Epidemiologic and Clinical Evaluation of the Bidirectional Link Between Molluscum Contagiosum and Atopic Dermatitis in Children

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PRACTICE POINTS

- There is a high prevalence of atopic dermatitis (AD) in children with molluscum contagiosum, with a strong bidirectional relationship between these conditions.
- Children with AD display a broader age range for molluscum contagiosum, greater lesion burden, increased local inflammatory responses, prolonged resolution time, and more extensive and severe disease.

Atopic dermatitis (AD) is recognized in clinical practice as a condition that increases a patient's susceptibility to molluscum contagiosum (MC) and predisposes them to more widespread infection; however, data remain limited. To clarify the relationship between MC and AD in children, a retrospective study was conducted analyzing medical records of pediatric patients diagnosed with MC, AD, or both between September 2013 and August 2022. Collected data included demographics, clinical manifestations, and disease duration. The findings highlight a strong correlation between MC and AD in children, underscoring the need for health care professionals to acknowledge this relationship and implement proactive strategies to optimize patient care.

olluscum contagiosum (MC), which is caused by a DNA virus in the *Poxviridae* family, is a common viral skin infection that primarily affects

children.¹⁻⁴ The reported incidence and prevalence of MC exhibit notable geographic variation. Worldwide, annual incidence rates per 1000 individuals range from 3.1 to 25, and prevalence ranges from 0.27% to 34.6%.²⁻⁷

Molluscum contagiosum is diagnosed clinically and typically manifests as smooth, flesh-colored papules measuring 2 to 6 mm in diameter with central umbilication. It can manifest as a single lesion or multiple clustered lesions, or in a disseminated pattern. The primary mode of transmission is through contact with skin, lesions, or contaminated personal items, or via self-inoculation. The majority of cases are asymptomatic, but in some patients, MC may be associated with pruritus, tenderness, erythema, or irritation. When present, secondary bacterial infections can cause localized inflammation and pain. 1,3,4 The pathogenesis hinges on MC virus replication within keratinocytes, disrupting cellular differentiation and keratinization. The virus persists in the host by influencing the immune response through various mechanisms, including interference with signaling pathways, apoptosis inhibition, and antigen presentation disruption.3,4

Molluscum contagiosum typically follows a selflimiting trajectory, resolving over several months to 2 years.^{3,4} The resolution timeframe is intricately linked to variables such as the patient's immune profile, lesion burden, and treatment approach. For symptomatic lesions, a

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This study was conducted following the principles of the Declaration of Helsinki and was approved by the local ethical committee (0104-09-LND). The data supporting the findings are available from the corresponding author on request due to privacy/ethical restrictions.

The eTables are available in the Appendix online at www.mdedge.com/cutis.

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variety of treatment options have been described, including physical ablation (eg, cryotherapy, curettage) and topical agents such as potassium hydroxide, cantharidin, imiquimod, and salicylic acid.^{3,4,8,9}

Atopic dermatitis (AD) is a common chronic relapsing inflammatory skin disorder. In the United States, its prevalence ranges from 15% to 30% in children and from 2% to 10% in adults, with ongoing evidence of a growing global incidence.10-14 While AD can emerge at any age, typical onset is during early childhood. The clinical manifestation of AD includes a spectrum of eczematous features, often accompanied by persistent itching. The pathogenesis is multifactorial, involving a complex interplay of genetic, immunologic, and environmental factors. Key contributors to this multifaceted process encompass a compromised epidermal barrier, alterations in the skin microbiome, and an immune dysregulation promoting a type 2 immune response. Epidermal barrier dysfunction can be attributed to various factors, including diminished ceramide production, altered lipid composition, the release of inflammatory mediators, and mechanical damage from the persistent itch-scratch cycle. 10-13,15 These factors or their interplay may enhance the susceptibility of patients with AD to infections.

Several studies conducted across various geographic regions examining the relationship between MC and AD have reported variable findings. ^{2,6,7,16-21} Published studies have reported a prevalence of AD in children with MC ranging from 13.2% to 43%. ^{2,6,7,16-21} Although some studies suggest a higher rate of atopy in patients with MC, not all research has confirmed this association. ^{16,21} Dohil et al² reported a greater number of MC lesions in children with AD than those without an atopic background. Silverberg²⁰ reported that in 10% (5/50) of children with MC, the onset of AD was triggered, and in 22% (11/50) MC was associated with flares of pre-existing AD.

In this study, we aimed to assess MC infection rates in children with AD, analyze the epidemiologic aspects and severity differences between atopic children with and without MC infection, and compare data from atopic and nonatopic children with MC.

Methods

In this retrospective cohort study, we analyzed the medical records of pediatric patients diagnosed with MC, AD, or both conditions at an outpatient dermatology practice in Netanya, HaSharon, Israel, from September 2013 to August 2022. Data were collected from the electronic medical records and included patient demographics, the clinical presentation of MC and/or AD at diagnosis, and the duration of both conditions. Only patients with complete data and at least 6 months of follow-up were included. Key epidemiologic characteristics assessed included patient sex, age at the initial visit, and age at the onset of MC and/or AD. Diagnoses of MC and AD were established through clinical examinations conducted by dermatologists. The clinical evaluation of AD encompassed the assessment of body surface area involvement (categorized as <5%, 5%-10%,

or >10%). Atopic dermatitis severity was classified as mild, moderate, or severe using the validated Investigator Global Assessment Scale for Atopic Dermatitis. Clinical evaluation of MC included assessment of the number of lesions (categorized as \leq 4, 5-9, or \geq 10), presence of inflammatory lesions, and resolution times for individual lesions (categorized as \leq 1 week, several weeks, or unknown), as well as the overall resolution time for all lesions (categorized as \leq 6 months, 6-12 months, 13-18 months, or \geq 18 months). The temporal relationship between the appearance of MC and AD also was assessed.

Statistical Analysis—Numbers and percentages were used for categorical variables. Continuous variables were represented by mean and standard deviation. Categorical variables were compared using the χ^2 test, and continuous variables between groups were compared using the Student t test. All statistical tests were 2-sided, with statistical significance defined as $P \leq .05$. Statistical analysis was performed using SPSS software version 28 (IBM).

Results

Study Population—A total of 610 children were included in the study; 263 (43%) were female and 347 (57%) were male. The patients ranged in age from 4 months to 10 years, with a mean (SD) age of 4.87 (1.82) years. Five hundred fifty-six (91%) patients had AD, and 336 (55%) had MC. Within this cohort, 274 (45%) children had AD only, 54 (9%) had MC only, and 282 (46%) had both AD and MC. Regarding the temporal sequence, among the 282 children who had both AD and MC, AD preceded MC in 203 (72%) cases, both conditions were diagnosed concomitantly in 43 (15%) cases, and MC preceded AD in 36 (13%) cases. For cases in which the MC diagnosis followed the diagnosis of AD, the mean (SD) time between each diagnosis was 3.17 (1.5) years.

Comparison of Atopic and Nonatopic Children With MC—Although a higher proportion of males were diagnosed with MC (with or without concurrent AD), the differences in sex distribution between the 2 groups did not reach statistical significance. Among all children with MC, the majority (81.5% [274/336]) were aged 1 to 6 years at presentation. Patients with MC as their sole diagnosis had a similar mean age compared with those with concurrent AD. However, a detailed age subgroup analysis revealed a notable distinction: in the group with MC as the sole diagnosis, the majority (95% [51/54]) were younger than 7 years. In contrast, in the combined MC and AD group, MC manifested across a wider age range, with 21% (58/282) of patients being older than 7 years. In MC cases associated with AD, a notably higher lesion count and increased local inflammatory response were observed compared to those without AD. The time for complete resolution of all MC lesions was substantially prolonged in patients with comorbid AD. Specifically, 93% (50/54) of patients with MC without comorbid AD achieved full resolution within 1 year, whereas 52% (146/282) of patients with comorbid AD required more than 1 year for resolution (eTable 1).

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Comparison of Atopic Children With and Without MC—Sex, age distribution, and disease duration showed no differences between atopic patients with and without MC. Atopic patients with MC exhibited greater body surface area involvement and higher validated Investigator Global Assessment Scale for Atopic Dermatitis scores compared to atopic patients without MC (eTable 2).

Comment

This study examined the relationship between MC and AD in pediatric patients, revealing a notable correlation and yielding valuable epidemiologic and clinical insights. Consistent with previous research, our study demonstrated a high prevalence of AD in children with MC.^{2,6,7,16-21} Previous studies indicated AD rates of 13% to 43% in pediatric patients with MC, whereas our study found a higher prevalence (84%), signifying a substantial majority of patients with MC in our cohort had AD. This discrepancy arises from factors such as demographic, genetic, and environmental differences, along with differences in access to medical care, referral practices, and diagnostic approaches across health care systems.¹⁴

Our temporal analysis of MC and AD diagnoses offers important insights. In the majority (72% [203/282]) of cases, the diagnosis of AD preceded MC, supporting previous research suggesting that the underlying pathophysiology of AD heightens susceptibility to MC. 15,17-20 Less frequently, MC was diagnosed before or concurrently with AD, indicating that MC may occasionally trigger or exacerbate milder or undiagnosed AD, as previously proposed. 20

A notable finding in our study was the expanded age range for MC onset in patients with AD, encompassing older age groups compared to patients with MC as their sole diagnosis, possibly due to persistent immune dysregulation. To the best of our knowledge, this specific observation has not been systematically reported or documented in prior cohort studies. Visible skin lesions of MC may have a psychological impact on patients, influencing self-consciousness and causing embarrassment and emotional distress. This may be more pronounced in older children, who are more aware of their appearance and social perceptions. ²³⁻²⁵ These considerations should play a role in the management of MC.

Our study revealed that children with AD and MC displayed higher lesion counts, increased local inflammatory responses, and a more protracted resolution period compared to nonatopic children. In more than 50% of children with AD, MC took more than 1 year for resolution, whereas the majority of those without AD achieved resolution within 1 year. These findings may be attributed to AD-related immune dysregulation, influencing the natural course of MC. Consequently, it suggests that while nonatopic children with MC usually are managed through observation, atopic patients may benefit from an intervention-oriented approach.

Comparing atopic patients with and without MC showed a heightened occurrence of severe and extensive

AD among those with concurrent MC. Several factors could contribute to this observation. On one hand, there could be a direct association between the extent and severity of AD, leading to an elevated susceptibility to MC. Conversely, MC might exacerbate immunologic dysregulation and intensify skin inflammation in atopic individuals.²⁰ Additionally, itching related to both disorders may exacerbate inflammation and compromise the epidermal barrier, facilitating the spread of MC. This interplay suggests that each condition exacerbates the other in a self-reinforcing cycle. The importance of patient and caregiver education is underscored by recognizing these interactions. To manage both conditions effectively, health care providers should counsel patients and caregivers on maintaining proper skin care practices such as gentle cleansing with mild, fragrance-free products, regular moisturization, and avoidance of irritants, encourage them to avoid scratching, and recommend adopting an active treatment approach.

Our study had notable strengths. Firstly, a substantial sample size enhanced the statistical reliability of our findings. Additionally, valuable insights into the epidemiology and clinical aspects of AD and MC were obtained by utilizing real-world data from an outpatient dermatology practice. In our study, clinical evaluations covered body surface area involvement and disease severity for AD while also assessing lesion counts and the presence of inflammatory lesions for MC. This comprehensive approach facilitated a thorough analysis of both conditions. The extended data collection period not only allowed for observation of their clinical course and duration, but also enabled a detailed assessment of their interplay.

Our study also had several limitations. Primarily, its retrospective design relied on the accuracy and comprehensiveness of medical records, which may have introduced bias. The exclusion of some patients due to incomplete data further increased the potential for selection bias. Additionally, this study was conducted in a single outpatient dermatology practice in Israel, resulting in a study population composed predominantly of Jewish patients (94%), with a minority (6%) of Arab patients. Other ethnic groups, including Black, Asian, and Hispanic populations, were not represented. This reflects the country's demographic composition rather than an intentional selection bias. However, the limited ethnic diversity reduces the generalizability of our findings. Differences in demographics, coding practices, health care utilization (eg, timeliness of seeking care, access to dermatology services), and treatment strategies also may impact the observed prevalence, clinical characteristics, and patient outcomes. Furthermore, while our study highlighted the potential advantages of a proactive treatment approach for atopic children with MC, it did not evaluate specific treatment protocols. Future research should aim to confirm the most efficacious therapeutic strategies for managing MC in atopic individuals and to include a more diverse population to better understand the applicability of findings across various ethnic groups.

Conclusion

Our study found a high prevalence of AD in children with MC and a strong bidirectional relationship between these conditions. Pediatric patients with AD display a broader age range for MC, greater lesion burden, increased local inflammatory responses, prolonged resolution times, and more extensive and severe AD.

Recognizing the interplay between MC and AD is crucial, highlighting the importance of health care providers educating patients and caregivers. Emphasizing skin hygiene, discouraging scratching, and implementing proactive treatment approaches can enhance the outcomes of both conditions. Further research into the underlying mechanisms of this association and effective therapeutic strategies for MC in atopic individuals is warranted.

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APPENDIX

eTABLE 1. Demographic and Clinical Comparison of Atopic and Nonatopic Children With MC

Variable	MC only (n=54)	AD+MC (n=282)	Total (N=336)	P value
Sex, n (%)				
Female	26 (48)	119 (42)	145 (43)	.42
Male	28 (52)	163 (58)	191 (57)	
Age at first visit, y				
Range	2.11-7.4	0.4-9.0	0.4-9.0	
Mean (SD)	4.63 (1.1)	4.86 (1.84)	4.82 (1.74)	.37
Age subgroup, n (%)				
Up to 3 y	16 (30)	68 (24)	84 (25)	.012ª
4-6 y	36 (67)	156 (55)	192 (57)	
7-12 y	2 (4)	58 (21)	60 (18)	
Ethnicity, n (%)				
Jewish	50 (93)	267 (95)	317 (94)	.77
Arab	4 (7)	15 (5)	19 (6)	
Inflammatory MC lesions, n (%)				
Present	16 (30)	122 (43)	138 (41)	.0008ª
Absent	36 (67)	94 (33)	130 (39)	
Unknown	2 (4)	66 (23)	68 (20)	
Number of MC lesions, n (%)				
≤4	33 (61)	96 (34)	129 (38)	.00006ª
5-9	19 (35)	109 (39)	128 (38)	
≥10	2 (4)	77 (27)	79 (24)	
Time to resolution of all MC lesions from onset, n (%)				
<6 mo	15 (28)	69 (24)	84 (25)	<.00001ª
6-12 mo	35 (65)	67 (24)	102 (30)	
13-18 mo	3 (6)	94 (33)	97 (29)	
>18 mo	1 (2)	52 (18)	53 (16)	
Duration of individual lesion resolution, n (%)				
≤1 wk	28 (52)	147 (52)	175 (52)	.27
>1 wk	18 (33)	135 (48)	153 (46)	
Unknown	8 (15)	0 (0)	8 (2)	

 $^{^{\}mathrm{a}}\!P$ values < .05 were considered statistically significant.

eTABLE 2. Demographic and Clinical Comparison of Atopic Children With and Without MC

Variable	AD only (n=274)	AD+MC (n=282)	Total (N=556)	P value
Sex, n (%)				
Female	118 (43)	119 (42)	237 (43)	.84
Male	156 (57)	163 (58)	319 (57)	
Age at first visit, y				
Range	0.3-10	0.4-9	0.3-10	
Mean (SD)	4.92 (1.92)	4.86 (1.84)	4.90 (1.88)	.71
Age subgroup, n (%)				
Up to 1 y	1 (0.4)	2 (0.7)	3 (0.5)	.80
2-3 y	66 (24)	66 (23)	132 (24)	
4-6 y	158 (58)	156 (55)	314 (56)	
7-12 y	49 (18)	58 (21)	107 (19)	
Ethnicity, n (%)				
Jewish	264 (96)	267 (95)	531 (95)	.45
Arab	10 (4)	15 (5)	25 (5)	
Duration of AD, y				
Range	0.4-8.5	0.3-7.2	0.3-8.5	
Mean (SD)	3.16 (1.51)	3.27 (1.46)	3.21 (1.48)	.38
BSA involvement by AD, n (%)				
<5	179 (65)	68 (24)	247 (44)	<.00001a
5-10	82 (30)	128 (45)	210 (38)	
>10	13 (5)	86 (30)	99 (18)	
vIGA-AD				
Mild	111 (41)	88 (31)	199 (36)	.039ª
Moderate	130 (47)	145 (51)	275 (49)	
Severe	33 (12)	49 (17)	82 (15)	

Abbreviations: AD, atopic dermatitis; BSA, body surface area; MC, molluscum contagiosum; vIGA-AD, validated Investigator Global Assessment Scale for Atopic Dermatitis.

 $^{^{\}mathrm{a}}\!P$ values $<\!.05$ were considered statistically significant.