and usually well-tolerated.¹⁰ It is a chemically destructive, vesiculating agent that is extracted from the Spanish fly (*Lytta* [formerly *Cantharis*] *vesicatoria*). It causes the activation or release of serine proteases, which leads to acantholysis and intraepidermal blistering.¹² Cantharidin is the treatment of choice for many clinicians.¹³ Chemically destructive therapies such as cantharidin can spare children from more aggressive

physical modalities. Cantharidin can be rapidly applied and does not cause bleeding. When properly used, major or long-term side effects generally do not occur. Cantharidin rarely is associated with pain, trauma, or scar formation, which gives it a distinct advantage over other forms of therapy in children. However, it can cause a variable degree of blistering, especially with improper use, and annoying postinflammatory alterations in pigmentation.

In a study of 300 patients treated with cantharidin, 90% had complete resolution and an additional 8% reported notable improvement after an average of 2.1 treatment visits.³ Six percent to 37% of patients reported treatment-associated side effects such as pain, erythema, and pruritus. However, 95% of guardians expressed satisfaction with cantharidin therapy and would choose it again if necessary.³ Conversely, another study (N=124) revealed that only 60% of patients and guardians were satisfied, with 19% experiencing adverse effects necessitating a switch in therapy. The authors of the latter study attributed the discrepancy to the length of application time.⁵

Cantharidin should only be applied vigilantly by a clinician; up to 20% of patients may require 3 or more applications for complete clearance.⁵ Therefore, it may be inconvenient or impractical for patients who do not reside nearby. Occasionally, cantharidin can incite a delayed reaction characterized by erythema, vesiculation, pruritus, burning, or pain, which may require prompt follow-up. If necessary, acetaminophen may be used to relieve pain associated with blistering. Postinflammatory pigmentation changes are potential side effects, but resolution should be expected within weeks to months.¹⁴ It is recommended that eruptions on the face and genitoanal area are not treated with this agent. Treated areas should be covered by a bandage to avoid contact with fingers. Cantharidin should never be combined with podophyllotoxin or salicylic acid because of potential toxicity.

Chemically destructive agents such as vitamin A derivatives, podophyllotoxin, lactic acid, salicylic acid, potassium hydroxide, hydrogen peroxide, silver nitrate, trichloroacetic acid, and phenol also are used for the treatment of MC. Chemically destructive therapy can spare children from the more aggressive physical treatment modalities. Vitamin A derivatives, such as tretinoin, have been successful in clearing infection. Tretinoin liquid 0.05% has produced the best results.¹⁵ Its proposed mechanism of action is the irritation it causes to the skin, which disrupts the protein-lipid membrane encasing the viruses. It also is thought to have immunomodulatory and antiviral activity.¹⁶ Application of tretinoin may cause drying

and peeling of the skin. When applied to sensitive areas such as the face, erythema and induration can occur.¹⁷

Podophyllotoxin is the main active antiwart ingredient of podophyllin, an herbal extract. Podophyllotoxin cream 0.5% is an effective, patient-administered therapy for MC. It results in a 92% cure rate after 4 weeks of treatment.¹⁸ Adverse effects such as mild pruritus and erythema frequently are present, with postinflammatory pigmentary alterations being an occasional concern. However, the alterations are tolerable and do not result in discontinuation. It is a safe, home-based therapy that some clinicians recommend as first-line treatment of MC.¹⁸

Keratolytic acids, such as lactic and salicylic acid, can be used individually or in combination. A study testing the efficacy of the combination of salicylic acid 16.7% and lactic acid 16.7% in flexible collodion resulted in a 100% cure rate after 2 visits. However, it was associated with a high incidence of side effects and a low rate of satisfaction.⁵

Potassium hydroxide has been shown to be an effective alternative for treating MC. The use of potassium hydroxide aqueous solution 5% resulted in complete clearance in 20 patients within a 6-week period.¹⁹ The solution with a 10% concentration is not recommended for use because of a stinging sensation during application and posttreatment alteration in pigmentation.

Silver nitrate aqueous solution or paste 40% has produced good results in the treatment of MC. It does not cause pain or scarring and is cost-effective. In a study of 389 patients with MC treated with silver nitrate paste 40%, the cure rate was 97.7%, with most patients having complete resolution after 1 application.²⁰ It is useful for treating widely disseminated MC and MC in intertriginous areas.

Trichloroacetic acid can be employed with caution. The depth of acid penetration is difficult to control; therefore, pain, irritation, and scarring frequently occur.²¹ However, trichloroacetic acid in concentrations of 35% or less appears to be an acceptable and effective adjuvant therapy for treating immunocompromised patients.²²

Phenol can cause considerable pain and discomfort. Although it is frequently cited as an acceptable form of treatment, it is not recommended because of its high rate of scarring. One study demonstrated that up to 81% (42/52) of treated papules resulted in scar formation.¹¹

Immunomodulatory Therapy

Immunomodulatory agents accelerate the clearance of MCV infection by enhancing the immune response

through the induction of antiviral cytokines or the influx of leukocytes capable of viral clearance. These agents include the commonly utilized imiquimod, rarely employed cimetidine, and interferon alfa. Imiquimod is an immune response modifier that acts by increasing the local release of proinflammatory cytokines.^{23,24} It is a self-administered topical therapy that is both efficacious and convenient. Imiquimod cream 5% appears to be safe and effective in children.²⁵⁻²⁸ The average of 9 studies on the rate of complete clearance was 42.2% (35/83).²⁶ To achieve therapeutic effect, some mild erythema, irritation, and pruritus may be necessary. However, these side effects are well-tolerated and rarely result in discontinuation. It is an acceptable alternative for patients who desire home-based therapy. This agent should be carefully applied with surrounding areas of noninfected skin covered in petroleum.¹⁷ It is especially useful for treating infections of the genitoanal area and other intertriginous regions. It seems to be particularly effective in patients with human immunodeficiency virus (HIV).^{29,30} However, it can be costly, especially for a 9-week supply usually employed. It also may take many months to achieve optimal results.³¹ Irritation may be intolerable in some children.

Cimetidine is a histamine-receptor antagonist that demonstrated clinical benefit in patients infected with varicella-zoster virus and herpes simplex virus. It is an immunomodulator that induces delayed hypersensitivity. The effectiveness of cimetidine is controversial. It may be successfully used for MC in immunocompetent children and children with atopic dermatitis³²; however, its value, particularly in the latter group, has been questioned.³³

Interferon alfa is a therapeutic option for immunocompromised patients with severe cases of MC resistant to standard treatment. It is a cell-signaling protein with immunomodulating, antiviral, and cytotoxic effects. Intralesional and subcutaneous interferon alfa has successfully treated patients with HIV and combined immunodeficiency, respectively.^{34,35}

Antiviral Therapy

Antiviral therapy is not commonly used for the treatment of MC. Highly active antiretroviral therapy (HAART) has been shown to effectively treat HIV and AIDS patients with recalcitrant MC. Resolution usually is achieved when CD4⁺ lymphocyte counts are consistently above 200 cells/mm³.³⁶ Since the advent of this therapeutic regimen, there has been a substantial decline in AIDS-related cases. For cases resistant to HAART, cidofovir is another therapeutic option. It is a nucleotide analogue of deoxycytidine monophosphate with broad antiviral activity against DNA viruses, including MCV. Both

systemic and topical forms have demonstrated clinical effectiveness in HIV patients unresponsive to standard therapy and HAART.³⁷⁻³⁹ However, systemic treatment carries a potentially serious side effect of nephrotoxicity. To maximize the effectiveness and bioavailability of the topical form, cidofovir 1% or 3% should be combined with a vehicle containing propylene glycol and affected skin should be occluded with adhesive tape for at least 12 hours.³⁸

Combination Therapy

Sodium nitrite 5% coapplied with salicylic acid 5%, also known as acidified nitrite, has resulted in a cure rate of 75% in a study conducted in 16 patients.⁴⁰ Acidified nitrite is a potent nitric oxide donor with antiviral effects. It is self-administered and painless but is associated with mild irritation and staining of the skin. Eruptions on the face should be avoided because of these potential side effects. Combination therapy with cantharidin and imiquimod also has been proven effective.⁶ Cantharidin can be used as the initial therapy with subsequent applications of imiquimod to residual papules. It is convenient for patients because it requires fewer office visits and costs less than using imiquimod alone. This regimen could be useful in patients with large numbers of papules or in those resistant to monotherapy.⁶ Iodine and salicylic acid applied together also has been successfully employed.⁴¹ According to a study using povidone iodine solution 10% and salicylic acid plaster 50%, all 20 patients were cured after an average of 26 days of therapy.⁴¹ It is a cost-effective alternative associated with no pain or scar formation and minimal adverse effects. This therapy is recommended for children, including patients with multiple papules.⁴¹

Comment

Symptoms associated with molluscum dermatitis can be treated with gentle skin care techniques similar to patients with atopic dermatitis and with corticosteroids or antihistamines. A thorough physical examination should be performed to identify and treat all areas of involvement to ensure complete resolution and prevent further spreading. Periocular eruptions should be left untreated in children. A disease-free period of 4 months has been suggested before the patient is considered cured.⁴² The management of this condition also should involve education to prevent transmission and autoinoculation. Patients should avoid communal bathing and public swimming. The sharing of towels or bath sponges should not be permitted.

Conclusion

The treatment of MC in pediatric patients involves destructive, immunomodulatory, and antiviral agents.

Treatment is essential to prevent transmission and to manage cosmesis; however, the treatment selected should be tailored to the patient, taking into consideration the patient's age, the cost of treatment, and the ability of the patient to access treatment.

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