

Molluscum Contagiosum Clears Atopic Dermatitis: A Case Report

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Practice Points

- Molluscum contagiosum virus (MCV) may infect the inflamed skin of patients with atopic dermatitis (AD).
- MC148 protein secreted by MCV is the molecule that might best explain the MCV-induced inhibition of AD observed in the patient presented here.
- The MCV-induced inhibition of AD may occur even in the presence of *Staphylococcus aureus* infection.

A 14-year-old patient with severe widespread atopic dermatitis (AD) and concurrent molluscum contagiosum virus (MCV) presented with MCV papules that were surrounded by dermatitis-free zones. It appeared that components inhibited the expression of AD, with inhibitory effects that persisted throughout 6 years of follow-up, even in the presence of a *Staphylococcus aureus* infection, which was proven by skin culture.

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Case Report

A 14-year-old patient presented with severe widespread atopic dermatitis (AD) characterized by variably scaly, reddish brown to dark gray-brown, excoriated, and mildly to markedly lichenified lesions. The patient was concurrently infected with molluscum contagiosum virus (MCV), with abundant MCV papules present both in loose groups and randomly scattered over the areas of dermatitis. Each MCV papule was surrounded by a clear zone of clinically normal skin extending 3 to 8 mm from the edge of the papule (Figure 1). A rough correlation between the size of the papule and the width of the corresponding clear zone was noted (ie, the larger

the papule, the wider the clear zone). The presence of culture-proven *Staphylococcus aureus* did not prevent the MCV-induced inhibition of AD. The dermatitis-free zones surrounding the MCV papules resembled the clear zones that appear around disks of penicillin on agar plates streaked with *Streptococci*.

Following more than 6 years of follow-up, there was no loss of the inhibition of AD around the

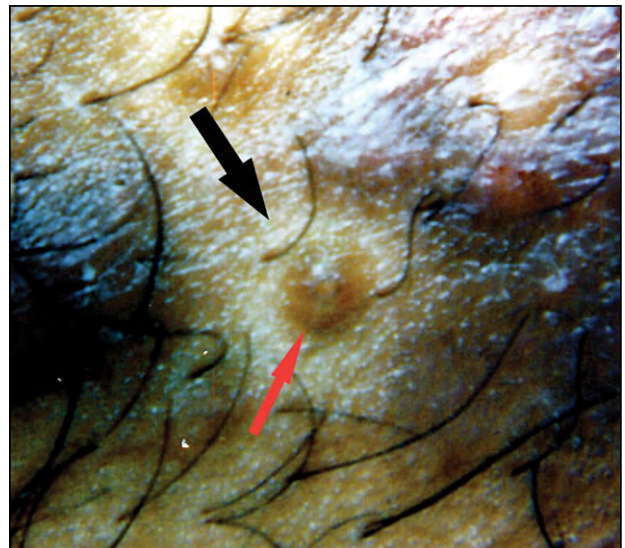


Figure 1. Clinical photograph showing a molluscum contagiosum virus papule surrounded by a clear zone with no atopic dermatitis. The red arrow indicates the edge of the molluscum contagiosum virus papule and the black arrow indicates the edge of the clear zone. The photograph was taken at a focal distance of 15 cm.

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The author reports no conflict of interest. Dr. Paslin holds a patent for "atopic dermatitis treatment method," but there is no company or product available.

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MCV papules. Some of the papules were intermittently removed via curettage, but as new MCV papules continued to appear, they retained the inhibitory function.

A photomicrograph of a biopsy taken at the edge of an MCV papule soon after the patient's initial office visit showed a paucity of mononuclear cells around small blood vessels of the superficial dermal plexus adjacent to the edge of a sample MCV papule (Figure 2). Molluscum bodies appeared as amorphous eosinophilic material within the cytoplasm of the keratinocytes of the papule. Mild to moderate acanthosis of the epidermis above and adjacent to the papule also was noted. A modified connective tissue stroma was present immediately adjacent to the MCV papule. In contrast to Figure 2 in which the dermis adjacent to the papule was almost devoid of inflammatory cell infiltrate, a concurrent photomicrograph depicted the heavy inflammatory cell infiltrate in the dermis in an area affected with AD that was remote from the MCV papule (Figure 3). In this image, the epidermis was markedly acanthotic with central adherent crust. There was a dense perivascular but also interstitial infiltrate of lymphocytes, mostly in the papillary and upper reticular parts of the dermis with lymphocytic exocytosis. Degranulated eosinophils were present in the interstitium.

Comment

Molluscum contagiosum is a poxvirus, but it has no known close viral relatives.¹ Similar to variola, MCV is limited to humans, but unlike variola, the infection usually is indolent, mild, asymptomatic, and almost always confined to skin. In the patient described here, the MCV infection may be viewed as commensal rather than destructive, living in but also benefiting the host.

The MCV genome consists of a tangle of double-stranded DNA. The genome sequence, which was initially described by Senkevich et al,² consists of 190,289 base pairs. It is submitted in the GenBank database (sequence accession U60315) (accessible at <http://www.viprbrc.org>) as comprising the entire genome, omitting only closed terminal hairpin loops. The genome has been estimated to encode 163 proteins that possess statistically predicted sequence similarity to proteins contained in databases.² Among these 163 putative proteins are 5 immune response-modifying proteins that are not present in other poxviruses.³ The genes from which these proteins are translated include MC054 whose protein product binds to IL-18 and inhibits its function; MC066 whose protein product hydrolyzes peroxides; MC080 whose protein product simulates

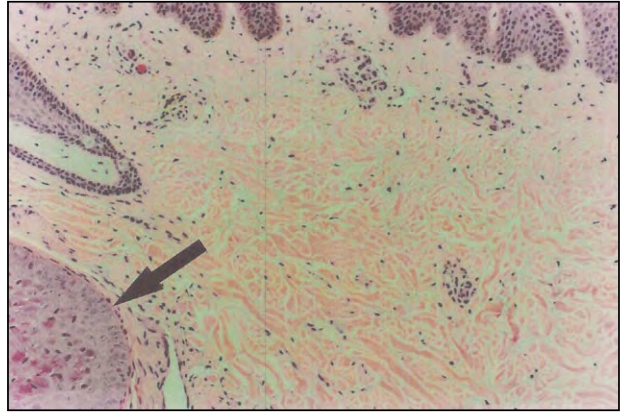


Figure 2. Photomicrograph showing the paucity of inflammatory cell infiltrate in the dermis adjacent to a molluscum contagiosum virus papule (arrow)(H&E, original magnification $\times 100$).

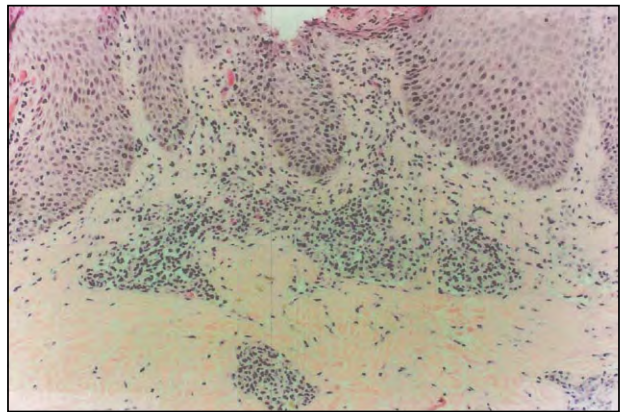


Figure 3. An inflammatory cell infiltrate of lymphocytes, macrophages, and eosinophils was present, characteristic of atopic dermatitis (H&E, original magnification $\times 100$). It was observed in an area affected with atopic dermatitis that was remote from the molluscum contagiosum virus papule.

the heavy chain of class I MHC antigens and binds to β_2 -microglobulin but lacks the amino acids necessary for peptide binding; MC148 whose protein product binds to chemokine receptor CCR8, thereby inhibiting chemotaxis of cells expressing CCR8; and MC159 whose protein product inhibits apoptosis of keratinocytes infected with MCV by binding to the intracytoplasmic protein Fas-associated death domain (FADD) to prevent FADD-induced activation of the apoptotic cascade.³

Atopic dermatitis is helper T cell (T_H2) dominant.⁴ Activated T_H2 cells, along with macrophages, interstitial dendritic cells, and Langerhans cells, contribute to atopic inflammation and express CCR8.⁵ The binding of CCR8 on the surface of these cells by the MC148 protein appears to inhibit access of these

cells to affected skin in patients with AD. Among the 5 immune-modifying proteins made by MCV, the action of the MC148 protein seems most likely to explain the clear zones surrounding the MCV papules in this patient.

The nucleotide sequence of MC148 open reading frame (ORF) in this patient is identical to the sequence deposited by Krathwohl et al⁶ in the GenBank database (sequence accession U96749). The MC148 protein is encoded by *MC148R* (R for reading right) ORF. *MC148R* is transcribed as an early gene. *MC148* messenger RNA is expressed in vivo as shown by reverse transcription-polymerase chain reaction of RNA extracted from MCV-infected human skin. MC148 protein is conserved in MCV isolates and is secreted from cultured mammalian cells using recombinant vaccinia virus harboring the *MC148* gene.⁷

Investigators at different laboratories have observed varying and at times conflicting actions of the MC148 protein. Based on the work of Krathwohl et al,⁶ MC148 protein is known as a CC chemokine homolog that binds to the MIP-1 α receptor but fails to activate the receptor due to the absence of the activation site in MC148 protein. The missing activation site is due to the absence of nonbasic amino acids between the extant amino acids at positions 24 and 25 from the amino terminal end of the MC148 protein as compared to the nonbasic amino acids present at the same activation sites of CC chemokines MCP-1, MIP-1 α , and MIP-1 β . The result was that MC148 protein blocked chemotaxis of peripheral blood mononuclear cells induced by MIP-1 α . Moreover, Damon et al⁸ reported that the MC148 protein possesses broad-spectrum capacity to inhibit both CC and CXC chemokines, not only by specifically impairing monocyte chemotaxis to the CC chemokines MCP-1, MCP-3, MIP-1 α , RANTES, and I-309 but also by specifically impairing both lymphocytic chemotaxis to the CXC chemokine SDF-1 and neutrophilic chemotaxis to the CXC chemokine IL-8. By contrast, the work of Lüttichau et al⁹ showed that the MC148 protein is

selective for binding to and inactivating CCR8 by the inhibition of chemotaxis of monocytes induced by I-309.

Conclusion

The inhibition of AD by MCV, as observed in the case described here, as well as the likelihood that MC148 protein in secretions from MCV prevented the expression of AD suggests that the MC148 protein may be useful in the treatment of AD. Studies are ongoing to test the capacity of MC148 protein to inhibit the inflammation of AD and perhaps other T_H2-related inflammatory and allergic disease states.

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