Mucopolysaccharide Keratin Dystrophy: Update on Pathogenesis and Microscopic Features

Mucopolysaccharide keratin dystrophy (MKD) is the alteration, frequently observed in the superficial layers of stratified squamous epithelium of the oral cavity. It is also known as plasma pooling. This epithelial change was first described by Toto as eosinophilic masses of homogeneous material that was confined to the superficial layers of mucosal epithelium.[1] Thus, it is also described as "Toto bodies." MKD replaces individual cell of the epithelium [Figure 1a and b].

Toto bodies are observed most commonly in reactive and inflammatory lesions of the oral mucosa, such as pyogenic granuloma, irritation fibroma (reactive fibrous hyperplasia), peripheral giant cell granuloma, peripheral ossifying fibroma, and epulis fissuratum [Figure 2a and b]. Sometimes, it is observed in leukoplakia, squamous cell carcinoma, and verrucous carcinoma of the oral cavity. However, this epithelial change has no diagnostic significance. It can be seen in any pathology where the mucosal epithelium is subjected to chronic irritation.

This epithelial change was earliest described by Toto as dystrophic complexes of acid and neutral mucopolysaccharides; hence, he termed them as keratin mucopolysaccharide dystrophy.[1]

After a decade of Toto's description, Buchner *et al*. suggested two different theories of origin for this epithelial change:[2]

1. As this change is frequently seen in reactive and inflammatory lesions, this might represent pooled ultrafiltrate of plasma, hence known as "plasma pooling"
2. Presence of –SH and –SS groups suggests similarity to protein secreted by cells. Thus, this material may be similar to keratin.

Immediately 1 year after Buchner's report, ultrastructural observations of Chen found that these bodies are located extracellularly in the intercellular spaces.[3] According to him, degenerative changes are induced in the superficial epithelial cells as a result of mucosal inflammatory reaction. This causes the cells to become compressible. The cell membranes of epithelial cells become thickened and less permeable to macromolecules, which precludes the discharge of intracellular materials such as keratin tonofilaments and keratohyaline granules in the extracellular space. These findings neutralized the concept that this material can be keratin.[4]

Recently, Padala *et al*. attempted to find out the chemical nature of the material with the help of special stains.[5] They employed Alcian blue, Periodic acid–Schiff (PAS), and Ayoub-Shklar stains to find out the chemical characteristics of Toto bodies. They found the highest intensity and diffuse distribution of Ayoub-Shklar stain in Toto bodies. Their findings are consistent with the concept that Toto bodies are of keratinaceous origin.

Beer *et al*. found the similar epithelial changes in fibroepithelial polyps of the anus and termed as "eosinophilic epithelial vacuolation." This change is morphologically similar to "glycogenic acanthosis of esophagus," "extramammary Paget's disease," and "white sponge nevus." However, MKD is a nonspecific reaction of the epithelium to mechanical trauma.[4] "Glycogenic acanthosis" and "extramammary Paget's disease" are extremely rare in the oral cavity.[6,7] "Glycogenic acanthosis" shows intracellular edema due to increased glycogen content within the cells of superficial epithelial layers. "Extramammary Paget's disease" is an intraepithelial form of adenocarcinoma, which shows "Paget's cells" (large cell with abundant amphophilic cytoplasm with centrally placed nuclei) scattered individually or in clusters within the epithelium. Paget's cells show positive reaction to PAS and mucicarmine stains.[8] However, MKD shows positivity to Ayoub-Shklar method in addition to PAS. "White sponge nevus" is a genokeratosis, which shows intracellular

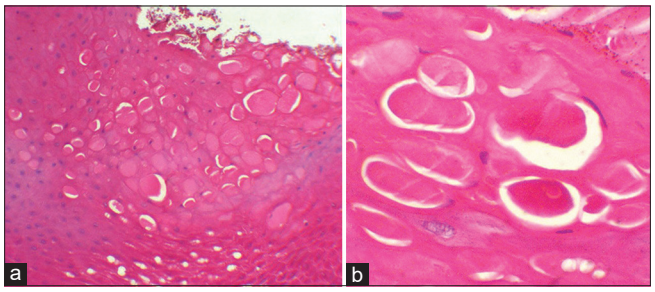

Figure 1: (a) Mucopolysaccharide keratin dystrophy involving superficial epithelial layers in pyogenic granuloma (H and E, ×10). (b) Mucopolysaccharide keratin dystrophy showing pool of amorphous eosinophilic material replacing individual epithelial cells (H and E, ×40)

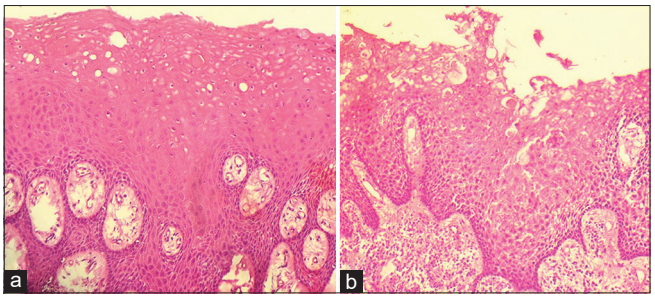

Figure 2: (a) Mucopolysaccharide keratin dystrophy involving superficial epithelium in reactive fibrous hyperplasia (H and E, ×10). (b) Mucopolysaccharide keratin dystrophy along with other features suggestive of reactive epithelium such as acanthosis and irregular epithelial rete ridges (H and E, ×4)

edema of the epithelial cells with perinuclear condensation of keratin tonofilaments. In contrast to all these, MKD does not show distinguished cytoplasmic membrane and nucleus. It represents as a well-circumscribed, amorphous, brightly eosinophilic material, replacing the individual cells in superficial epithelial layers.

Thus, even after many years, the origin and pathogenesis of this epithelial change have remained controversial. Toto bodies represent reaction of the epithelium to chronic trauma or mechanical irritation. They are of unknown significance. MKD is commonly encountered in oral lesions. However, histopathologists must be aware of this feature to avoid diagnostic confusion because it resembles many other lesions.

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Conflicts of interest

There are no conflicts of interest.

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