Brief Communication

Lifting the lid over the pearl: A histological insight

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Abstract Epithelial pearls and Keratin pearls are pathognomonic of squamous cell carcinoma. However, their histogenesis is not well understood. Only a handful of studies have been conducted in the past in this regard. This brief communication aims to understand the formation of these pearls with a few of our own experiences.

Keywords: Cellblock, epithelial pearl, keratin pearl

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Submitted: 14-Sep-2022, **Revised:** 14-Oct-2022, **Accepted:** 17-Oct-2022, **Published:** 13-Jul-2023

INTRODUCTION

Keratins are one of the many intermediate filaments which form the cytoskeleton of epithelial cells. These fibrous structural proteins are specific and characteristic of epithelial cells. The protein is highly insoluble and tough; and is present in a variety of structures such as skin, nails, hairs, horns, scales feathers, and beak to name a few. Cytokeratin (CK) is the single subunits that chemically join together to form keratin. Their utility in diagnosis lies in the fact that their immunohistochemical expression in any altered pathological cell is indicative of that cell's ectodermal origin.

CKs are numbered 1 to 20 and classified on the basis of their chemical nature and molecular weight.

	Basic CK	Acidic CK
High molecular weight CK	1,2,3,4,5,6	9,10,12,13,14,15,16,17
Low molecular weight CK	7,8	18,19,20

They are usually found in pairs and different combinations have been reported in different epithelial cells. One such group of epithelia is stratified squamous epithelium comprising both keratinized and non-keratinized. These epithelial cells are known as keratinocytes, due to their ability to produce surface keratin. The difference between the two types lies in the ability of the cells to aggregate the CK filaments in thicker aggregates.[1]

The process of keratinization is different from apoptosis. The cellular and extra-cellular cascades are not activated in keratinization in contrast to apoptosis. Also, the dead superficial cells are intact while apoptotic cells are fragmented. The pathologies which are associated with the process of cornification are hyperkeratinization, lack of keratinization, and dyskeratosis. Out of all these, dyskeratosis is the least discussed and one of the most intriguing topics in pathology.[2]

Dyskeratosis is defined as an event where an individual cell or a group of cells undergo maturation before reaching the surface. Keratin pearls and epithelial pearls are variants of dyskeratosis, found in the connective tissue in cases of squamous cell carcinoma.[2] The histogenesis of both events is different and will be explained in subsequent paragraphs.

Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/jomfp.jomfp_389_22

How to cite this article: Narayan B, Rajoria S, Urs AB, Kumar P, Augustine J. Lifting the lid over the pearl: A histological insight. J Oral Maxillofac Pathol 2023;27:399-401.

CK13 and CK19 are expressed in stratum spinosum and stratum basale respectively while CK 17 and 16 expression, in normal conditions, are absent in the epithelium. Mikami *et al*.[3] reported that CK 13 and 19 disappear in reciprocation with the emergence of the CK 17 and 16 in oral epithelial malignancies. Therefore, positive immunostaining for CK 17/16 is critical in the diagnosis of neoplastic conditions of epithelial tissue.

EPITHELIAL PEARL FORMATION IN CARCINOMA *IN SITU*

Epithelial pearls are characteristic histological features of carcinoma *in situ* (CIS) and are characterized by a central dyskeratotic cell surrounded by whorls of epithelial cells. The histopathogenesis has been described by Al-Eryani *et al*.[4] They postulated that the epithelial cells proliferate in the epithelial rete ridges confined by the basement membrane in the lesion of CIS before invasion into the lamina propria. These rete ridges grow extensively to entrap the blood vessels in the connective tissue papilla where these vessels are now known as intra-epithelially entrapped blood vessels (IEBVs). Due to the continued proliferation of the epithelial cells, these entrapped blood vessels collapse secondary to the narrowing of the connective tissue space. As a consequence, erythrocytes from these ruptured IEBVs are extravasated in the epithelium. These extravasated erythrocytes evoke haemolysis-derived oxidative stresses coordinated with haemophagocytosis which results in epithelial cells undergoing keratinization with induction of CK 17 expression. They emphasized that abundant IEBVs are a prerequisite for the formation of epithelial pearls in CIS.

KERATIN PEARL FORMATION IN CONNECTIVE TISSUE

Keratin pearls are whorl-shaped structures that are seen in histopathological examination of well-differentiated squamous cell carcinoma as concentric rings of keratin around a central core of keratin. It has been proposed that in an epithelial pearl, the malignant epithelial cells as a result of loss of cohesion, get arranged in a concentric manner.[2] When these cells undergo keratinization, keratin pearl is formed. The other school of thought states that a single malignant epithelial cell undergoes keratinization or degeneration, thus acting as a nidus around which other keratinized cells are arranged centrifugally in a circular fashion making a whorl of keratin as seen in psammoma bodies.

We normally prepare cytological smears and cell blocks from the aspirate taken from the pathological lesions reporting to the department. To corroborate the above theory, we made cytological smears and cell blocks from the aspirate taken from metastatic lymph nodes. The cytological smears showed polygonal epithelial cells arranged individually and in groups [Figure 1a]. The remaining aspirate was centrifuged to make a cell block and histopathological slides were made. The sections showed numerous keratin pearls in a fibrinous background [Figure 1b].

To further substantiate our claim, we made cell blocks from the aspirate of a few odontogenic keratocysts (OKCs). Keratin pearls have never been reported in OKC but the histopathological slides of the cell block showed keratin pearl formation [Figure 2]. This reconfirms the hypothesis that a single cell acts as a nidus around which other cells are arranged in a concentric centrifugal pattern.

To conclude, cell blocks are good adjuncts to conventional aspiration cytology to get better cellular and architectural details. Through this experiment, we have shown that

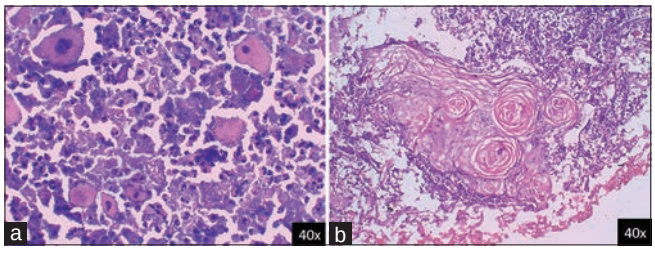

Figure 1: (a) Photomicrograph shows scattered individual epithelial cells in a cytological smear from metastatic lymph node (40x). (b) Photomicrograph shows keratin pearls in a slide made from cell block (40x)

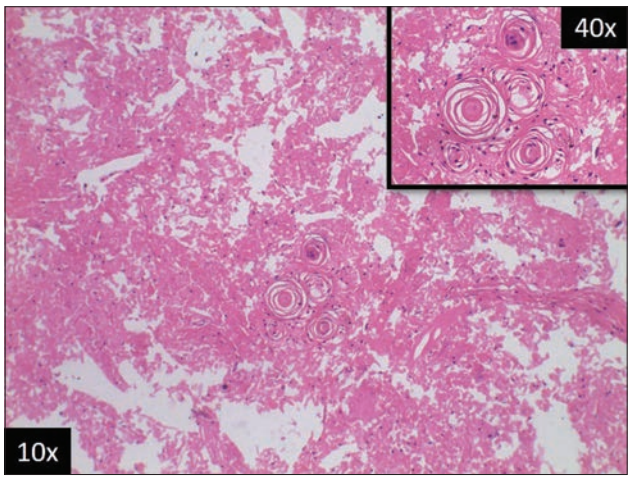

Figure 2: Photomicrograph shows keratin pearl formation in a cell block prepared from aspirate taken from Odontogenic Keratocyst (10x). [Inset: 40x magnification]

keratin pearls are formed around a central nidus in a concentric pattern, irrespective of the type of pathology. However, more extensive studies on a larger sample size of aspirates need to be executed to further substantiate this hypothesis.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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