Experience With Molluscum Contagiosum and Associated Inflammatory Reactions in a Pediatric Dermatology Practice

The Bump That Rashes

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Objective: To investigate the frequency, epidemiology, clinical features, and prognostic significance of inflamed molluscum contagiosum (MC) lesions, molluscum dermatitis, reactive papular eruptions resembling Gianotti-Crosti syndrome, and atopic dermatitis in patients with MC.

Design: Retrospective medical chart review.

Setting: University-based pediatric dermatology practice.

Patients: A total of 696 patients (mean age, 5.5 years) with molluscum.

Main Outcome Measures: Frequencies, characteristics, and associated features of inflammatory reactions to MC in patients with and without atopic dermatitis.

Results: Molluscum dermatitis, inflamed MC lesions, and Gianotti-Crosti syndrome–like reactions (GCLRs) occurred in 270 (38.8%), 155 (22.3%), and 34 (4.9%) of the patients, respectively. A total of 259 patients (37.2%) had a history of atopic dermatitis. Individuals with atopic dermatitis had higher numbers of MC lesions (50.6% vs 31.8%; P < .001). In patients with molluscum dermatitis, numbers of MC lesions increased during the next 3 months in 23.4% of those treated with a topical corticosteroid and 33.3% of those not treated with a topical corticosteroid, compared with 16.8% of patients without dermatitis. Patients with inflamed MC lesions were less likely to have an increased number of MC lesions over the next 3 months than patients without inflamed MC lesions or dermatitis (5.2% vs 18.4%; P < .03). The GCLRs were associated with inflamed MC lesion (P < .001), favored the elbows and knees, tended to be pruritic, and often heralded resolution of MC. Two patients developed unilateral laterothoracic exanthem–like eruptions.

Conclusions: Inflammatory reactions to MC, including the previously underrecognized GCLR, are common. Treatment of molluscum dermatitis can reduce spread of MC via autoinoculation from scratching, whereas inflamed MC lesions and GCLRs reflect cell-mediated immune responses that may lead to viral clearance.

Published online August 20, 2012.

MOLLUSCUM CONTAGIOSUM (MC) is a self-limited viral skin infection that typically presents as umbilicated papules and occurs most commonly in children. A recent population-based study found that 20% of Japanese children developed MC by 6 years of age. In surveys of general practitioners in the Netherlands (1987 and 2001) and the United Kingdom (1994-2003), the cumulative incidence of MC by 15 years of age was approximately 17%, with slightly higher incidence rates in more recent years. Only 5% to 10% of MC cases in these studies occurred in individuals older than 14 years. In most affected children, MC spontaneously resolves within a few months to years; however, a variety of treatments have been used to speed its clearance in patients with bothersome symptoms or cosmetic concerns. Up to 39% of adults in the general population have antibodies to the MC virus, suggesting a high rate of mild or subclinical infections.

Several types of inflammatory reactions can occur in association with MC. Lesions of MC may become inflamed and are often surrounded by eczematous dermatitis (“molluscum dermatitis”). Gianotti-Crosti syndrome–like reactions (GCLRs) have also been reported in a few patients with MC. Although inflammatory reactions are well-recognized manifestations of MC infection, there are a paucity of published data on their frequency, epidemiolog-
ogy, clinical spectrum, and prognostic significance. Furthermore, the effects of previous and concurrent atopic dermatitis (AD) on the incidence, spread, and response to treatment of MC have varied in different studies.1-5,14-18

To better characterize the demographic and clinical features of inflammatory responses to MC and the relationship between AD and MC, we performed a retrospective study of 696 patients with MC seen in our university-based pediatric dermatology practice over a 5-year period; MC-associated GCLR occurred in 34 patients, and its relevance to the course of the infection was noted. Data on the number, location, and duration of MC in patients with and without AD and inflammatory reactions were collected. In addition, the treatments used for MC and associated dermatitis were documented.

METHODS

A retrospective review was performed of the medical charts of patients at the New York University Pediatric Dermatology Faculty Practice who were diagnosed from January 1, 2005, through December 31, 2010, as having “molluscum contagiosum” according to the International Classification of Diseases, Ninth Revision, Clinical Modification. Data were gathered on these patients’ demographics (age, sex), medical and family histories, number and distribution of MC, presence of active AD and other inflammatory skin reactions, laboratory studies, treatment modalities, and MC course and duration. Qualitative estimates of the number of MC lesions were converted to quantitative ranges as follows: 5 or fewer lesions for “few”; 6 to 15 lesions for “multiple”; 16 to 50 lesions for “many”; and more than 50 lesions for “numerable” (there were no quantitative estimates for the 16-30 category). In less than 10 patients to whom cimetidine was administered and the number of MC lesions was not specified, it was estimated that there were 31 to 50 lesions, as it is our practice to give cimetidine only to patients with more than 30 MC lesions. Time periods charted as “a few” weeks or months were converted to 3 weeks or months, and MC course and duration. Qualitative estimates of the number of MC lesions were converted to quantitative ranges as follows: 5 or fewer lesions for “few”; 6 to 15 lesions for “multiple”; 16 to 50 lesions for “many”; and more than 50 lesions for “numerable” (there were no quantitative estimates for the 16-30 category). In less than 10 patients to whom cimetidine was administered and the number of MC lesions was not specified, it was estimated that there were 31 to 50 lesions, as it is our practice to give cimetidine only to patients with more than 30 MC lesions. Time periods charted as “a few” weeks or months were converted to 3 weeks or months, respectively.

Approval by the New York University Medical Center institutional review board was obtained prior to beginning the medical chart review. There was no direct patient contact, and no identifiable patient data were recorded from the medical chart. Statistical analysis was performed via calculation of descriptive frequencies and use of 2-tailed χ² tests (using commercially available software) for comparisons between groups.

RESULTS

PATIENT CHARACTERISTICS

A total of 696 patients (336 boys, 360 girls) with MC were identified. The mean age at presentation was 5.5 years (median age, 5 years [range, 7 months to 17 years]) (Figure 1). Two children had immune disorders (IgA deficiency and familial Mediterranean fever treated with colchicine). Five other patients were taking at least 1 systemic immunosuppressive medication: prednisone (2 patients), mycophenolate mofetil (2 patients), cyclosporine, and 6-mercaptopurine. None of the patients were known to be infected with the human immune deficiency virus (HIV).

A total of 307 (44.1%) had a history of atopy. This included 259 patients (37.2%) with AD and 138 patients (19.8%) with asthma or allergies (environmental or food). Among patients with a history of AD, 169 (65.3%) had active dermatitis: 53.9% only at sites of MC, 22.5% only at other sites, and 23.7% at both sites of MC and other sites. A total of 293 patients (42.1%) had a family history of atopy (AD, asthma, or environmental allergies), and 179 patients (25.7%) had 1 or more household members with MC (176 siblings, 2 parents, and 1 grandparent). Figure 2 depicts the duration of MC prior to presentation in the 434 patients for whom these data were available.

LOCATION AND NUMBERS OF MC LESIONS

The distribution of the patients’ MC lesions is presented in Table 1. Molluscum contagiosum lesions were limited to 1 region in 213 patients (30.6%), most often the extremities (125 patients [18.0%]) or trunk (39 patients [5.6%]). Molluscum contagiosum lesions were present on both the trunk and extremities in 302 patients (43.4%). Most patients’ peak number of MC lesions was less than 50 (Figure 3).

Several patterns of inflammation were associated with having more than 50 MC lesions. Fifty-one of 259 patients (19.7%) with AD (whether or not it was active) had more than 50 MC lesions vs 22 of 437 patients (5.0%) without AD (P < .001). Similarly, 46 of 270 patients...
(17.0%) with molluscum dermatitis had more than 50 MC lesions vs 27 of 426 patients (6.3%) without molluscum dermatitis (P < .001). In addition, 25 of 155 patients (16.1%) with inflamed MC lesions had more than 50 MC lesions vs 48 of 541 patients (8.8%) without inflamed MC lesions (P < .02). In contrast, patients with a GCLR were not more likely than those without this type of reaction to have more than 50 MC lesions (3 of 34 [8.8%] vs 70 of 662 [10.6%]; P > .99).

INFLAMED MC LESIONS

A total of 155 patients (22.3%) had at least 1 inflamed MC lesion, and 102 patients (14.7%) had at least 2 inflamed MC lesions. Inflamed MC lesions were characterized by substantial erythema and swelling, including pustular or fluctuant lesions. The locations of these lesions are shown in Table 1. A systemic antibiotic was administered to 24 children with inflamed MC lesions owing to suspicion of infection (furunculosis [22 patients] or cellulitis [2 patients]). A pathogenic organism (Staphylococcus aureus) was isolated in only 2 of 10 culture samples performed of purulent exudate from these lesions. Inflamed MC lesions were equally common in patients with and without AD (57 of 259 [22.0%] vs 98 of 437 [22.4%], P = .93).

Among the 58 patients who were seen in follow-up within 3 months of presenting with inflamed MC lesions, the overall number of MC lesions increased in 3 patients (5.2%), remained the same in 12 patients (20.7%), and decreased in 43 patients (74.1%). On average, the number of MC lesions decreased 65.0% in the latter group, and complete resolution occurred in 12.1% of these patients. The number of MC lesions was less likely to increase over the subsequent 3 months in patients with inflamed MC lesions (3 of 58 patients [5.2%]) than in those without inflamed MC lesions or dermatitis (16 of 87 patients [18.4%]; P < .03) (Table 2).

MOLLUSCUM DERMATITIS

Molluscum dermatitis (eczematous dermatitis surrounding MC lesions) was present in 270 patients (38.8%). Patients with a history of AD, when compared with those without a history of AD, were more likely to have dermatitis associated with their MC lesions (50.6% vs 31.8%; P < .001). The locations of molluscum dermatitis are shown in Table 1. A total of 249 patients with molluscum dermatitis (92.2%) were treated with a topical corticosteroid (primarily low to mid potency agents). Among the 146 patients with molluscum dermatitis who were seen in follow-up within 3 months (Table 2), the number of MC lesions increased in 32 of 137 patients (23.4%) who received topical corticosteroid therapy and 3 of 9 patients (33.3%) who were not treated with a topical corticosteroid (P = .44). Although a smaller proportion of patients without dermatitis (19 of 113 [16.8%]) had an increased number of MC lesions after 3 months of follow-up compared with those with dermatitis (35 of 146 [24.0%]), the difference was not significant (P = .16).

GIANOTTI-CROSTI SYNDROME–LIKE REACTIONS

Thirty-four patients (12 girls and 22 boys) developed a GCLR during the course of their MC. The GCLRs were characterized by an eruption of numerous monomorphous, edematous, erythematous papules or papulo-

<table>
<thead>
<tr>
<th>Body Site</th>
<th>MC Lesions (n = 696 Patients)</th>
<th>Molluscum Dermatitis (n = 270 Patients)</th>
<th>Inflamed MC Lesions (n = 155 Patients)</th>
<th>MC Lesions in Patients With a GCLR (n = 34 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk</td>
<td>379 (54.5)</td>
<td>79 (29.3)</td>
<td>53 (34.2)</td>
<td>21 (61.8)</td>
</tr>
<tr>
<td>Extremities</td>
<td>542 (77.9)</td>
<td>186 (68.9)</td>
<td>83 (53.5)</td>
<td>24 (70.6)</td>
</tr>
<tr>
<td>Face</td>
<td>123 (17.7)</td>
<td>17 (6.3)</td>
<td>6 (3.9)</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Scalp</td>
<td>4 (0.6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Buttocks</td>
<td>153 (22.0)</td>
<td>27 (10.0)</td>
<td>19 (12.3)</td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Groin</td>
<td>107 (15.4)</td>
<td>12 (4.4)</td>
<td>17 (11.0)</td>
<td>5 (14.7)</td>
</tr>
<tr>
<td>Neck</td>
<td>97 (13.9)</td>
<td>14 (5.2)</td>
<td>6 (3.9)</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>Axilla(e)</td>
<td>98 (14.1)</td>
<td>30 (11.1)</td>
<td>10 (6.5)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Palms or soles</td>
<td>5 (0.7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviation: GCLR, Gianotti-Crosti syndrome–like reaction.
vesicles separate from MC lesions (Figure 4). The mean age of these patients was 5.6 years (median age, 5.5 years [range, 11 months to 12 years]). Pruritus was a prominent feature of the GCLR in 27 patients (79.4%). The eruption was present at the initial visit in 17 patients (50.0%), and in the others it developed a mean of 1.7 months after their first visit. Treatment of the MC had been initiated within the month prior to the onset of the GCLR in 13 patients (38.2%).

The GCLR involved the extremities in 32 patients (94.1%), affecting the arms in 30 patients and legs in 29 patients. The eruption was bilateral in all patients. Twenty-three patients (67.6%) with a GCLR had exclusive involvement of the extensor aspects of the extremities, and lesions were limited to the knees and/or elbows in 12 patients (35.3%). Palmoplantar lesions occurred in only 1 patient. Other areas affected by the GCLR included the face (7 patients), trunk (5 patients), and buttocks (4 patients). Two patients (1- and 4-year-old boys) initially had involvement primarily on 1 side of the trunk that resembled a unilateral laterothoracic exanthem (ULTE). In 1 of these children, the MC lesions were limited to the same truncal region, and a more classic GCLR affecting the extensor aspects of the extremities later developed.

The locations of MC lesions in patients with a GCLR (Table 1) were similar to those in the study population overall. In patients with a GCLR, the number of MC lesions was 5 or fewer in 23.5%, 6 to 15 in 11.8%, 16 to 30 in 35.3%, 31 to 50 in 14.7%, and more than 50 in 8.8%. A GCLR was equally common in patients with and without AD (13 of 259 [5.0%] vs 21 of 437 [4.8%]; P > .99).

A biopsy was performed of the GCLR in 1 patient. Histologic evaluation showed a superficial and mid-dermal perivascular infiltrate composed of lymphocytes, histiocytes, and scattered eosinophils (Figure 5). Some lymphocytes extended into the overlying epidermis. Spon-

**Table 2. Change in Number of Molluscum Contagiosum (MC) Lesions in Patients Who Had Follow-up Visits Within 3 Months**

<table>
<thead>
<tr>
<th>Type(s) of Associated Inflammation</th>
<th>Decrease in the No. of MC Lesions</th>
<th>No Change in the No. of MC Lesions</th>
<th>Increase in the No. of MC Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflamed MC, n = 58</td>
<td>43 (74.1)</td>
<td>12 (20.7)</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>Inflamed MC + dermatitis, n = 32</td>
<td>26 (81.3)</td>
<td>6 (18.8)</td>
<td>0</td>
</tr>
<tr>
<td>Inflamed MC, no dermatitis, n = 26</td>
<td>17 (65.4)</td>
<td>6 (23.1)</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Molluscum dermatitis, n = 146</td>
<td>91 (62.3)</td>
<td>20 (13.7)</td>
<td>35 (24.0)</td>
</tr>
<tr>
<td>Molluscum dermatitis with topical corticosteroid therapy, n = 137</td>
<td>85 (62.0)</td>
<td>20 (14.6)</td>
<td>32 (23.4)</td>
</tr>
<tr>
<td>Molluscum dermatitis without topical corticosteroid therapy, n = 9</td>
<td>6 (66.7)</td>
<td>0</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>No molluscum dermatitis or active atopic dermatitis, n = 113</td>
<td>74 (65.5)</td>
<td>20 (17.7)</td>
<td>19 (16.8)</td>
</tr>
<tr>
<td>No inflamed MC, molluscum dermatitis, or active atopic dermatitis, n = 87</td>
<td>57 (65.5)</td>
<td>14 (16.1)</td>
<td>16 (18.4)</td>
</tr>
</tbody>
</table>

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**Figure 4.** Patients with Gianotti-Crosti syndrome–like reactions to molluscum contagiosum. Pruritic, edematous, pink papules on the elbow (A) and knees (B). Central crusts are evident in some lesions. Note the coalescence to form a plaque on the elbow and koebnerization secondary to scratching on the knee.

**Figure 5.** Histologic findings of a Gianotti-Crosti syndrome–like reaction. A perivascular infiltrate composed of lymphocytes, histiocytes, and a few eosinophils is evident in the superficial and mid-dermis. Some lymphocytes extend into the overlying epidermis, where there is spongiosis, intraepidermal vesiculation, and focal scale crust. No molluscum bodies are present, further differentiating this reaction pattern from inflamed molluscum lesions (hematoxylin-eosin, original magnification ×10).
giesis, intraepidermal vesiculation, and focal scale-crust were evident.

The mean duration of the GCLR was 6 weeks in the 13 patients for whom this information was available. The eruption lasted less than 1 month in 5 of these patients and a mean of 2 months in the other 8 patients. The GCLR was typically treated with a topical corticosteroid of mid-potency or higher and usually responded with substantial improvement within 1 week. The mean time between onset of the GCLR and resolution of the MC lesions was 2 months (median, 5 weeks [range, 1-8 months]) in the 12 patients for whom these data were available. In addition, a substantial (50%-95%) reduction in the number of MC lesions occurred in all 9 patients with a GCLR who were followed for at least 2 months after its onset, but they were lost to follow-up prior to complete resolution of the MC lesions.

RELATIONSHIPS AMONG DIFFERENT TYPES OF INFLAMMATORY REACTIONS

Inflamed MC lesions were observed in 22 of 34 patients (64.7%) with a GCLR, compared with only 133 of 662 patients (20.1%) without a GCLR (P < .001). In contrast, patients with and without a GCLR were equally likely to have molluscum dermatitis (12 of 34 [35.3%] vs 258 of 662 [39.0%]; P = .67). Similar proportions of patients with and without molluscum dermatitis had inflamed molluscum (70 of 270 [25.9%] vs 85 of 426 [20.0%]; P = .08).

TREATMENT AND COURSE

Data on the treatments administered are presented in Figure 6. Cantharidin (0.7% in a collodion base) was applied in 475 patients (a mean of 1.9 treatment sessions per patient [range, 1-10]; treated areas were washed with soap and water 2 to 3 hours after application), and curettage was used in 100 patients (a mean of 1.4 treatment sessions per patient [range, 1-5 sessions]). A second agent was later added in some patients who were treated initially with cantharidin or curettage, including imiquimod cream in 35 patients, a topical retinoid in 17 patients, and oral cimetidine (approximately 40 mg/kg daily divided into 2 doses, a maximum of 1600 mg daily) in 111 patients. None of the patients experienced a serious adverse effect related to any of the treatments administered. In the 42 patients (treated with various modalities) for whom data on the timing of both the onset and resolution of the MC were available, the MC lesions were present for a mean of 8.0 months (median, 6.6 months [range, 1.5-29.0 months]).

This study further characterizes both classic and more recently recognized types of inflammatory reactions associated with MC. Data from other large series of pediatric patients with MC that described the frequencies of inflamed MC lesions, molluscum dermatitis, and AD are summarized in Table 3.13,14,15,17,19-22

Inflamed MC lesions typically present as erythematous, edematous papules and papulonodules that may become pustular or fluctuant. In this study and the previous large MC series that provided data on this reaction pattern (Table 3), 20.8% of patients overall (343 of 1646) were noted to have inflamed MC lesions.13,17 Despite their furuncle-like appearance, the results of the current study
confirm that the purulent exudate from inflamed MC lesions is usually sterile. However, superinfections with S aureus occasionally occur, and antibiotic administration (as well as drainage when appropriate) should be considered when there is lymphangitic streaking or spread of erythema suggestive of cellulitis.

Inflammation usually leads to regression of affected MC lesions and sometimes heralds clearance of the entire eruption, including lesions that do not develop clinically evident inflammation. In this study, patients with inflamed MC lesions were significantly less likely to have an increased number of MC lesions during the next few months than those without inflamed MC lesions. Cell-mediated immunity presumably plays a role in the clearance of MC, explaining the increased likelihood of widespread, severe and persistent MC in patients with HIV infection. Histologically, inflamed MC lesions demonstrate a dense, mixed inflammatory infiltrate (eg, lymphocytes, histiocytes, and neutrophils). In the current study, the presence of inflamed MC lesions was associated with the development of a GCLR, which can also be a harbinger of MC clearance and likely also has a cell-mediated immune basis but not molluscum dermatitis. Unfortunately, the limited follow-up data in this retrospective study and previous series have precluded a more thorough analysis of the duration of MC in patients with and without inflamed lesions, especially considering that patients whose MC lesions resolve are unlikely to return for follow-up visits.

Molluscum dermatitis presents as a pruritic eczematous eruption in the skin surrounding MC lesions. The dermatitis can be diffuse or nummular and may be more prominent than the MC lesions themselves, with MC lesions obscured by dermatitic patches and plaques. Molluscum dermatitis was evident in 38.8% of the patients in this study and in 9% to 47% of those in previous MC series, with an overall mean incidence of 27% (505 of 1896; Table 3). Like the study by Osio et al, the current study found that molluscum dermatitis is more likely to develop in children with a history of AD, affecting most (50.6%) patients in this subgroup. However, an association between molluscum dermatitis and the development of inflamed MC lesions or a GCLR was not observed, suggesting different inflammatory pathways for these noneczematous reactions. Patients with molluscum dermatitis were more likely to have a large number of MC lesions, likely related at least in part to spread of MC lesions by scratching due to increased pruritus.

In the current study, a history of AD was associated with the development of inflamed MC lesions or a GCLR, explaining most (50.6%) patients in this subgroup. However, an association between molluscum dermatitis and the development of inflamed MC lesions or a GCLR was not observed, suggesting different inflammatory pathways for these noneczematous reactions. Patients with molluscum dermatitis were more likely to have a large number of MC lesions, likely related at least in part to spread of MC lesions by scratching due to increased pruritus.

There is evidence that MC is more common in children with AD than in those without AD. The prevalence rates of AD in this study and other pediatric MC series based in the United States, South America, Europe, Australia, and Japan have ranged from 18% to 45% (Table 3), with an overall mean of 36% (944 of 2656). These rates are higher than the estimated AD prevalence of approximately 10% to 20% in pediatric populations. However, MC-infected children with a history of AD may be more likely to see a physician for skin problems, which could potentially affect the results of MC series based on medical records. A 2010 population-based study of nursery school children in Japan found a 1.6-fold increased likelihood of MC (95% CI, 1.00-2.68) in children with AD. In the current series, children with a history of AD were more likely to have a large number of MC lesions than those without AD. Likewise, in a recent study of curettage treatment for MC, patients with AD had more lesions and more frequent relapses than those without AD. In contrast, a history of AD was not associated with the number of MC lesions or recurrence of MC in a recent large French series. In the current study, a history of AD was associated with having dermatitis surrounding MC lesions (as discussed in this section) but not with the development of inflamed MC lesions or a GCLR.

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients With MC, No.</th>
<th>Ages (Mean), y</th>
<th>AD, % of Patients</th>
<th>Molluscum Dermatitis, % of Patients</th>
<th>Inflamed MC Lesions, % of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>696</td>
<td>0.6-17 (5.5)</td>
<td>36</td>
<td>39</td>
<td>22</td>
</tr>
<tr>
<td>Osio et al,2011</td>
<td>650</td>
<td>0.5-15 (6)</td>
<td>34</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Seiz et al,2011</td>
<td>113</td>
<td>1-15 (5.5)</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Hayashida et al,2010</td>
<td>180</td>
<td>1-6 (3.6)</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Dohil et al,2006</td>
<td>302</td>
<td>≤5 in 53% and ≤8 in 80% of patients</td>
<td>24</td>
<td>24</td>
<td>NA</td>
</tr>
<tr>
<td>Kakourou et al,2005</td>
<td>110</td>
<td>0.5-11 (4.9)</td>
<td>18</td>
<td>15</td>
<td>NA</td>
</tr>
<tr>
<td>Laxmisha et al,2003</td>
<td>137</td>
<td>0.5-14 (6.2)</td>
<td>NA</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Agromayor et al,2002</td>
<td>107</td>
<td>1-14 (6)</td>
<td>45</td>
<td>45</td>
<td>NA</td>
</tr>
<tr>
<td>Silverberg et al,2000</td>
<td>300</td>
<td>NA (4.7)</td>
<td>41</td>
<td>41</td>
<td>20</td>
</tr>
<tr>
<td>Choong and Roberts,2019</td>
<td>198</td>
<td>0.5-47 (7.8)</td>
<td>32</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviation: NA, data not available.

aLimited to series of at least 100 patients with MC.

### Table 3. Data on the Prevalences of Atopic Dermatitis (AD) and Inflammatory Reactions in Patients With Molluscum Contagiosum (MC)

- Present study: 696 patients, 0.6-17 (5.5) years, 37% AD by history, 39% AD active, 24% inflamed MC lesions
- Osio et al, 2011: 650 patients, 0.5-15 (6) years, 43% AD by history, 19% AD active, 21% inflamed MC lesions
- Seiz et al, 2011: 113 patients, 1-15 (5.5) years, 34% AD by history, 47% AD active, 12% inflamed MC lesions
- Hayashida et al, 2010: 180 patients, 1-6 (3.6) years, 21% AD by history, 21% AD active, 21% inflamed MC lesions
- Dohil et al, 2006: 302 patients, ≤5 in 53% and ≤8 in 80% of patients, 24% AD by history, 24% AD active, NA, NA
- Kakourou et al, 2005: 110 patients, 0.5-11 (4.9) years, 18% AD by history, NA, NA
- Laxmisha et al, 2003: 137 patients, 0.5-14 (6.2) years, NA, NA, 9% inflamed MC lesions
- Agromayor et al, 2002: 107 patients, 1-14 (6) years, 45% AD by history, NA, NA
- Silverberg et al, 2000: 300 patients, NA (4.7) years, 41% AD by history, 20% inflamed MC lesions
- Choong and Roberts, 1999: 198 patients, 0.5-47 (7.8) years, 32% AD by history, NA, NA

- 5 in 53% and ≤8 in 80% of patients

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characteristics, distribution, and pruritus of GCLRs in the setting of MC are indeed reminiscent of id reactions (eg, disseminated eczema associated with allergic contact dermatitis or a dermatophyte infection). Compared with classic Gianotti-Crosti syndrome, GCLRs triggered by MC tend to exhibit more prominent pruritus, a relatively localized distribution (eg, limited to the elbows and knees), and a better response to topical corticosteroid therapy. The histologic findings in the patient described herein whose GCLR was biopsied and 1 previously reported patient included epidermal spongiosis and a dermal perivascular lymphohistiocytic infiltrate, which would be compatible with either Gianotti-Crosti syndrome or an id reaction.\(^{11}\)

The observation of GCLRs in 5% of the patients with MC in the current series suggests that this inflammatory response to MC is more common than suggested by the paucity of previous reports. The association of GCLRs with MC may be underrecognized when the MC lesions are few in number, in “hidden” sites (eg, the axillae or groin), masked by inflammation, or obscured by dermatitis. Because the papules or papulovesicles of a GCLR can resemble MC lesions, a GCLR may even be mistaken (especially by parents) for a sudden increase in the number of (inflamed) molluscum. Dermoscopy can help to identify MC lesions, which are characterized by a multilobulated, white to yellow, amorphous central structure surrounded by a “crown” of blood vessels.\(^{29}\)

Molluscum-associated GCLRs tend to be relatively short-lived, lasting a mean of 6 weeks in the patients in this study who returned for follow-up visits and 3 or fewer weeks (following removal of MC lesions via curettage) in the 2 previous reports. The development of a GCLR in a patient with MC seems to be a good prognostic sign. All of the patients with GCLR for whom follow-up data were available experienced a dramatic reduction in the number of MC lesions, with complete clearance of the MC lesions occurring a median of 5 weeks after onset of the GCLR.

Two patients in this series had a reactive papular eruption that initially involved 1 axilla and the ipsilateral trunk, resembling an ULTE. Like Gianotti-Crosti syndrome, ULTE is thought to have a viral trigger, but no etiologic agent has been consistently demonstrated. Affected children present with a morbilliform or eczematous eruption that initially involves 1 axilla and the adjacent trunk and/or upper arm, eventually becoming bilateral. There have been 2 previous reports\(^{12,13}\) of a predominantly unilateral truncal exanthem lasting 1 to 2 months in children with MC in the same distribution and negative results from serologic studies for other viruses. In the current study, the MC lesions resolved within 2 weeks of onset of the ULTE-like eruption in the patient with this reaction who returned for follow-up.

Osió et al\(^{15}\) noted that use of topical corticosteroids within the previous 3 months was associated with a higher risk of recurrence following treatment of MC. Among patients in the current study with molluscum dermatitis, the number of MC lesions increased during the following 3 months in 23.4% of those who were treated with a topical corticosteroid and in 33.3% of those who were not treated with a topical corticosteroid (Table 2). A smaller proportion (16.8%) of patients without dermatitis had an increased number of MC lesions during this time frame. These results suggest that the eczematous dermatitis itself, rather than immunomodulatory effects of the corticosteroid used to treat it, was responsible for the development of new MC lesions. The association between topical corticosteroid use and recurrence of MC observed by Osió et al\(^{15}\) may be explained by autoinoculation of MC virus related to pruritus and resultant scratching of the dermatitis that was being treated. Using a topical corticosteroid could also make MC lesions previously obscured by dermatitis become visible, providing another possible explanation for an apparent “recurrence” of MC. Observations in the current study and experiences of other pediatric dermatologists suggest that control of surrounding dermatitis may help to prevent the spread of MC that often occurs secondary to scratching.\(^{29,30}\)

In series of children with MC, the proportion of patients with known immune disorders (eg, HIV infection, primary immunodeficiencies) or taking a systemic immunosuppressive medication has been extremely low. For example, only 7 of the 696 patients (1.0%; none with HIV infection) in this series and none of the 661 pediatric patients with MC in the largest previous study were immunocompromised.\(^{19}\) At a tertiary care center, patients with complicated medical histories (including immune disorders and receipt of immunomodulatory therapy) would likely account for a larger proportion of patients with MC than in the general community. In a 5-year population-based study of Native Americans and Alaskan Natives, only 13 of 13 700 visits (<0.1%) for MC over a 5-year period involved patients with HIV infection.\(^{31}\)

There is no gold standard for the treatment of MC, as reflected in the variety of destructive and immunomodulatory methods that are used.\(^{29,30,32}\) Although watchful waiting is often appropriate given the self-limited nature of MC, treatment can help to alleviate pruritus and discomfort, prevent spread via autoinoculation or transmission to other children, and eliminate the social stigma of visible lesions.\(^{29,30,32}\) In a recent survey of members of the Society for Pediatric Dermatology,\(^{32}\) the most common therapeutic methods used for MC were cantharidin, imiquimod, and curettage (used by 95%, 85%, and 72% of respondents, respectively). Each of these modalities was frequently used in the current study (Figure 6), which represents the largest published experience with cantharidin (475 patients) to date. This and other series, such as the report of cantharidin therapy in 300 patients with MC by Silverberg et al in 2000,\(^{17}\) provide support for its safety and efficacy.

The tendency for spontaneous resolution of MC makes it difficult to determine the effectiveness of treatment in retrospective series and uncontrolled studies. One prospective randomized study found that curettage (following use of a topical anesthetic with or without systemic sedation) required fewer patient visits for elimination of MC and had a lower rate of adverse effects than topical application of cantharidin or imiquimod.\(^{33}\) Randomized studies have also shown that imiquimod therapy for MC has efficacy similar to that of cryotherapy or topical application of potassium hydroxide.\(^{34,35}\) Although cryotherapy (when performed weekly) may result in more rapid clearance of MC lesions than imiquimod (eg, 3-6 weeks vs 6-12 weeks), the former modality produces more
discomfort and pigmented sequelae. Additional prospective controlled studies are needed to evaluate the benefits and patient tolerance of different treatments for MC.

In conclusion, this series documents the frequencies and clinical presentations of inflammatory reactions to MC, highlighting their relationships with one another, AD, and the course of the MC infection. The incidence, features, and prognostic implications of the recently recognized GCLR in patients with MC are characterized for the first time. Better understanding of the pathogenesis of these inflammatory reactions and their effects on the natural history of MC may help to develop more effective treatment options for this common childhood infection.

Accepted for Publication: May 25, 2012.

Published Online: August 20, 2012. doi:10.1001/ARCHDERMATOL.2012.2414

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Author Contributions: All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Berger, Orlow, and Schaffer. Acquisition of data: Berger and Schaffer. Analysis and interpretation of data: Berger, Orlow, Patel, and Schaffer. Drafting of the manuscript: Berger, Orlow, and Schaffer. Critical revision of the manuscript for important intellectual content: Berger, Orlow, Patel, and Schaffer. Statistical analysis: Berger and Schaffer. Administrative, technical, and material support: Berger, Orlow, and Schaffer. Study supervision: Orlow, Patel, and Schaffer.

Financial Disclosure: None.

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