Pediatric Molluscum Contagiosum: Reflections on the Last Challenging Poxvirus Infection, Part 1

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Molluscum contagiosum (MC) is a common dermatologic infection that usually affects school-aged children, sexually active young adults, and immunocompromised individuals. It is a benign and self-limiting disease, with most cases undergoing spontaneous resolution within 6 to 9 months. However, a more severe and prolonged course is associated with immunosuppression or atopic dermatitis (AD). Management can be challenging; it needs to be decided whether to treat MC or let it run its natural course. It may be managed with reassurance and benign neglect; however, therapeutic intervention may be indicated to prevent autoinoculation and transmission, especially in patients at risk for severe disease. Guardians concerned about cosmesis should understand that therapy may leave pigmented alterations and sometimes scars. The 3 major therapeutic modalities employed are physical destruction, immunomodulation, and antiviral agents. Combinations of these therapies may be employed. Therapeutic modalities will be discussed in part 2.


Molluscum contagiosum (MC) is a common viral infection of the skin and mucous membranes that predominantly affects school-aged children, sexually active young adults, and immunocompromised individuals. It is considered a benign and self-limiting disease, though it can have a severe and protracted course in patients with an impaired immune system or atopic dermatitis (AD). Molluscum contagiosum is caused by the molluscum contagiosum virus (MCV), a highly contagious poxvirus. This infection spontaneously resolves within months in children with normal immune systems, but it can persist for years.1 Its prolonged course, associated symptoms, and lack of cosmesis can be bothersome to patients and may cause concern to patients and parents/guardians.

A continuous debate exists about the management of this disease. Some physicians believe it should be left alone to take its natural course, while others support the use of therapeutic measures. We often favor treating this condition, not only for cosmetic reasons but also to prevent transmission, reduce autoinoculation, and relieve associated symptoms. Many effective therapeutic options currently are available. They can be broadly subdivided into 3 types: destructive, immunomodulatory, and antiviral. Treatment should be individualized based on patient and physician preference. Occasionally, MC can present therapeutic challenges. Patients treated with destructive therapy can experience a recurrence several months later because of the prolonged incubation period of the virus.2 Immunocompromised patients may be refractory to standard treatment and may fail to clear the infection indefinitely.

Molluscum Contagiosum Virus

The MCV is a large, brick-shaped, double-stranded DNA virus of the family Poxviridae. With the eradication of smallpox, MCV is the only member of this family to commonly cause human morbidity.3 Although the virus is thought to exclusively
infect humans, rare cases in chimpanzees, horses, and kangaroos have been reported. Molluscum contagiosum virus has not been grown in tissue cultures or animals; however, infected human foreskin has been grafted onto athymic mice. The incubation period ranges from 2 weeks to 6 months. Molluscum contagiosum virus is composed of a 190-kilobase pair genome that encodes 163 proteins, 103 of which are homologous to the smallpox virus. Four major subtypes of MCV have been described: MCV-1, MCV-2, MCV-3, and MCV-4, with the latter 2 being extremely rare. Molluscum contagiosum virus subtype 1 accounts for the majority of infections in children, while MCV-2 is responsible for causing MC in immunocompromised patients and sexually active individuals. 

The virus has a predilection for the epidermis and replicates within the cytoplasm of keratinocytes where it induces hyperplasia and hypertrophy of these cells. Characteristic viral inclusion bodies termed molluscum bodies or Henderson-Patterson bodies are present within infected keratinocytes and are diagnostic for MC.

**Epidemiology**

Molluscum contagiosum has a worldwide distribution but tends to occur more frequently in tropical climates. Poverty, poor hygiene, and overcrowding may contribute to the increased prevalence in some areas. The incidence in childhood is on the rise in the United States and worldwide. The annual incidence is reported to be between 2% and 10%. In the Netherlands, there is a cumulative incidence of 17% by 15 years of age. However, its true incidence may be remarkably underestimated because many patients do not seek medical attention if cases are mild or subclinical, as papules often can go unnoticed or heal spontaneously. Molluscum contagiosum can occur sporadically or in localized outbreaks. One epidemic took place in a rural Israeli community where 34 individuals were infected, mostly children aged 2 to 9 years. No notable difference has been found in sex distribution. Studies on seasonal variation have conflicting results.

Virus transmission occurs by direct contact with infected skin or fomites and through autoinoculation. In adolescents, the virus generally is contracted during sexual activity. Clothing, bath sponges, towels, and gymnastic equipment have been implicated in spreading the infection. Multiple cases have been linked to swimming pools and public baths. The exact mechanism of spread at swimming pools is unknown. Sports that involve direct skin-to-skin contact such as wrestling also are associated with increased transmission.

Certain dermatologic conditions, such as AD, predispose children to this infection. Children with Darier disease or a genetic or acquired immunodeficiency also have increased susceptibility. An estimated 5% to 18% of patients infected with human immunodeficiency virus (HIV) are coinfected with MCV. The incidence and severity of MC in patients with HIV infection and AIDS is inversely proportionate to the CD4 lymphocyte count, with an associated incidence of 30% in those with less than 100 cells/mL.

**Clinical Description**

Molluscum contagiosum is characterized by 1- to 5-mm papules that are smooth, firm, and dome-shaped with central umbilication. They appear pearly white, pink, or flesh-colored (Figure 1). Central umbilication may not be evident in young children, though it can develop as the papule increases in size.
Cutaneous eruptions can be solitary or multiple and usually occur in clusters. Although MC typically is asymptomatic, some patients may report pruritus or burning pain. In one study of 537 children with MC, up to 33% of patients reported symptoms or presented with an associated rash. The average number of papules is 10 to 20, with a range of 1 to several hundred. Molluscum contagiosum can manifest on any part of the skin; however, eruptions on the palms and soles are rare. The most common sites include the trunk, antecubital fossae, axillae, and popliteal fossae. Small children may appear to have an acneform eruption. When the infection is transmitted during sexual activity, it is evident on the groin, genital area, upper thighs, and lower abdomen (Figure 2). Mucous membrane involvement is uncommon, with infrequent reports of MC affecting the oral mucosa, conjunctiva, and genital mucosa. Infections on the eyelid can lead to unilateral chronic conjunctivitis or keratoconjunctivitis. Cutaneous eruptions tend to show minimal or no signs of inflammation, though some papules may appear to be erythematous. There can be a surrounding area of localized eczema, especially in patients with AD. This clinical finding is termed molluscum dermatitis; its incidence ranges from 10% to 75%. It is associated with pruritus and scratching, thus increasing the risk for autoinoculation. Occasionally, papules can arise from hair follicles with comedo formation that can develop into a secondary abscess following manipulation.

Molluscum contagiosum commonly undergoes spontaneous regression within several months in immunocompetent patients, though it may persist for years. Typically, scarring does not occur. Patients with AD may have a prolonged course with widespread cutaneous involvement. Immunocompromised children can develop extensive MC with atypical clinical findings. Their eruptions frequently occur on the face, eyelids, and neck. They may appear unusually large, verrucous, or as coalescent plaques that ulcerate and may be disfiguring. These patients are at increased risk for bacterial superinfection and secondary inflammation. Giant molluscum (>1 cm in diameter) is a variant observed in patients with HIV/AIDS or rarely as a solitary nodule in immunocompetent individuals. It may be a marker for advanced HIV infection with a decreasing CD4 lymphocyte count.

**Natural History**

The natural course of infection is complete spontaneous resolution within 6 to 9 months, though the rate of clearance is highly variable. Individual papules usually clear by 2 months. The condition can reappear after a period of spontaneous remission or following a course of apparently successful treatment. In certain cases, solitary papules can persist for up to 5 years.

Patients with impaired cellular immunity tend to have a more severe and protracted course, indicating that the cell-mediated immune response plays a pivotal role in the clearance of infection, which is further supported by the increased prevalence of MC associated with the AIDS epidemic during the 1980s. Moreover, the high incidence of MC in patients with AD has been attributed to the relative suppression of the type 1 immune response on eczematous skin. The role of humoral immunity, on the other hand, remains unclear. Many patients have clinically apparent infections despite high levels of MCV antibodies.

The virus' inability to be cultured and lack of animal models has limited study on the pathogenesis of this disease. The absence of inflammation in most cases of MC suggests local immunosuppression caused by the virus. Using a panel of monoclonal antibodies, several studies have shown a lack of immune cells within the papules. Sequencing the MCV genome demonstrated that the virus encodes a number of proteins that allow it to evade the host immune response and promote its survival. These molecules include MC54, MC148, MC013L,
MC159, MC80, and MC66. The molecule MC54 is a protein homologous to the human IL-18–binding protein. Through its interaction with IL-18, it prevents the production of IFN-γ by macrophages, thus inhibiting inflammation. The molecule MC148 belongs to the cysteine-cysteine family of chemokines and is structurally similar to human macrophage inflammatory protein-1β. However, this protein lacks the NH2-terminal that is needed to activate monocytes. It acts as a chemokine antagonist to the chemokine receptor 8 and interferes with monocyte and natural killer cell invasion. The molecule MC013L may promote viral replication by inhibiting the differentiation of infected keratinocytes by blocking the action of glucocorticoids and vitamin D that normally inhibit proliferation and promote terminal differentiation of keratinocytes, respectively. The molecule MC159 is thought to inhibit apoptosis induced by the cellular proteins Fas, tumor necrosis factor, and tumor necrosis factor–related apoptosis-inducing ligand. It acts by binding to caspase 8 or Fas-associated death domain protein, which are key enzymes in the apoptosis pathway. The molecule MC80 is a class I major histocompatibility complex homolog that is unable to present peptides on the surface of infected cells because of the lack of conserved amino acids necessary for peptide binding. This viral protein competes with host major histocompatibility complex molecules, thereby preventing the presentation of MCV-specific peptides and protecting it from being killed by cytotoxic T cells. The MCV genome also encodes the protein MC66, a molecule similar to human glutathione peroxidase, which is thought to protect the virus and infected cells from oxidative damage by peroxides. This virus is known to induce epidermal hyperplasia and hypertrophy. An epidermal growth factor–like polypeptide has been postulated to play a role in cell proliferation.

**Diagnosis**

The diagnosis of MC is primarily based on clinical evaluation. However, some cases may be difficult to diagnose. When central umbilication is not clear, a magnifying lens can be used to improve visualization. Histologic examination may be necessary in uncertain cases. A curetted papule is crushed on a slide and stained with Wright, Giemsa, Gram, or Papanicolaou stain. Microscopy reveals a well-circumscribed collection of infected keratinocytes with discrete ovoid intracytoplasmic molluscum bodies (Figure 3). These structures are initially eosinophilic and become basophilic toward the superficial epidermis. The histologic pattern of MC is so typical that staining may not be necessary to recognize its features. Alternatively, a Tzanck smear preparation also can be performed on scrapings from a papule. If the diagnosis is still in doubt, electron microscopy can help provide a definitive answer.

Molluscum contagiosum in children rarely is associated with immunodeficiency; no other evaluation usually is necessary. It can occur as an opportunistic infection in patients with HIV and may be indicative of impaired cellular immunity. An extensive or refractory case should alert the clinician of a possible underlying immunodeficiency. For adolescents who present with MC in the lower abdominal and genital area, coexisting sexually transmitted diseases should be sought.

**Differential Diagnosis**

Molluscum contagiosum can closely resemble other dermatologic diseases. Cases of MC with an associated dermatitis and bacterial superinfection can resemble AD or pyoderma. Eruptions in the genital area can appear similar to condyloma acuminatum. A solitary giant nodule can easily be confused with basal cell carcinoma, keratoacanthoma, verruca vulgaris, warty dyskeratoma, or an epidermal inclusion cyst. If the nodule becomes inflamed, it can mimic pyogenic granuloma. Benign appendageal tumors, including syringomas, hydrocystomas, and trichoepitheliomas, may require differentiation. Infections on the eyelid can appear similar to a chalazion, a lid abscess, or a foreign body granuloma. In immunocompromised patients, cutaneous fungal infections, including...
cryptococcosis, histoplasmosis, coccidioidomycosis, and penicilliosis, can mimic the clinical features of MC.\textsuperscript{2,3,5,6} Thus a skin biopsy specimen of apparent MC in this setting may be desirable.

**Conclusion**

Molluscum contagiosum is a common dermatologic infection that usually affects school-aged children, sexually active young adults, and immunocompromised individuals. Management can be challenging; however, therapeutic intervention may be indicated to prevent autoinoculation and transmission.

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*This article is the first of a 2-part series. The second part providing a therapeutic update will appear in a future issue of Cutis*\textsuperscript{8}.

**REFERENCES**


