Abstract

Civatte bodies (CBs) are found in various characteristic skin lesions, and their presence is suggestive of disorders characterized by interface dermatitis. These are eosinophilic hyaline ovoid bodies which are often found within the epidermis/epithelium or sometimes in the subepidermal papillary/connective tissue/dermis regions. They are called CBs when present intra epidermal or within epithelium, and as colloid bodies or hyaline bodies when located within the connective tissue or dermis. These bodies contain characteristic deposits of the most common immunoreactant type IgM, which can be characteristically diagnosed using immunofluorescence. Colloid bodies with immunoreactant deposits can be found in various diseases in the connective tissue, but strong intensity and high quantity favors interface dermatitis. Although colloid bodies are found in a lot of disease conditions, they leave important diagnostic clues in diagnosis of disease conditions like Lichen planus and Discoid Lupus Erythematosus, where reaching clear diagnosis is often difficult. This review highlights various aspects of CBs from origin and pathogenesis, morphological characteristics and associated diseases.

Key words: Civatte bodies, colloid bodies, IgM, interface dermatitis, skin lesions

Introduction

Civatte bodies (CBs) are eosinophilic hyaline ovoid bodies found characteristically in the dermal or connective tissue regions, and also within epidermis or epithelium. These bodies are found principally associated in patients with various dermatoses like Lichen planus and Discoid lupus erythematosus, which have definite oral manifestations. These CBs are apoptically damaged basal keratinocytes having keratin intermediate filaments, and invariably covered with immunoglobulin, chiefly IgM.1, 2, 3

Origin and pathogenesis of CBs

Sabouraudin explained their formation early in 1910.4 These CBs are generally believed to be derived from two origins based on their locations. They are:

- CBs located both in epidermis and papillary dermis: They originate from apoptosis of keratinocytes, caused by epithelial damage created by circulating disorders.
- CBs located in papillary dermis: These are the result of the destruction of thickened basement membrane which are found only in papillary region of dermis.2,3

The generation of CBs is a result of keratinocytes that occurs in interface dermatitis, where basal cell damage is common. The dead apoptotic cells are eliminated from epidermis transepidermally to the stratum corneum, or expelled towards dermis if apoptotic cells are situated in the basal layer. These eliminated apoptotic cells that are dropped off are

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subsequently phagocytosed by macrophages, or they provide a ground for deposition of substances like immunoglobulin, complement fragments and fibrin, which are result of fibrinogen cascade resulting in complement fixation.

**Role of apoptosis**

Active physiological process of genetically programmed cell death is called apoptosis. The apoptotic mechanism is an essential way by which skin regulates keratinocytes proliferation and epidermal growth. The apoptotic process by which keratinocytes undergoes apoptosis is a multistep mechanism. Amongst the mechanisms, one of the step is by binding specific death ligands to death receptors on target cells, such as FasL expressed on activated cytotoxic T cells to Fas expressed keratinocytes. The other mechanism is mediated by effector cell granule release like cytolytic molecule perforin and serine proteases like granzymes. In skin, multiple apoptotic stimuli may trigger different apoptotic pathways.

In Lichen planus, dysfunctional apoptotic process with formation of colloid bodies represents apoptotic keratinocytes. The infiltrating cytotoxic T cells are seen to be responsible for damage of basal keratinocytes, whereas it is the autoimmune mechanisms which precedes in conditions of Lupus Erythematosus.

**Synonyms**

CBs are also known as colloid bodies, cytoid bodies and hyaline or keratin bodies according to literature search. They are called as CBs when present in epithelium/epidermis, whereas they are called colloid bodies or hyaline bodies when present within connective tissue or dermis. The concept of colloid bodies with respect to various dermatoses develop as a result of damage to epithelium, caused by various factors, which include trauma, pathological process and circulatory disorders, with subsequent hypoxia or anoxia. Dyskeratosis, pyknosis and fibrinoid necrosis of damaged cells occurs, and the nuclei disintegrates. The colloid bodies so formed may coalesce, scatter or are expelled from the epithelium according to the principle of apoptosis. These expelled apoptotic cells are phagocytosed by macrophages within connective tissue or dermis, and acts as ground for deposition of immunoglobulins, fibrin and complement fragments.

**Morphological characteristics**

*Light microscopy:* CBs appear as rounded, homogenous eosinophilic masses on routine haematoxylin and eosin (H and E) sections, lying either in deeper parts of epidermis/epithelium and more frequently in connective tissue or dermis. They are placed mostly within or above the inflammatory cell infiltrate. In Lichen planus they appear very large because a number of keratinocytes are seen lying in clusters in the upper most part of dermis/connective tissue region. These isolated epithelial cells appear shrunken with eosinophilic cytoplasm, and contains pyknotic nuclear fragments or are anucleated as a result of fibrinoid necrosis of damaged basal cells (Figure 1). When stained with Periodic Acid Schiff Stain (PAS), these bodies give positive reaction, and are seen to be diastase resistant in nature.

*Electron microscopy:* CBs, ultra-structurally, are made up of 60-80 Å diametric distinctive filaments or whorls, which are attached to desmosomes with a lost nuclei in them. The nuclei in them are lost either by condensation, or by diffuse disintegration along with presence of a vacuolated cytoplasm. The adjoining phagocytes also show filaments in their cytoplasm which form the CBs. These CBs also contain centrioles, chromosomes, nuclear membrane particles and spindle tubules. Morphological diversity of nuclear material appearance within

![Figure 1: H and E stained section of Lichen planus with CBs (40X)](image-url)
these apoptic bodies indicate high probability of these cells getting converted to CBs.3,4

**Immunofluorescence microscopy:** This diagnostic adjunct is also helpful in achieving diagnosis when microscopic diagnosis is difficult. This holds true for various mucocutaneous lesions with similar clinical and difficult microscopic features. Nearly 10% of the skin biopsies shows CBs on direct immunofluorescence (DIF) microscopy. These CBs are seen as scattered or clustered bodies in the epidermis/epithelium, along or underneath the dermal epidermal junction or epithelium connective tissue interface. Researches in the past has demonstrated immunoreactant deposits at CBs in a wide variety of disease conditions.

Various immunoglobulin subclasses like IgG, IgA, IgM, complement (C3) and fibrinogen were demonstrated on CBs, but IgM was identified as the most common immunoglobulin deposit in Lichen planus, bullous pemphigoid and erythema multiforme.6,7,8 Immunoreactant deposits in CBs are found in various diseases (Table 1), but strong intensity and high quantity favor diagnosis of interface dermatitis.9

**Table 1: Role of CBs in various diseases**

| CBs with dermal epidermal junction (DEJ) deposits | Interface dermatitis |
| CBs more common with shaggy fibrinogen deposition at DEJ/basement membrane zone | Lichen planus |
| CBs less common, with DEJ deposits and superficial vessels | Discoid Lupus Erythematosus |

It is important to consider the CBs based on their quantity - such as few or numerous arrangement like clusters of 10 or more in the papillary dermis, and based on their intensity to immunoreactant IgM like bright or dull along with combination of fibrin deposition or a combination of various types of immunoreactants at various locations. Some lesions of Lichen planus does not show cytoid bodies due to phagocytosis of these apoptotic bodies in older lesions.10,11,12

**Stains for Civatte/cytoid bodies:**
- Routine Hematoxylin and Eosin
- PAS positive, diastase resistant
- Positive for Keratin

Extensive studies in the past has demonstrated immunoreactant deposits in CBs in variety of diseases. Immunoglobulin subclasses like IgG, IgA, IgM and complement components were demonstrated, but majority had IgM as immunoreactant deposit, especially in diseases like Lichen planus, bullous pemphigoid and erythema multiforme.1,2,7-9

**Diseases associated with presence of CBs**
The spectrum of diseases associated with CBs include Lichen planus, lupus erythematosus, erythema multiforme, graft versus host response, drug reactions, eczema, bullous pemphigoid, herpes simplex, herpes zoster, varicella, dermatitis herpetiformis, keratosis follicularis, familial benign chronic pemphigus, toxic Epidermolysis bullosa, sweets syndrome, lichen pilo-planaris, actinic cheilitis, cutaneous amyloidosis, rheumatoid arthritis and even normal skin. (Table 2)10,11,15-18

**Table 2: Diseases associated with CBs**

<table>
<thead>
<tr>
<th>Diseases which reveal CBs</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen planus, lupus erythematosus, bullous pemphigoid, Graft versus host response, erythema multiforme, eczema, sweets syndrome, rheumatoid arthritis</td>
<td>Immune mediated inflammatory disorders</td>
</tr>
<tr>
<td>Drug reactions</td>
<td>Drug related disorders</td>
</tr>
<tr>
<td>Herpes Simplex, Herpes Zoster, Varicella</td>
<td>Infections –Viral</td>
</tr>
<tr>
<td>Toxic Epidermolysis bullosa, Dyskeratosis follicularis, Familial Benign Chronic Pemphigus</td>
<td>Genetic/ inherited disorders</td>
</tr>
<tr>
<td>Cutaneous Amyloidosis</td>
<td>Others</td>
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</tbody>
</table>

**Conclusion**
The CBs are helpful in achieving pathological diagnosis based on their number, size and arrangement, location and based on the immunoreactivity to specific immunoglobulin and complements. In absence of clear diagnosis, these bodies definitely leave a clue to achieve accurate diagnosis, and are thus considered to be important in diagnostic finding, especially in diseases like Lichen planus and Discoid lupus erythematosus.
References

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