Molluscum Contagiosum: The Need for Physician Intervention and New Treatment Options

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Molluscum contagiosum is an infection caused by a poxvirus that gives rise to small, benign, white, pink, or flesh-colored, umbilicated, raised papules or nodules located in the epidermal layer of the skin. The disease can be transmitted by direct bodily contact including sexual activity, fomites, or self-inoculation. There has been continued debate about whether physicians should actively treat molluscum contagiosum. Many dermatologists recommend treatment to reduce the incidence of contagious transfer and reduce self-inoculation. Furthermore, individuals with weakened immune systems (eg, patients with human immunodeficiency virus infection) not only are at greater risk for secondary inflammation and bacterial infection but also are prone to lesions that typically persist for prolonged periods. In addition to the commonly administered treatments (ie, physical and chemical destruction), novel treatment opportunities exist, including immunomodulated therapy with imiquimod.

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Key characteristics of molluscum contagiosum are shown in Table 1. Lesions may be found as single or multiple mollusca. The incidence of molluscum contagiosum is increasing, though current statistics are lacking. The number of private physician office visits due to molluscum contagiosum in the United States from 1966 to 1983 increased from 1.2 to 11 per 100,000 patient visits for individuals older than 15 years.[1] The incidence of this disease in patients with human immunodeficiency virus (HIV) infection is higher than in the general population, reportedly as much as 5% to 18%.[2] Although the peak incidence of disease is most commonly observed in children younger than 10 years, it can occur at any age.[2]

When molluscum contagiosum lesions appear, they occur singly or in groups (usually <30 papules) and can be detected anywhere on the body. Lesions typically are observed on the face, neck, abdomen, arms, thighs, axilla, and genital areas but rarely are observed on the palms of the hands or soles of the feet (Figure 1). However, patients who are immunocompromised may present with atypical manifestations.

Treatment Options

Debate continues about whether physicians should treat molluscum contagiosum or let the disease spontaneously resolve. Many dermatologists recommend treatment to reduce both autoinoculation and the incidence of transfer to other individuals. Although lesions generally will resolve if left untreated, it may take from 6 months to 5 years for lesions to disappear.[2] Furthermore, individuals with weakened immune systems, including patients with HIV infection, not only are at greater risk for secondary inflammation and bacterial infection but also are prone to lesions that typically persist for prolonged periods. In addition, some patients experience pain and discomfort that adversely affect quality of life. There also can be emotional and psychological discomfort associated with the disease, particularly embarrassment that may result from lesion locations (eg, face). Therefore, it would

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Table 1.

Characteristics of Molluscum Contagiosum

Family
Poxviridae
Genus
Molluscipoxvirus
Clinical presentation
Small, benign, white, pink, or flesh-colored, umbilicated, raised papules (1–5 mm in diameter) or nodules (6–10 mm in diameter)
Three subtypes (molluscum contagiosum types 1, 2, and 3)
Subtype 1 is most commonly observed
Clinical presentation is similar for all 3 subtypes
Transmission
Direct bodily contact
Fomites
Self-inoculation
Incubation period
14–50 d

be advantageous for physicians to treat molluscum contagiosum if the treatment was safe, effective, painless, and convenient to administer.

Several options are available for treating molluscum contagiosum lesions (Table 2). Physicians typically employ the same modalities popular for the treatment of warts. Physical destruction of small lesions is common. It involves electrosurgery, curettage, or cryosurgery performed in a physician's office[3] and employs an electric needle, laser, or curette for removal of small papules. Even with application of a local anesthetic, these procedures are associated with pain, irritation, soreness, and mild scarring. Cryosurgery, for example, involves the application of liquid nitrogen by spray, probe, or cotton-tipped applicator. This treatment can be painful and also may result in skin irritation. Furthermore, as with all physical destruction techniques, repeated lesion treatment requiring additional office visits may be required. Because of the pain and discomfort, these procedures typically are performed only on adolescents and adults. Furthermore, the efficacy of physical destruction of lesions has not been supported by placebo-controlled clinical trials. Success rates of physical ablation in uncontrolled studies are difficult to interpret and usually are similar to those observed with placebo.[4] In addition to physically removing papules from the skin, application of caustic agents also has been used.

Chemical agents such as vesicants or blistering agents, retinoic acid (regulates cell proliferation), and alkalis have been used to remove molluscum contagiosum papules. Cantharidin is a potent vesicant that has been used with or without occlusion for the removal of lesions.[5] It should be used sparingly as it may cause blistering, tingling, or burning within a few hours of application, and the lesion site may remain tender for 2 to 6 days.[6] For example, blisters occurred at the application site in 92% (276/300) of patients treated with cantharidin, and 6% to 37% of patients experienced burning, pain, erythema, or pruritus.[5] Furthermore, cantharidin should not be applied to more than 3 to 4 lesions initially because some patients may be particularly sensitive to the medication and may develop serious erosions.[3]

Another form of chemical treatment, retinoic acid (tretinoin), also has been used topically to remove lesions by exfoliation.[7] However, retinoic acid may cause skin drying, peeling, irritation, and soreness.[6] Potassium hydroxide, a strong alkali agent, also has been investigated in the treatment of molluscum contagiosum.[8] Administration of topical potassium hydroxide 10% twice daily in children with molluscum contagiosum resulted in successful removal of lesions in 32 of 35 patients after a mean treatment of 30 days. However, 3 patients discontinued treatment—2 because of severe stinging of lesions and 1 because of a secondary infection at the application site. Therefore, as with other chemical treatments such as retinoic acid, pain and skin irritation may occur, and physicians should consider more tolerable treatment options that minimize skin irritation to surrounding tissues. One such therapeutic option is imiquimod cream 5%.

Imiquimod is a member of a new class of drugs, immune response modifiers, and is approved as a 5% cream for the treatment of external genital and perianal warts/condyloma acuminatum in adults. Although the mechanism of action of imiquimod has not been elucidated completely, studies suggest that imiquimod indirectly activates antiviral activity by inducing cytokines, including interferon alfa.[9,10] Antiviral activity has been demonstrated in human cell culture models and several virus-infected animal models.[11,12] Because physicians typically have used similar techniques for the treatment

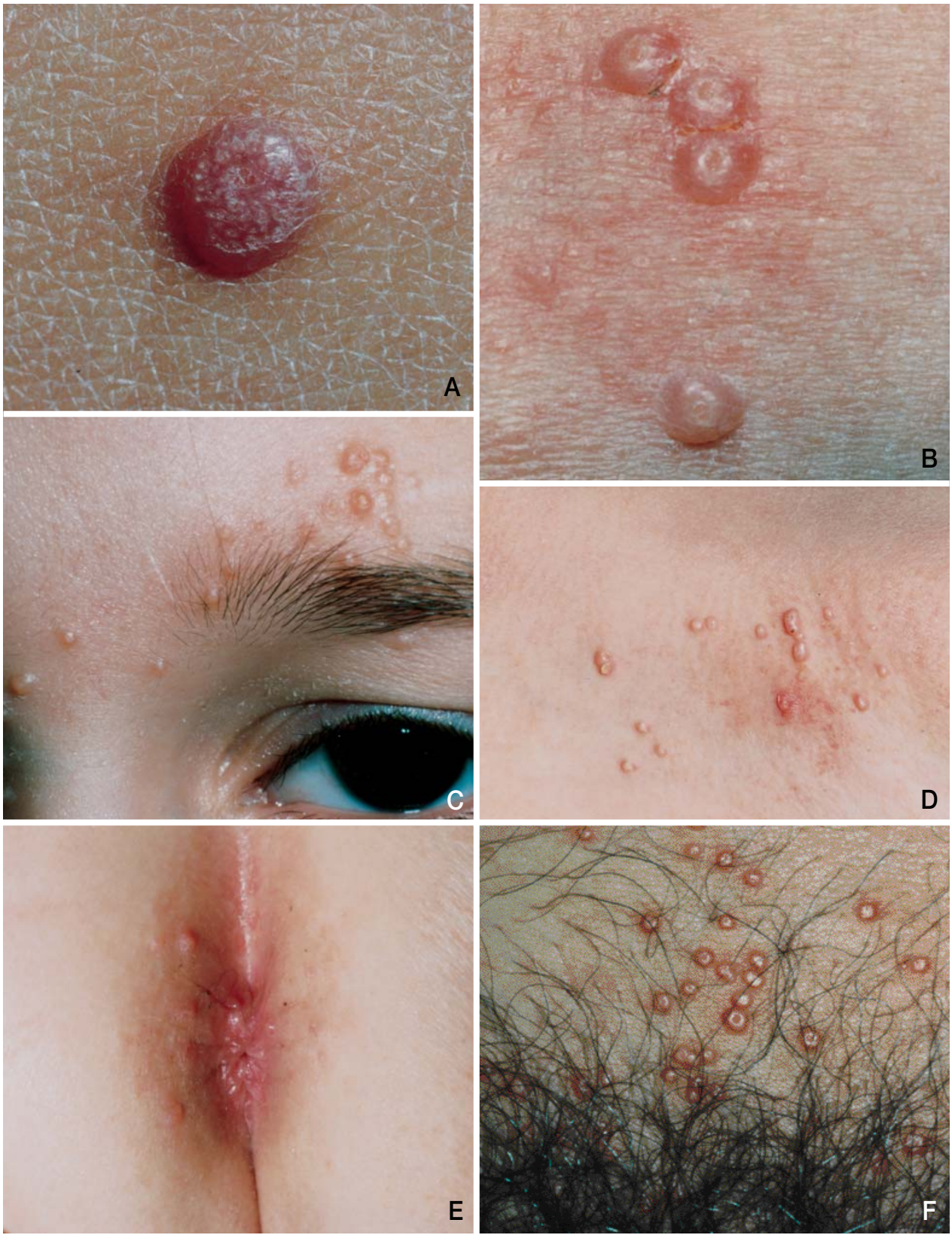

Figure 1. Molluscum contagiosum lesions: classic pink, umbilicated papule (A); multiple umbilicated, flesh-colored papules (B); multiple lesions on the face of a 4-year-old boy (C); axillary vault of a 7-year-old girl with multiple inflamed and noninflamed lesions (D); perianal nonsexually transmitted lesions on a 3-year-old child (E); and sexually transmitted suprapubic lesions in a young boy (F).

Table 2.

Treatment of Molluscum Contagiosum Lesions

Physical destruction
Electrosurgery
Curettage
Cryosurgery
Chemical destruction (physician applied)
Blistering agent (eg, cantharidin)
Alkali agent (eg, potassium hydroxide)
Topical therapy (patient applied)
Retinoic acid
Imiquimod cream (immune response modifier)

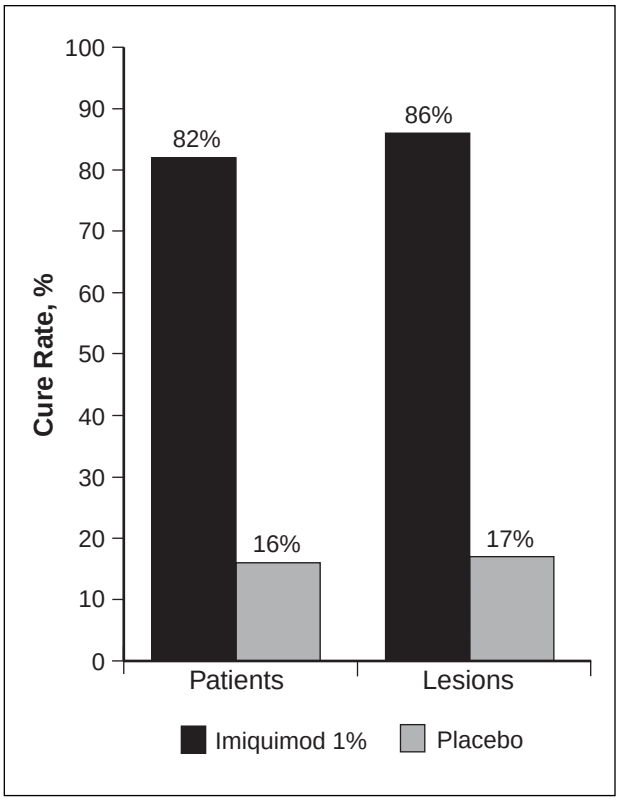

Figure 2. Percentage of patients (N=100) and molluscum contagiosum viral lesions (N=733) cured by week 4 with imiquimod 1% vs placebo.

of warts and molluscum contagiosum lesions, imiquimod cream also might be effective for the treatment of poxviruses. A small number of published clinical trials have studied the safety and efficacy of imiquimod cream in the treatment of molluscum contagiosum.[13-15]

In a double-blind, randomized, placebo-controlled study, 100 males (mean age, 16.3 years; range, 9–27 years) with a total of 733 (mean, 7.3) 2- to 5-mm molluscum contagiosum lesions were treated with imiquimod cream 1% or placebo.[13] Patients applied the medication at home 3 times daily for 5 consecutive days for a total of 4 weeks (maximum of 60 topical applications). Patients were followed weekly for 12 weeks, then followed monthly for 9 months. Treatment with imiquimod cream resulted in a complete response or cure in 82% (41/50) of patients and eliminated 86% (309/358) of lesions in this treatment group compared with 16% (8/50) of patients and 17% (63/375) of lesions treated with placebo at week 4 ($P<.001$)(Figure 2). Furthermore, imiquimod cream was well tolerated, and there were no treatment discontinuations. Only 18% (9/50) of patients treated with imiquimod cream experienced mild adverse events. All 9 of these patients experienced mild fever, and 6 also experienced mild pruritus. In addition, the lesion responses were lasting. Only 1 of the 41 patients successfully treated with imiquimod cream relapsed (during month 10).[13] The study administered imiquimod cream 1%, which contains less active agent than the imiquimod cream 5% approved for the treatment of warts. However, open-label studies have investigated the use of imiquimod cream 5% in the treatment of molluscum contagiosum.

An open-label safety study reported on 13 patients (mean age, 7 years; range, 4–10 years) treated with imiquimod cream 5% nightly for 4 weeks.[14] Of the 12 patients completing the study, 7 (58%) experienced localized adverse events—most commonly nominal to mild erythema, occurring in 6 (50%) patients. In addition, there was no evidence of systemic toxicity (eg, leukopenia, headaches, myalgia). Furthermore, although the study was not designed to test efficacy, complete resolution of the target lesions occurred in 33% (4/12) of patients by the end of week 4.[14]

In an additional study, 15 patients with molluscum contagiosum resistant to standard therapeutic treatment (eg, salicylic acid, local surgery, cryotherapy, laser ablation) self-administered imiquimod cream 5% nightly 5 days per week for 4 to 16 weeks.[15] Eighty percent (12/15) of patients achieved either a complete clearance of lesions (8 patients) or a greater

than 50% reduction in lesion size (4 patients). Of the 7 children participating, 6 (86%) achieved total clearance of lesions. In addition, there was no correlation of response to HIV serostatus, gender, or atopic predisposition. Furthermore, consistent with previous results, only one patient developed a recurrence (at week 10) after initial complete clearance of lesions. These studies suggest that imiquimod cream may be used in the treatment of molluscum contagiosum in children and adults and provides a novel treatment opportunity, particularly in patients who experience adverse reactions or who are refractory to other forms of treatment. Further comparative studies are warranted to determine the efficacy of imiquimod cream in the treatment of molluscum contagiosum.

Comment

Molluscum contagiosum is a common viral infection of the skin's epithelial layer. Multiple papules can develop at multiple locations. The disease can be spread by direct bodily contact with an infected person, by fomites, and by self-inoculation. Lesions are typically found on the face, extremities, and trunk in children, whereas sexual transmission typically results in lesions on the genitals or surrounding area in adolescents and adults. Furthermore, patients with compromised immune systems, such as patients with HIV infection, tend to have increased difficulty in resolving the infection and may experience secondary complications such as bacterial infections. Although debate continues regarding the value of therapeutic intervention, physicians should treat this contagion, particularly in light of the availability of safe, efficacious, and convenient treatment options.

Several treatment strategies used in the treatment of warts also have been applied to molluscum contagiosum lesions. However, treatments such as physical and chemical destruction result in pain and irritation and are inconvenient because of the need for several office visits. A new class of drugs, immune response modifiers, of which imiquimod is a member, has been approved for the treatment of external genital and perianal warts. Clinical studies in molluscum contagiosum have indicated that imiquimod is well tolerated and efficacious in treating molluscum contagiosum papules. Furthermore, the medication can be administered in the privacy of a patient's own home, providing added convenience and reducing patient embarrassment or stress, particularly in children and adolescents. With the novel treatment opportunities currently available or in development, physicians have the tools available to improve patient quality of life while providing patients with a convenient, well-tolerated, easily administered treatment regimen.

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