

Papules, craters and umbilication: molluscum contagiosum

Molluscum contagiosum

(MC) is a cutaneous contamination with a pox virus discovered in children.¹ Bateman first scripted the entity in 1817.² Individuals with a normal immune function tend to recover spontaneously, though the disease can prolong for months. The therapeutic options are numerous including simple observation.¹ Efficacious therapies may be mechanical, chemical, immune-modulation or antiviral.

Determinants

Molluscum Contagiosum originates from a pox virus of the mollusci pox genus belonging to the pox viridae family. Molluscum contagiosum virus (MCV) is a sizable, brick shaped, double stranded DNA virus of 200-3000 nm dimension. The virus genome is covalently coupled at both edges and encodes 182 proteins with 105 direct analogues with the ortho pox virus (3) Molluscum contagiosum virus has 4 major subclasses: MCV 1 as a subclass occurs frequently (75-96%) with MCV 2 (5%), MCV 4(9%) and MCV3(11%). Paediatric patients are generally infected with MCV subclass 1. MCV subclass 2 induces a sexually transmitted disease, prevalent in teenagers and adults. MCV subclass 2 is antecedent to nearly 60% of the viral disorders co-infected with HIV. Thus molluscum contagiosum when co-exists with HIV, does not imply a reoccurrence in paediatric infections. Usually an individual represents infectivity of a single viral subclass.³

Existence

Molluscum Contagiosum is prevalent worldwide. However it frequently inhabits tropical and humid climates.^{1,4} The irrefutable reservoir for Molluscum contagiosum is humans MCV infection is recorded in 1% of the diagnosed dermatological disorders. The paediatric cases such as the pre school/ elementary school children are implicated with 5% to 11.5% prevalence.¹ MC is infrequent below 1 year of age as is congenital MC. Both genders are equally incriminated. Poor hygiene, poverty, cramped living conditions predispose to MC. Physical touch, autoinoculation and contaminated fomites (clothing, bath sponges, towels and wet skin) help to disseminate the virus.⁵ Autoinoculation with a bunch of lesions ensue due to rubbing and scratching and is a probable mode of transmission in children. The virus is sexually transmitted in adults via tattoos and in swimming pools with the lesions elucidating a bathing suit distribution. Vertical dissemination of the virus from the mother to the foetus via an infected birth canal or an ascending infection with premature rupture of membranes is described.³ The MCV infection emanates in the first six weeks of life. Immune deficiency (HIV infection) or atopic dermatitis predispose to the viral disease.^{1,6} 5-18% of the patients display a co-infection of HIV with MCV.

Clinical phenomenon

Incubation varies from 2-7 weeks and the infection can manifest in up to 26 weeks. The classic lesions of MC evolve as discrete, firm, smooth, dome-shaped waxy papules with a typical central umbilicus occluded with oozing, cheesy matter comprised of dead epithelial cells and virus particles.¹ The lesions can be pearly white,

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yellow, flesh coloured, translucent, pink or red (inflamed).¹ The moist zones or areas of abrasion are implicated especially the extremities (intertriginous region), trunk and face in the children. The adults manifest the lesions in the lower abdomen, upper thighs, pubic area, anus and genital region. Uncommonly the nipples, areolae, conjunctiva, lips, eyelids, oral mucosa, scalp and soles of the feet are incriminated. Numerically the papules are <20 and range from 1-5 mm in diameter. The lesions may be asymptomatic but can undergo inflammation, accumulation and display a linear pattern with autoinoculation. Occasionally, they may be solitary. Miniscule papules and paediatric patients may not demonstrate a central crater.¹ The rare congenital lesions exhibit a halo about the scalp.³ A pallid, hypopigmented halo or a ring (Woronoff ring) abutting the viral papules is noted (halo phenomenon). At the site of retrogression, the lesions are oedematous, inflamed and erythematous.⁷ "BOTE" Beginning of the end is a term utilized for the regressing, inflammatory lesions which is defined by the variable immune reaction to the viral ingress instead of a secondary bacterial contagion, in patients with adequate immunity. Lesions in the immune-compromised are extensive, preponderantly >1cm in diameter (giant molluscum contagiosum) and may exhibit an anomalous representation and location such as a verrucous or a hypertrophic emergence. The protuberant papules develop rapidly, disseminate, recur and are resistant to therapy.⁸

Interpretation

Physical inspection and clinical examination are the mainstay of diagnosis. The discrete, smooth, flesh coloured, dome shaped papules with a central umbilicus are characteristic. A magnifying lens or a dermatoscope assists in viewing the central umbilicus which depicts a poly-lobular or four leaf clover-like yellowish white amorphous configuration with tangential reddish, linear or branching blood vessels. These attributes are not visible to the un-aided eye. Molecular techniques such as the Polymerase Chain Reaction (PCR) are beneficial in correlating the clinical features and epidemiology of the pox virus infection. However, the technology lacks utilization in daily practice.⁹

Excision biopsy

Excision biopsy is advantageous in problematic lesions with anomalous morphology. Histopathology elucidates the typical enormous, eosinophilic, intra-cytoplasmic inclusion bodies visualized on routine H & E stained sections. The centric corpus is detailed with exudation of pearly, keratinous material. Light microscopy defines a

dermis notched by the epithelial proliferation. Cellular differentiation within the papule packs the cytoplasm with a granular, eosinophilic expansion which dislocates the nucleus. The signature molluscum bodies are composed of viral fragments identical in size and disposition to poxviruses. The circumferential dermis is profoundly inflamed, configuring as an abscess or a pleomorphic T cell infiltrate which may resemble a lymphoma /leukaemia proliferation. Metaplastic ossification may be detected. Light microscopy also delineates a lobular, circumscribed lesion with epithelial hyperplasia, prominent keratinisation and a transposed basement membrane. The encompassing stroma ranges from being fibrous, adenomatous and myxomatous. A dense, fine vasculature can be elucidated in the viral lesions on immunohistochemistry (IHC) and CD34 monoclonal antibodies. Vacuolated, amphophilic cytoplasm with prominent nucleoli are evident. The epithelial hyperplasia and keratinocytes exhibit multiple discrete, ovoid, large, eosinophilic intracytoplasmic inclusion bodies (Henderson-Patterson or Molluscum Bodies) with a condensed nucleus stretched across the cell membrane, thus developing a signet ring appearance. Follicular neo-genesis has been hypothesized as the originator of the pox virus infection by virtue of the foci of circumferential hair bulb differentiation with sporadic sebaceous gland discrimination.¹⁰ However zones of minimal /absent hair follicles such as the palm may elucidate the condition, thereby signifying epidermal transformation. The hand held reflectance confocal microscope is a rapid, non-invasive mechanism which can be utilized for the detection of the disorder.

Electron microscopy

Demonstrates typical brick shaped viral particles within the intracytoplasmic inclusion bodies. MCV multiplies in the epidermal stratum spinosum following infection of the epidermis. The keratinocytes hypertrophy and in conjunction with viral replication, display the distinctive intra-cytoplasmic viral inclusion bodies. Innumerable virions are enclosed in the intracellular compartment enclosed within a collagen and lipid rich vesicle. The eosinophilic intra-cytoplasmic inclusions can be demonstrated on H& E stained sections.⁶ The host cell, when breached on extermination, dispenses the viral particles in order to contaminate fresh epithelium (Figures 1–5).

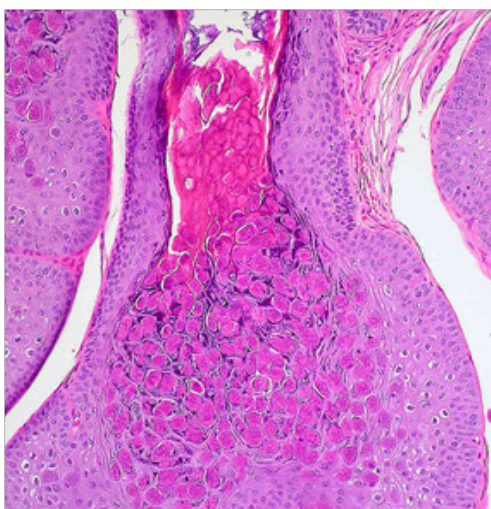


Figure 1 Epithelial hyperplasia with a central crater.

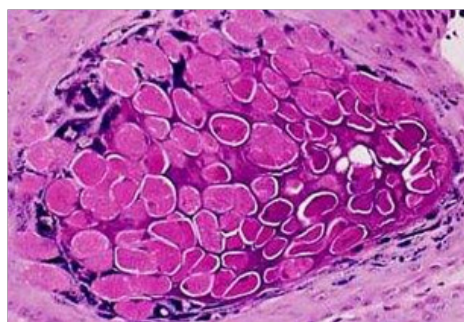


Figure 2 Viral particles as intracytoplasmic inclusions.

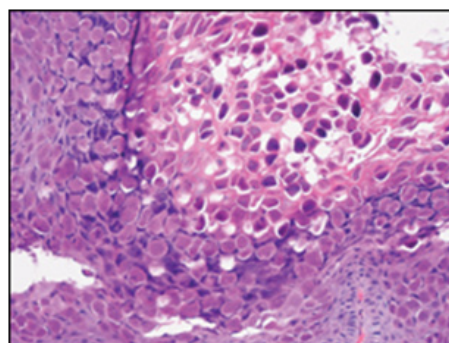


Figure 3 Central crater with hypertrophic keratinocytes.

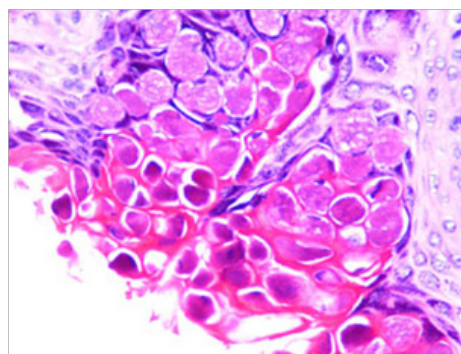


Figure 4 Pox virus particles as eosinophilic inclusions.

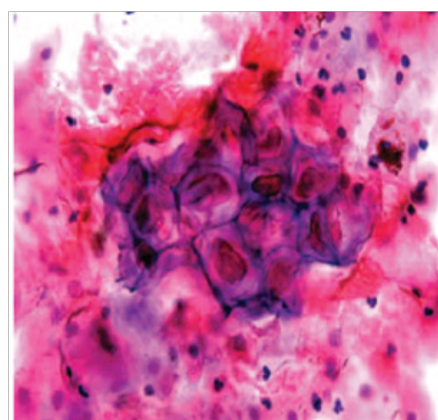


Figure 5 Molluscum of the Cervix with inclusions and inflammation- Cytology smear.

Ramifications

The papules can be hideous and distressing. Giant, expansive, external lesions may motivate parental apprehension. Secondary bacterial infection (aftermath of irritation induced impetiginisation), irritation, inflammation, conjunctivitis and superficial punctate keratitis are implicated.^{1,3} Eczematous dermatitis is demonstrated in 10% cases at the perimeter of the lesions. The dermatitis recedes spontaneously with the elimination of the viral lesions.³ Folliculitis, erythema multiforme, erythema annulare centrifugum and infected epidermoid cyst secondary to the pox virus ingress is infrequent.

Conclusions and substitution

Besides the Table 1, alternatives that require distinction are:

Acantholytic acanthoma: Asymptomatic benign skin tumours with typical acanthosis and acantholysis usually elucidate as keratotic papules or nodules on the torso. The elderly are predisposed with Male: Female proportions at 2:1.

Epidermoid cyst: is a fluctuant, indolent, firm, dome shaped lesion adherent to the skin excluding the subcutaneous tissue. A central core may be visible.

Subepidermal calcified nodule: Commences as a dome shaped, firm, solitary, yellowish white or erythematous, well circumscribed, papule or nodule with a smooth or a verrucous crust generally appearing in the head and neck.

Immune-deficiency: Delineates fungal contamination such as cryptococcosis, histoplasmosis, penicillosis, aspergillosis and coccidiomycosis in varied organs.

Table 1 Inflammatory

Lesion	Clinical features	Gross examination	Gross examination	Preferential sites
Acne Vulgaris	Non inflammatory follicles papules, comedones	Inflammatory Papules, Pustules, Nodules.	Comedones open/closed	Upper Chest, Face, Back.
Occurs in Adolescence				
Chicken Pox	Rose coloured Macules, Papules, Vesicles, Dew drops on rose petals	Pustules on crust, new lesions in 1-2 days,	250-500 lesions. Pruritus with skin rash. Scarring.	Central distribution, trunk
Common Warts (Verruca Vulgaris)	Asymptomatic, small, well circumscribed, papule, nodule, hyperkeratotic/verrucous surface	Yellow/gray/brown, flesh coloured.	Peels to punctate black dots due to thrombosed capillaries	Fingers, dorsum of the hands, toes, elbows knees, face.
Papular acrodermatitis (Gianotti-Crosti Syndrome)	Acute onset, multiple, monomorphic, flat topped lesions.	Pink to red brown papules or papulo-vesicles	Symmetrical and typical distribution on the extensor surface of extremities.	Lesions on the trunk are mild
Milia	Small < 3mm, white, benign, dome shaped, superficial keratinous cysts	Congenital milia favour the nose	Primary milia of children	Prefer eyelids.
Syringoma	Small, soft to firm, skin coloured or yellowish papules	Papules 1-3 mm in diameter, asymptomatic and symmetric	Solitary/multiple, localized or generalized	Localized common & periorbital. Generalized chest, neck forearms.
Fordyce Spots	Asymptomatic, isolated or grouped minute, discrete, creamy yellow papules	Bilateral and Symmetrical	Thick, chalky, cheesy material expressed	Vermilion border of the lips, Penis, scrota, labia,
Eruptive Xanthoma,	Abrupt onset, yellow orange papules, crops	Hyperlipidemia		Extensor surface of extremities and buttocks
Papular Urticaria	Intense pruritus, grouped or discriminative urticarial papules	Hypersensitivity to insect bites and stings	Central crater	3-10 years, summer or late spring
Steatocystoma Multiplex	Asymptomatic Multiple, smooth round, movable, soft, yellow (superficial) or skin coloured (deeper) papules and nodules	Few mm to centimetres, slow growing. No central umbilicus	Oily or creamy content. Overlying epidermis is normal	Chest, neck, axilla, proximal extremities and groin.
Folliculitis	Small, discrete pustules, erythematous base,			Around hair follicles
Condylomata Acuminata	Soft, flesh coloured, flat, ragged papules	Warty Papules, Cauliflower growths, velvety plaques		Peri-anal area
Lichen Striatus	Abrupt onset Discrete, flesh, pink, tan erythematous flat topped papules	1-3mm, continuous or interrupted linear bands which may curve		
Lichen Planus	Pruritus, purple, planar or polygonal plaque or papules	Lacy, reticular white lines : Wickham's Striae	Symmetric, Koebner's phenomenon	Flexor aspect of the wrist and ankles Dorsa of the hand, trunk, shins, glans penis

Therapeutics

Generic preventions: Communal use of bed linen, towel, sponges, bath tubs, swimming pools, contact sports should be circumvented. Abstinence from scratching, rubbing, picking and squeezing the lesions with finger nails is necessary as the central plugs are fraught with the viral particles inducing dispersal.

Simple observation: Spontaneous recovery is anticipated particularly with temperate disease and in fragile regions such as the face & groin.

Progressive intervention: Molluscum Contagiosum is a self limiting condition. Active intervention is required for cosmetic purposes and to relieve irritation, itching, transmission and inoculation.^{1,4,5}

Mechanical measures: Cryo-therapy with liquid nitrogen, curettage and pulsed dye laser therapy are efficacious though painful and morbid.¹ Topical anaesthesia with eutectic mixtures of local anaesthetics can also be employed. Adverse reaction to Liquid nitrogen are pain, erythema, vesicle formation and de-pigmentation. Curettage may result in pain, minor bleeding and scarring. Pulse dye laser therapy is a competent and safe method appropriate for refractory lesions.

Chemical composites: Substitutes such as Cantharidin, KOH, podophyllotoxin, benzoyl peroxide, tretinoin, trichloroacetic acid, lactic acid, glycolic acid, salicylic acid can be anointed but a local inflammation may ensue. Cantharidin may incite uneasiness, pain, blister formation and a post inflammatory de-pigmentation. Application of cantharidin at intertriginous regions should be restricted as it escalates the inflammation.

Immune modulatory: Methods such as Topical Imiquimod, Interferon alpha, Cimetidine disperse cytokines. Alpha interferon, a glycoprotein cytokine, annihilates the virus particles so the viral infection retrogresses. It is utilized in immune-deficient patients elucidating severe, recalcitrant lesions. It can be administered as subcutaneous or within the lesion.

Antiviral therapy: With Topical or Intravenous Cidofir can be employed in a severe, refractory disease. Topical application is adopted as the intravenous mode is nephrotoxic. Adverse reactions such as irritation, erosion, post inflammatory alterations and superficial scarring at the site of administration can be delineated. Cochrane systematic review provides inadequate evidence with respect to the efficacy or excellence of a specific treatment modality.⁴ The preferential therapy varies with the physician's comfort level, selective treatments, patients' age, severity and site of lesions, the inclination of the patients besides comprehensive effectiveness, disbursement, adverse reactions, manageable and possible administration. Anti-viral drugs are recommended for treating the refractory lesions.

Outcome

Majority of the cases recover automatically without progression in 6.5 to 13 months but may persevere for decades.

Acknowledgements

None.

Conflict of interest

The author declares that there is no conflict of interest.

References

1. Leung AK. Molluscum Contagiosum. *Current Paediatric Review*. 2012;8(4):346–9.
2. Bateman F. *Molluscum Contagiosum*. In: Shelley WB, Crissy T, Editors. *Classic in Dermatology: Springfield Illinois*. Charles C Thomas. 1953. 20 p.
3. Nguyen HP. Treatment of Molluscum Contagiosum in adult, paediatric and immune-deficient population. *J Catan Med Surg*. 2014;18(5):299–306.
4. Van Der Wouden JC. Interventions for cutaneous Molluscum Contagiosum. *Cochrane Database Systematic Review*. 2009;4:CD004767.
5. Jones S. Treatment of Molluscum Contagiosum and Herpes Simplex Virus Cutaneous Infection. *Cutis*. 2007;79(Suppl 4):11–7.
6. Rush J. New discoveries and guidelines regarding management of bacterial soft tissue infections, Molluscum Contagiosum and Warts. *Curr Opin Paediatr*. 2016;28(2):250–7.
7. Berger EM. Experience with Molluscum Contagiosum and associated inflammatory reactions in paediatric dermatology practice: The bump that rashes. *Arch Dermatol*. 2012;148(11):1257–64.
8. Erickson C. Efficacy of Intravenous cidofovir in the treatment of giant molluscum contagiosum in patients with Human Immune-Deficiency. *Arch Dermatol*. 2011;147(6):652–4.
9. Alexander K Leung. Molluscum Contagiosum: An Update. Recent patients on inflammation and allergy drug discovery. 2017;11(1):22–31.
10. Reed RJ, Parkinson RP. The histogenesis of Molluscum Contagiosum. *Am J Surg Pathol*. 1977;1(2):161–166.