

# Pathogenesis of Molluscum Contagiosum: A new concept for the spontaneous involution of the disease

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## ABSTRACT

**Background:** Molluscum contagiosum is a common viral skin disease that usually has a self-clearing course. **Objectives:** to study the process of involution of molluscum contagiosum through utilizing histological examination. **Patients and Methods:** Different sizes and stages of evolution of lesions from 50 patients with molluscum contagiosum were included. Deep shave biopsies were taken from each patient for histopathological examination. **Results:** All lesions showed a single punctum and this was confirmed by histopathological examination. Each individual lesion showed an epidermal hyperplasia consisting of many lobes which subdivided into lobules that contain the molluscum bodies. The intra-cytoplasmic molluscum inclusion bodies increase in the number and size as the cells differentiate toward the surface of the epidermis to accumulate at a central meeting point equivalent to the clinical sign of umbilication at which the infected cells undergo cytoidal disintegration releasing its viral contents into the skin surface. The general histological architecture resemble that of keratoacanthoma. **Conclusion:** The central umbilication represent the site of the future involution that contains the final growth phase of the infected epidermal cells where it ends by a process of cellular death and disintegration releasing its viral contents into the surface of the skin at the craterform opening which is called punctum. This process of self-involution may resemble that of keratoacanthoma where there are many similar pathological features in both conditions.

**Key words:** Molluscum contagiosum; Molluscum body; Keratoacanthoma

## INTRODUCTION

Molluscum contagiosum (MC) is a common cutaneous viral disease that caused by pox virus [1]. It can affects both children and adults through direct contact or indirectly via fomites, swimming pools and towels in addition to the sexual transmission which can occurs in adults [2].

Clinical presentation starts by the appearance of a single or multiple, small, pearly white, discrete papules that located anywhere on body but especially on the face or genital region [3]. Central umbilication is considered to be a characteristic feature of MC lesions through which a cheesy white material can be evacuated mechanically [4]. Some authorities proposed a follicular pattern of MC disease where the virus

has the tendency to infect the follicular epithelium (Fig. 1) [5]. Spontaneous clearance usually occurs during the natural course of the disease [6]. However,



**Figure 1:** Follicular molluscum contagiosum affecting the beard of a young man.

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till now there is no explanation for this self-limiting fate and there is no comment about the feature of MC umbilication and its relation to the pathogenesis of the disease. It has been reported that the mean duration of the single lesion of MC is 2 months while the mean duration of the infection process can last from 8 months to more than one year [7].

During our routine clinical and histopathological work, we noticed that early MC lesions are usually umbilicated papules that become gradually larger and eventually involute and clears up spontaneously with a characteristic histopathological picture. Hence we arranged for the present work to correlate the different clinical stages of MC evolution with its corresponding pathological appearance so that we can discuss the spontaneous resolving course of the disease with emphasis on the pathogenesis of a single MC lesion.

## MATERIAL AND METHODS

This prospective case series study included 50 patients, 29 males and 21 females with clinical diagnosis of molluscum contagiosum between February-December 2013 in Department of Dermatology, Baghdad Teaching Hospital - Baghdad College of Medicine. Their ages ranged from 1-46 years with a duration of their disease ranged from 1-14 months. All patients had no history of immunosuppressive diseases. All patients were checked up for the presence of punctum or so called umbilication by the naked eye with or without using magnifying lens.

Deep shave biopsies were taken from lesions in 50 patients at different stages of evolution of MC disease, from very early papular lesion to mature large lesion. These were stained with hematoxylin and eosin (H & E) stain for the dermatopathological evaluation. The study was approved by the departmental ethical committee and the patients were informed about the nature of the study where they gave their consent to participate in this scientific work. Statistical analysis was done using scientific calculator.

Prior to the study, every patient gave written consent to the examination and biopsy after having been informed about the procedure and aim of the study. The study design was accepted by the Institutional Review Board of the Department of Dermatology, University of Baghdad- College of Medicine.

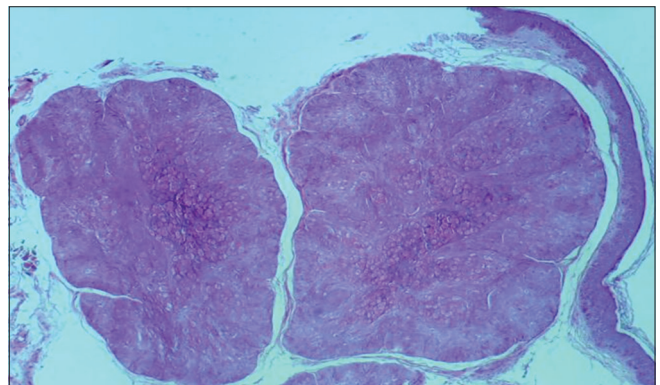
## RESULTS

All lesions whether large or very small lesions had a single punctum using naked eye with or without using magnifying glass and these punctae had been confirmed by histopathology assessment in all lesions.

The results of the histological picture of MC lesions at its different stages of evolution were as follow:

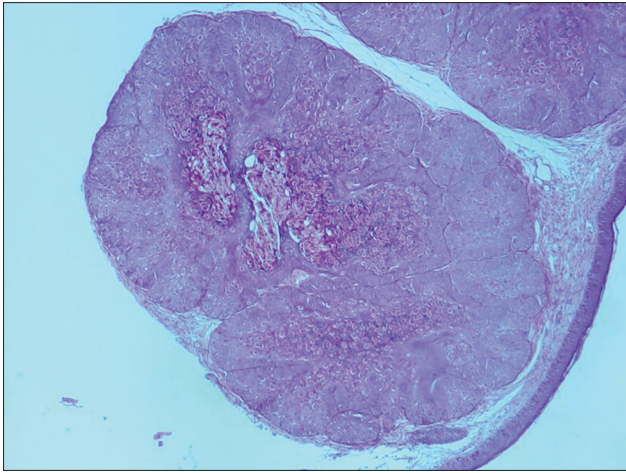
Each single MC lesion consisted of many lobes of acanthotic hyperplastic epidermal tissue that descend downward into the dermis and each lobe made up of many lobules that separated from each other by distinct basement membrane (Fig. 2).

The infection of keratinocytes started usually at the base of the lobule causing swelling of the cells and forming intracytoplasmic inclusion bodies (MC bodies) that pushed the nucleus to the periphery of the keratinocytes. These MC bodies enlarge in size and increases in its number as the cells differentiate toward the stratum corneum where all the lobules meet at a central meeting point corresponding clinically to the punctum (Fig. 3). At this umbilicated point, the cells from all lobules accumulate as a large bulky cells filled with viral particles and then attempt cytocidal degeneration where the lobules get rid of the necrotic material into the surface of the skin through the punctum (Fig.4). There was no obvious infiltration of inflammatory cells in the infected epidermis or in the surrounding dermis. The general histopathological architecture is similar to that of keratoacanthoma where both of them had epidermal hyperplasia, epidermal shouldering at the periphery of lesion and a central depression as a crater that opens to the surface (Fig. 5).

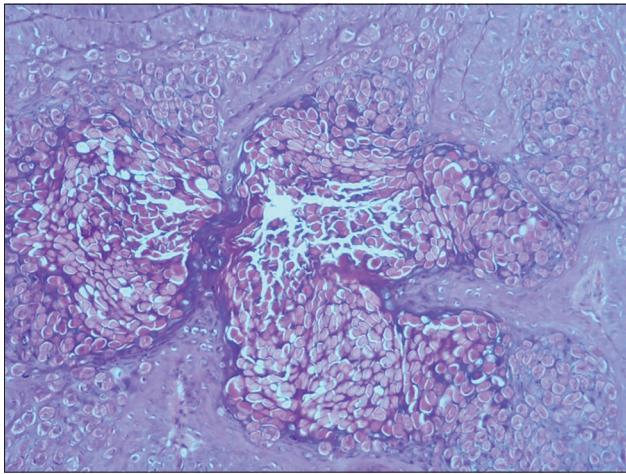


**Figure 2:** Histopathology of a single Molluscum contagiosum lesion composed from epithelial lobes that subdivided into many lobules separated from each other by clear basement membrane zone (H & E)  $\times 40$ .

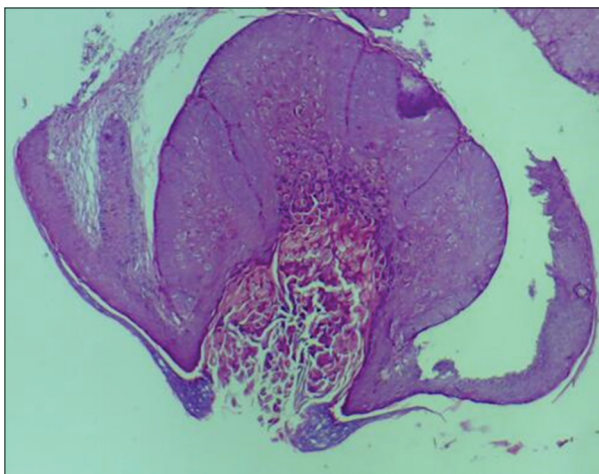




**Figure 3:** Cross section of MC lobe showing the umbilication point as a central channel draining the intracytoplasmic MC inclusion bodies from all lobules to meet at the corresponding clinical punctum (H & E)  $\times 100$ .



**Figure 4:** The central umbilication point at a closer view demonstrating the final growth phase of the infected keratinocytes with its degeneration releasing the viral content (H & E)  $\times 400$ .



**Figure 5:** Molluscum contagiosum histological architecture resembling that of keratoacanthoma with a cup shape epidermal hyperplasia and shouldering of the epidermal surface and craterform opening at its center (H & E)  $\times 40$ .

In some sections, the general pattern of MC lesion showed an acanthotic epidermis simulating that of the hair follicle where its ostium like opening filled with degenerated keratinous material and molluscum bodies (Fig. 6).

## DISCUSSION

Molluscum contagiosum is a self-healing disease and many medical authorities don't recommend any treatment for it especially in children [8]. Clinical inflammation has been observed as preliminary step for spontaneous regression of some MC lesions [9].

A study by Vermi and colleagues presented evidence of brisk immunological response as a mechanism of self-resolution of the inflammatory MC lesions [10]. Meanwhile, not all involuting MC lesions have a preceding clinical inflammation to complete its resolving course [11]. Also, no well explanation for the spontaneous resolution of the disease exists in the medical literature relating the presence of umbilication to the pathogenesis of MC infection.

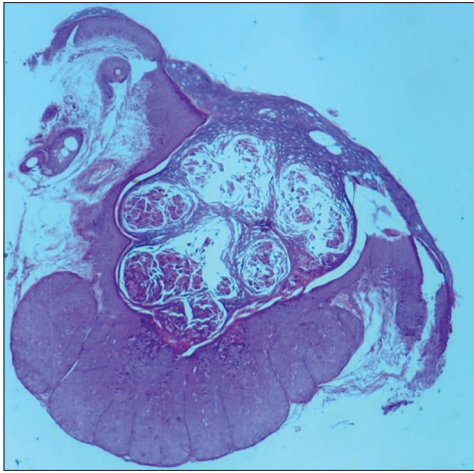
The present study that included 50 cases of MC lesions of different size and evolutions showed no inflammatory reaction. This finding encouraged us to think about alternative theory to explain the resolution of lesions especially the non-inflammatory MC disease.

Although punctum could not be seen clinically by naked eye in all cases of MC lesions, the present work showed the presence of punctum histopathologically in all cases of MC lesions regardless the size or stage of development.

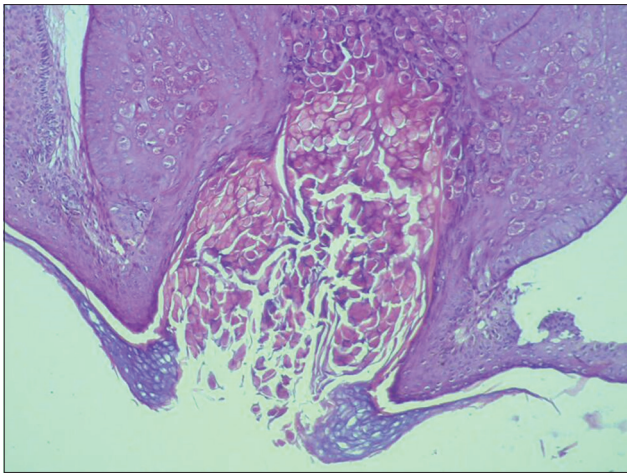
Ianhez et al demonstrated the presence of punctum in 204 MC lesions out of 211 (96.68%) through using dermoscopy while they were able to diagnose the presence of punctum by clinical examination only in half of their cases [12].

Hence, punctum must be present as a channel through which the virion loaded keratinocytes discharge its content as they reach into the cutaneous surface. Meanwhile the individual MC lesion ends spontaneously via the same process of degeneration of the infected epidermal cells at the umbilication point.

Accordingly, punctum represent the site of death of MC lesions and at the same time is a source of viral infection spread (Fig. 7). These results suggest that



**Figure 6:** Histopathological pattern of molluscum contagiosum lesion showing epidermal acanthoma similar to hair follicle with central ostium full with viral particles and keratinous debris ready to be discharge to the outer surface (H & E) x40.



**Figure 7:** The craterform opening of molluscum contagiosum lesions discharges its degenerated cells and the viral particles into the surface of the skin (H & E) x400.

the self-healing process of MC disease is not related to the size of the lesion where punctum was present in all cases regardless the stage of development of MC disease. Individual single MC lesion can persist an average period of 2 months, however the patient can still develop new lesions by inoculation via trauma or scratching for up to 8-12 months or even longer [7].

From these results, we can hypothesize the nature of the regressing course of MC as the viral infection stimulate the lobulated hyperplasia of the epidermis which contain the intracytoplasmic virion until it reaches the central meeting point of all lobules at the umbilication point to undergo cytotoxic degeneration where it discharges its content into the cutaneous surface. This hypothesis might explain many cutaneous diseases that

heal spontaneously like keratoacanthoma (KA) as the present study demonstrated some similarities between the pathological pattern of MC and KA. The process of involution in KA could simulate that of MC in the following points;

- The etiology of KA is unknown but viral theory is suggested [13].
- In both conditions there are rapid proliferation of epidermal tissue followed by involution which is well demonstrated by the presence of cellular degenerations, apoptosis and disintegration of cells at the craterform opening [14].

The general pattern of MC growth mimics that of follicular neogenesis where the pale palisading basal cells of the MC lobules resemble the cells of the outer root sheath of the hair follicle and the central punctum of MC lesion simulate the ostium of the hair follicle [15]. The similarity of MC lesion to the hair follicle, the holocrine secretion of MC bodies into the surface, their ability to produce immune-modulators and the affinity of the virus to infect the follicular epithelium support our speculation to adopt the follicular stem cell theory as alternative one for the involution of the MC disease especially the non-inflammatory MC lesions. We can suggest that the infection originate in the hair follicle where the virus will prompt release of growth factors that induce rapid proliferation of epidermal cells producing a picture similar to anagen phase of hair follicle, subsequently the growth phase might end by involution and degeneration of keratinocytes similar to telogen phase of hair growth cycle. Further support of the follicular theory comes from a recent study that reported resolution of MC lesions by just pricking them with a sharp needle producing a cure rate of 82% where this new treatment proposed that trauma to MC lesion may induce growth arrest similar to the catagen and telogen phase of the hair cycle or alternatively the pricking action may break the barrier allowing the exposure of the hidden MC antigen to the local immune system [16].

In conclusion, the present study hypothesizes a new speculation of the growth and involution of MC lesions where each single MC lesion runs a uniform fixed course of infection that started with lobulated hyperplasia of the epidermis with central umbilication producing a follicular pattern of growth. The central crater represents the area of viral discharge into the surface of the skin and the site of future involution of MC lesions.



## Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

## Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

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