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Does Molluscum Contagiosum Need to be Managed Differently in Atopic Children?

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The association between molluscum contagiosum and concomitant atopic dermatitis and its impact on clinical features and treatment outcomes remains unclear. This retrospective study, conducted in the paediatric dermatology clinic of a tertiary medical centre, aimed to compare molluscum patients with and without atopic dermatitis. A total of 615 children with molluscum were included, 13.17% of whom had atopic dermatitis. While the latter group exhibited higher lesion count and itchiness (p=0.026 and p=0.044, respectively), no significant differences were observed in average lesion diameter, ulceration, purulence, and erythema (p=0.239, p=0.730, p=0.682, and p=0.296, respectively). Both groups showed comparable responses to molluscum-specific and supportive treatments, with no distinct difference in outcomes or recurrence of visits. It was concluded that atopic dermatitis does not exacerbate molluscum morbidity, inflammation markers, treatment outcomes or recurrence rates.

Key words: atopic dermatitis; molluscum contagiosum; paediatric dermatology.

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SIGNIFICANCE

We studied 615 children with molluscum contagiosum and found that 13.17% also had atopic dermatitis. When having both conditions, patients had more molluscum lesions and reported more itchiness. However, there were no differences in the size of the lesions or their inflammation between the two groups. We found that both groups responded similarly to molluscum-specific and supportive treatments. We concluded that atopic dermatitis does not seem to affect other aspects of molluscum infection, treatment outcomes or recurrence rate. This information is valuable for managing molluscum, especially when it coexists with atopic dermatitis.

Molluscum contagiosum (MC) is a viral infection frequently observed in the pediatric population (1). Its pathophysiology has been extensively documented. Upon invading the host, the double-stranded MC virus infects keratinocytes located in the stratum basale. As keratinocytes undergo differentiation from the stratum basale to the stratum corneum, the virus is released from the stratum corneum layer, leading to hypertrophy and hyperplasticity of the epidermis (2). This projection above the surface results in the formation of small papules (2). The incubation period for the virus varies, typically spanning from 2 to 6 weeks (1).

Because MC gains access through breaks in the skin, its prevalence tends to be higher among individuals with dry skin or those dealing with conditions such as atopic dermatitis (AD) (1). Nevertheless, this connection has sparked recent debates as studies present conflicting findings. A study conducted on Brazilian children revealed no discernible difference in MC frequency between those with and without AD (5). However, Olsen et al. (6) discovered that children with AD have a 13% higher likelihood of developing MC than their non-AD counterparts. Furthermore, another study found that patients with a history of AD were more likely to have a higher number of MC lesions (7) as well as a higher prevalence of molluscum dermatitis (8). Finally, Leshem et al. (9) recently identified an increased probability of MC in AD patients compared with those without AD.

Conversely, in individuals with pre-existing AD, MC has been found to exacerbate their condition, resulting in a higher occurrence of widespread lesions. This phenomenon has recently been investigated in children, where the risk of AD appeared to be highest when MC lesions were localized in intertriginous or flexural areas (10). Therefore, understanding the correlation between AD and MC is crucial for improving the care management of patients presenting with both conditions.

In this study, we aimed to compare MC patients with and without AD. By examining distinct characteristics associated with these two groups of MC patients, we anticipate that we might offer additional insights and bridge the knowledge gap in the correlation between MC and AD.

MATERIALS AND METHODS

This research was conducted at the paediatric dermatology clinic of Soroka University Medical Center (SUMC), a university-affiliated referral centre in Southern Israel, directly serving a

population of 600,000 and acting as a tertiary hospital for over 1 million people. Data were gathered from the medical records of patients at SUMC, and the study was conducted under the IRB number SOR-0305-21.

We retrospectively reviewed all cases of children (aged 0–18) diagnosed with MC between 2013 and 2022. Inclusion criteria encompassed individuals who received assessment or treatment for MC lesions at the paediatric dermatology clinic in SUMC during this period, while those aged 18 years and older and those not evaluated at the clinic were excluded. Demographic information, including age, ethnicity, gender, and age at MC diagnosis, was initially collected. Subsequently, various parameters related to MC lesions were evaluated, covering location, number, size, and the presence of erythema, ulceration, pruritus, or purulence. Treatment details and associated outcomes such as hypopigmentation, hyperpigmentation, and scarring were analysed, along with the number of clinic visits to assess resistance or reinfection. Evaluation criteria for treatment response encompassed a reduction in lesion size by at least 50% compared with the initial measurement, absence of scarring, and clinical improvement, as assessed and recorded by the treating physician. Clinical improvement parameters extended beyond alterations in lesion size and scarring to encompass changes in induration, ulceration, and erythema. Recurrent visits due to MC complaints were also assessed after discounting people who did not receive any treatment. This modification aimed to mitigate any bias in visit frequency for patients who did not receive treatments but were nonetheless scheduled for routine follow-ups at the office.

All treatments within the study were categorized into two groups: MC treatments (curettage, topical retinoids, fluorouracil with salicylic acid, imiquimod, podophyllotoxin, trichloroacetic acid, and liquid nitrogen) and supportive treatments (topical and systemic steroids and antibiotics). There was no disparity in the length of MC treatment prescribed between patients with AD and those without AD. However, it is important to note that MC patients with AD may have already been receiving treatments for their underlying condition before seeking treatment for their MC.

JASP (https://jasp-stats.org/) was utilized for descriptive statistical univariate analyses. Normality was assessed, when applicable, through Shapiro–Wilk tests. To examine distinctions between atopic and non-atopic patients, univariate analysis employed either one-tailed or two-tailed χ^2 tests, a Fisher's exact test or Student's *t*-test. Statistical significance was set at $p < 0.05$.

RESULTS

The study comprised 615 children, with a mean age of 7.9 years and an MC diagnosis at 5.1 years old. Within the population, 51.8% were male, 95.2% identified as Jewish, while the remaining 4.8% were Arabs. AD was present in 13.17% of patients, while 86.83% of patients did not have AD.

When comparing individuals with and without AD, several notable findings emerged. First, AD patients exhibited a significantly higher quantity of lesions compared with non-atopic patients (21.75 vs 12.39 lesions, $p=0.026$, see **Fig. 1**), although there was no discernible difference in the average lesion diameter (4.58 mm vs 5.61 mm, $p=0.239$). Second, most inflammation markers, including ulceration, purulence, and erythema, demonstrated similar levels between atopic and non-atopic patients ($p=0.730$, $p=0.682$, and $p=0.296$, respectively). However, AD patients were found to have significantly greater itchiness than their non-atopic counterparts ($p=0.044$). All data are summarized in **Table I**.

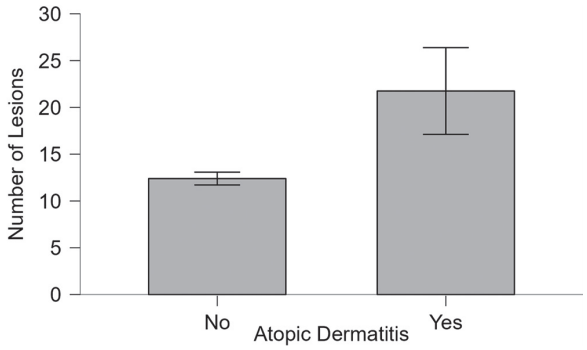

Fig. 1. Difference in the average number of molluscum contagiosum lesions between atopic dermatitis and non-atopic dermatitis patients. The bars around the mean indicate the standard error.

Our findings indicate that patients lacking AD received a notably higher proportion of treatments in general compared with those with AD (88.5% vs 11.5%, $p=0.002$). More specifically, no significant distinctions between atopic and non-atopic MC patients were noted upon segregating patients into those receiving MC treatments and those receiving only supportive treatment ($p=0.567$). The most frequently utilized treatments in both atopic and non-atopic patients were curettage (16.1% and 20.4%, respectively) and the combination of salicylic acid with fluorouracil (16.1% and 9.7%, respectively). However, no significant differences in the utilization of these treatments were observed between the two groups ($p=0.116$). Finally, the recurrence of return visits after treatments showed no significant difference between patients with and without AD ($p=0.498$).

Furthermore, the application of treatments in both atopic and non-atopic patients did not yield significant changes in outcomes concerning the reduction of ulceration ($p=0.782$), itchiness ($p=0.919$), and erythema ($p=0.102$). Furthermore, treatment outcomes such as hyperpigmentation ($p=0.167$), hypopigmentation ($p=0.530$), or residual scarring ($p=0.395$) were the same in patients both with and without AD (see Table I).

Table I. Comparison of key characteristics and treatment outcomes of patients with molluscum contagiosum with atopic dermatitis (AD) vs non-AD

Characteristics	AD	Non-AD	*p*-value
Number of lesions, mean	21.75	12.39	0.026
Lesion diameter, mm, mean	4.58	5.61	0.239
Ulceration, *n* (%)	7 (12.1)	62 (13.7)	0.730
Purulence, *n* (%)	9 (14.5)	78 (16.5)	0.682
Itchiness, *n* (%)	20 (30.8)	91 (19.9)	0.044
Erythema, *n* (%)	44 (60.3)	265 (53.8)	0.296
Recurrence	21 (33.9)	177 (38.3)	0.498
Treatment – outcome, *n* (%)			
Ulceration	4 (18.2)	32 (23.5)	0.782
Itchiness	8 (38.1)	48 (36.9)	0.919
Erythema	11 (47.8)	37 (30.3)	0.102
Hyperpigmentation	2 (66.7)	5 (21.7)	0.167
Hypopigmentation	3 (15.0)	12 (10.3)	0.530
Residual scarring	5 (21.7)	17 (14.7)	0.395

Moreover, we aimed to contextualize our findings more broadly by comparing MC patients with a history of any atopy in their medical records to those without any history of atopy. Our analysis revealed no statistically significant differences in inflammation markers such as erythema, itchiness, ulceration, and purulence between the two groups ($p=0.534$, $p=0.156$, $p=0.246$, and $p=0.449$, respectively). Following treatment, there was no discernible distinction between the two groups when assessing reductions in ulceration (p=0.122) and itchiness ($p=0.391$). However, patients with a history of atopy had a significant reduction of erythema following treatment compared with patients without a history of atopy ($p=0.035$). Post-treatment outcomes include hypopigmentation ($p=0.431$), hyperpigmentation ($p=0.883$), and residual scarring ($p=0.480$, **Table II**).

DISCUSSION

In this retrospective analysis, we thoroughly examined significant distinctions among MC patients with and without AD. Our results revealed that MC patients with AD displayed a higher quantity of lesions and reported increased itchiness compared with MC patients without AD. However, no disparities were identified in terms of lesion diameter, ulceration, purulence, and erythema. A comparable outcome was observed when examining recurrence, with atopic patients showing no tendency to revisit the hospital more frequently than non-atopic patients following treatment. Furthermore, despite a higher proportion of MC patients without AD receiving treatment, no variations were observed in the specific use of MC treatment or supportive treatment with the AD group. Similarly, no differences were found in treatment outcomes.

Our study contributes new insights to the ongoing debate in the literature, shedding light on previously conflicting perspectives. In their multiple logistic regression analysis, Hayashida et al. (11) found no notable distinction in the occurrence of molluscum contagiosum (MC) between children with AD and those without. Similarly, separate investigations conducted in a specialized dermatology clinic revealed a low prevalence of AD associated with MC and no statistically significant variance in recurrence rates linked to MC between patients with and without AD (5, 12). Our study aligns with these findings, indicating that MC patients, irrespective of the presence of AD, do not exhibit a higher recurrence of visits to our dermatology clinics. Moreover, our results distinctly provide new clinical insights into the limited pool of data in the literature regarding the similarities in ulceration, erythema, purulence, and lesion diameter between MC patients with AD and those without.

Nevertheless, several studies have presented evidence of the coexistence of AD and molluscum contagiosum (MC), along with clinical correlations between the two conditions. McCollum et al. demonstrated that individuals with MC were more likely to have a history or concurrent diagnosis of eczema (13). Another study reported a prevalence of AD in children with MC as high as 43% based on the review of cases from outpatient clinics (12). Additionally, Dohil et al. suggested that children with AD were prone to an increased number of MC lesions (7). Despite our study supporting the notion that more lesions may be present on atopic skin compared with non-atopic patients, only 13% of our MC patients were identified with AD, representing a substantial deviation from existing literature.

While our study generally supports prior research indicating a relatively modest impact of AD on the progression of MC, our findings stand out as unique. They demonstrate that the administration of treatments to both atopic and non-atopic patients did not lead to significant changes in terms of outcomes. The improvements in AD management in recent years may have played a role in these results. The existing literature proposes that effective AD management rapidly improves skin barrier function, potentially diminishing occurrence and MC morbidity (14). This could act as a factor in reconciling any differences that might have been observed in atopic dermatitis patients who are either non-compliant or untreated.

However, our findings do not endorse one treatment over another, aligning with 2 recent comprehensive analyses that found no variations in the effectiveness of various molluscum contagiosum (MC) treatments (15, 16). Our results expand on these findings within the context of AD, demonstrating that MC-specific and supportive treatments exhibit no discernible differences between AD and non-AD patients. Hence, we show that, despite the application of different treatments based on practicality, clinical judgement, or the preferences of physicians or patients, the choice between treatments does not impact the resolution of MC in the context of AD. Nonetheless, we contend that considering treatment in AD is warranted, given the higher number and increased pruritus of MC lesions compared with non-AD patients. While there is no evidence indicating that MC itself inherently induces more itchiness in AD patients than

Table II. Comparison of clinical characteristics of patients with molluscum contagiosum with and without an atopy history

Characteristics	Atopy history	No atopy history	*p*-value
Ulceration (*N*)	8 (8.6%)	52 (12.9%)	0.246
Purulence (*N*)	12 (12.4%)	65 (15.4%)	0.449
Itchiness (*N*)	25 (24.8%)	75 (18.5%)	0.156
Erythema (*N*)	63 (56.3%)	232 (53.0%)	0.534
Treatment – outcome			
Ulceration (*N*)	6 (18.6%)	30 (24.6%)	0.122
Itchiness (*N*)	9 (30.0%)	45 (38.5%)	0.391
Erythema (*N*)	15 (48.4%)	32 (28.3%)	0.035
Hyperpigmentation (*N*)	2 (25.0%)	5 (27.7%)	0.883
Hypopigmentation (*N*)	4 (15.4%)	11 (10.0%)	0.431
Residual scarring (*N*)	6 (20.0%)	16 (14.7%)	0.480

in non-AD patients, we acknowledge that this observation could be clarified by acknowledging the pruritic nature of AD, which may serve as a confounding factor in interpreting these findings. This heightened pruritic response may potentially lead to subsequent scratching of the MC papules, increasing the risk of autoinoculation (1). This perspective offers a plausible explanation for why MC patients with AD may exhibit a higher lesion count compared with those without AD.

While there is a lack of studies specifically exploring the relationship between atopy and skin infections, existing literature points to Th2 cytokines, such as IL-4 and IL-13, as potential contributors to an elevated risk of skin infections in patients with atopy (17). The results of our study do not contradict this notion, although they reveal no noticeable differences in inflammation markers and their reduction post-treatment, except for erythema. It is conceivable that children with atopy undergo more comprehensive and prolonged treatment overall (18), potentially leading to a long-term reduction in erythema. Furthermore, our analysis showed no notable differences in itchiness between MC patients with and without a history of atopy. The presence of a significant number of MC patients without AD but with a history of atopy in our findings may offset any statistical differences between MC patients with and without a history of atopy. This suggests that atopy alone may not be a decisive factor in the management of MC patients.

Strenghts and limitations

Our study possesses notable strengths. First, it encompasses a substantial number of patients, enabling the collection of a significant amount of data on both MC and AD, thereby enhancing the robustness of our analyses. Second, the retrospective nature of our study facilitates a more comprehensive evaluation of our AD patients, given that retrospective studies are inherently more effective for conditions with a prolonged latency period, such as AD. Finally, our methodology allowed us to assess the recurrence of MC complaints, which is an important factor in the follow-up and management of the disease. However, our study also has limitations. Children with AD and MC might visit clinics more frequently due to the lesions' easily spreadable or persistent nature, potentially introducing referral bias in a hospital-based study like ours and thereby limiting the generalizability of our findings to the broader population. This also holds true for patients without atopic dermatitis, who were also referred to the hospital because of more extensive MC infections, further prompting the need for increased treatments. Furthermore, due to its unavailability during the study period, our research could not draw comparisons with newer treatments recently approved by the Food and Drug Administration, such as cantharidin (19) and berdazimer gel (20). Subsequent studies are necessary to assess their impact, specifically within the context of atopic patients. Finally, our data collection did not include information regarding the severity of AD among patients, which limited our ability to stratify our findings based on AD severity. Further studies are necessary to gain a deeper understanding of how MC influences AD-related symptoms in affected patients.

Conclusion

In summary, our study offers valuable insights into the association of MC in children with AD. While AD may contribute to increased inconvenience in terms of the number of lesions and associated itchiness with MC, our findings reveal no significant differences in inflammation markers, treatment outcomes, and recurrence rates that could exacerbate MC morbidity when compared with non-atopic patients. Similarly, our results refrain from favoring one treatment over another regardless of atopic status, marking a significant advancement in MC management within the context of atopy. Further research is essential to validate these assertions.

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Data sharing statement: all data may be available upon request to the authors.

Ethical statement: Approval from Soroka Medical Center's institutional review board was obtained prior to the study which complied with the 1964, 1975, and 2013 revisions of the Helsinki Declaration (approval number SOR-0305-21).

Use of large language models: The authors declare that they used ChatGPT to assist with grammar.

The authors have no conflicts of interest to declare.

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