ORIGINAL ARTICLE

Desmosomes: A light microscopic and ultrastructural analysis of desmosomes in odontogenic cysts

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ABSTRACT

Introduction: Desmosomes together with adherens junctions represent the major adhesive cell–cell junctions of epithelial cells. Any damage to these junctions leads to loss of structural balance. **Aim:** The present study was designed to analyze the desmosomal junctions in different odontogenic cysts and compare them with their corresponding hematoxylin and eosin (H and E) stained sections. **Materials and Methods:** Ten cases each of odontogenic keratocyst (OKC), dentigerous cysts (DCs), radicular cysts (RCs) and normal mucosa were stained with hematoxylin and eosin. Scanning electron microscopy (SEM) analysis of the sections was then carried out of all the sections. The area of interest on H and E stained section was marked and this marking was later superimposed onto the corresponding unstained sections and were subjected to SEM analysis. **Results and Observations:** OKC at ×1000 magnification showed many prominent desmosomes. However, an increase in the intercellular space was also noted. SEM analysis demonstrated similar findings with the presence of many desmosomes, though they were seen to be damaged and fragile. H and E stained DC under oil immersion did not show any prominent desmosomes. SEM analysis of the same confirmed the observation and very minimal number were seen with a very condense arrangement of the epithelial cells. RC at ×1000 magnification revealed plenty of desmosomes, which were again confirmed by SEM. **Conclusion:** The number and quality of desmosomal junctions in all the cysts has a role in the clinical behavior of the cyst.

Key words: Desmosomes, electron microscopy, odontogenic cysts

INTRODUCTION

Desmosomes are intercellular junctions that tether intermediate filaments (IFs) to the plasma membrane. Desmogleins and desmocollins, members of the cadherin super family, mediate adhesion at desmosomes.[1] It is an adhesive intercellular junction that is crucial to tissues that experience mechanical stress, such as the myocardium, bladder, gastrointestinal mucosa and skin. The desmosome was first observed in the spinous layer of epidermis by the Italian pathologist Giulio Bizzozero (1846–1901). Bizzozero's observations of these small dense nodules, subsequently named "nodes of Bizzozero," led him to the insightful interpretation of these structures as adhesive cell–cell contact points.[2,3]

The term was coined by Josef Schaffer in 1920 (Schaffer, 1920) and derives from the Greek word "desmos", meaning "bond", "ligament", or "fastening", with some meaning "body".[4,5] Epithelial desmosomes are usually small (200–350 nm), electron-dense, symmetrical, disk-like structures, which link the keratin IF systems within cells to the plasma membrane and to adjacent cells [Figure 1]. Their molecular weight ranges between 15,000 and 230,000 daltons. Desmosomes comprise of proteins from at least three distinct gene families: Cadherins, armadillo proteins and plakin family of cytolinkers. The coordinated establishment of specific cell–cell junctions is a driving force for morphogenesis and cell positioning during development and for maintenance of tissue integrity in adult organisms.

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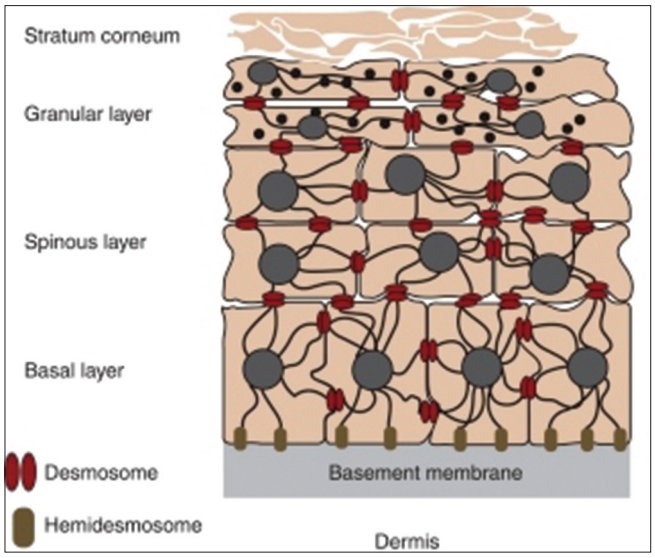

Figure 1: Schematic representation of normal desmosomes (courtesy: Delva E, Tucker DK, and Kowalczyk AP. The desmosome. Cold Spring Harb Perspect Biol 2009;1:a002543)

Desmosomes together with adherens junctions represent the major adhesive cell–cell junctions of epithelial cells. The primary function performed by desmosomes is to provide strong cell–cell adhesion. They also link the IF cytoskeletons between cells and play major role in cell signaling, tissue morphogenesis and wound repair.[6,7]

Desmosomes resist mechanical stress because they adopt a strongly adhesive state in which they are said to be hyperadhesive and which distinguishes them from other intercellular junctions; desmosomes are specialized for strong adhesion and their failure can result in diseases of the skin and heart. The desmosomal IF complex may be divided into three components, two intracellular and one intercellular. Intracellularly there are the IFs that link with the the desmosomal adhesion molecules; intercellularly there is the adhesive bond provided by the desmosomal adhesion molecules. They are also dynamic structures whose adhesiveness can switch between high and low affinity adhesive states during processes such as embryonic development and wound healing, the switching being signaled by protein kinase C. Desmosomes may also act as signaling centers, regulating the availability of signaling molecules and thereby participating in fundamental processes such as cell proliferation, differentiation and morphogenesis.[8]

Mutations in genes encoding desmosomal constituents can have devastating effects on tissue integrity, but it would be a mistake to assume that desmosomes are simply adhesive structures; much evidence now indicates that they play an important part in the regulation of cell proliferation and differentiation. Furthermore, there is a strong possibility that desmosomes influence epithelial cell invasion and metastasis.[9]

The three most commonly found odontogenic cysts were selected for the study, that is, radicular cyst (RC), dentigerous cyst (DC) and odontogenic keratocyst (OKC) and were studied for the desmosomal attachment. The OKC has already been categorized as benign epithelial tumor according to the World Health Organization (WHO) classification of odontogenic tumors in 2005.[10] Although all these lesions arise from odontogenic apparatus, OKC behaves in an aggressive manner as compared to the other two lesions.

Aim

The present study was designed to analyze the desmosomal junctions under light and electron microscope in OKC, DC, RC and normal mucosa. The study aimed to analyze whether the desmosomes have any role to play in the aggressive behavior of OKC as compared to the dentigerous and RC. The structural integrity of desmosomes was also analyzed by scanning electron microscopy (SEM).

MATERIALS AND METHODS

The study was conducted on 10 cases each of OKC, DC, RC and normal mucosa that were retrieved from the archives of our department. The tissues were obtained on the slide by routine microtomy and stained with H and E. The stained sections were compared with the tissues of normal mucosa. SEM analysis of the sections was then carried out for all the specimens. SEM is helpful in analyzing the surface morphology of tissues and is routinely used for hard tissue specimens. But, as our study included soft tissue specimens, the routine protocol could not be followed. The sections had to be thin, approximately of 3–4 μm and absolutely free of moisture. Also, the width of the section created problems as the area of interest tended to get lost. Thus, to simplify the procedure, few modifications were adopted.

The area of interest, that is, the epithelium on H and E stained section was first marked and this marking was later superimposed onto the corresponding unstained section. This glass slide with unstained section was then cut into an approximately size of 1 cm × 2 cm. The unstained section was then passed through various changes of xylene and brought to absolute alcohol. This absolute alcohol served as an excellent medium of transport of the slides. The slides were removed from alcohol just before sputtering, which is the initial step before SEM analysis.

OBSERVATION AND RESULTS

H and E stained section of normal mucosa under ×1000 magnification revealed numerous desmosomes between the epithelial cells [Figure 2]. The same field on SEM analysis confirmed the findings and intact and numerous desmosomes were seen linking the epithelial cells [Figure 3].

OKC at ×1000 magnification in H and E section showed many prominent desmosomes. However, an increase in the intercellular space was also noted [Figure 4]. SEM analysis demonstrated similar findings with the presence of many desmosomes [Figure 5], though they were seen to be damaged and fragile. H and E stained DC under ×1000 did not show any desmosome [Figure 6]. SEM analysis of the same confirmed the observation and very minimal number were seen with condensed arrangement of the epithelial cells [Figure 7]. RC at ×1000 magnification in H and E sections revealed plenty of desmosomes, which were seen linking the epithelial cells [Figure 8]. The findings of the RC were confirmed by SEM [Figure 9].

DISCUSSION

Desmosomes help in maintaining the structural integrity of the epithelium. They represent adherens type of junctions which hold the cells together, but the intercellular space in these junctions is maintained at approximately 20 µm.[11] Their loss and destruction is the reason for clinical behavior of various lesions, especially the skin lesions. In this study, RCs showed similar number of desmosomes as compared to the normal mucosa and they were seen to be intact for most part of the epithelium. In RCs, inflammation is a contributory factor for proliferation of the odontogenic epithelial lining. These cells proliferate and mature as their normal counterpart. Thereby, the desmosomal junctions seen were similar to those seen in normal mucosa.

In case of DC, the desmosomes seen were very minimal in number and the epithelial cells were condensely packed together. This may be because of the increased pressure from the cystic fluid, which leads to compression of reduced enamel epithelial cells, making the intercellular junctions less evident. Also, the reduced enamel epithelial cells have very minimal proliferative activity. Thus, the scanty number of desmosomes along with the compact arrangement of epithelial cells may explain the non recurrent behavior of DC.

The number of desmosomes in OKC was more as compared to others, but they were seen to be fragile and damaged at

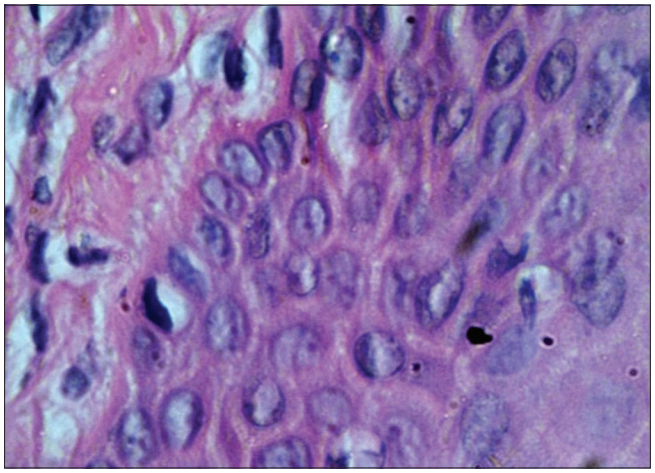

Figure 2: Desmosomes in normal oral mucosa (H&E stain, x1000)

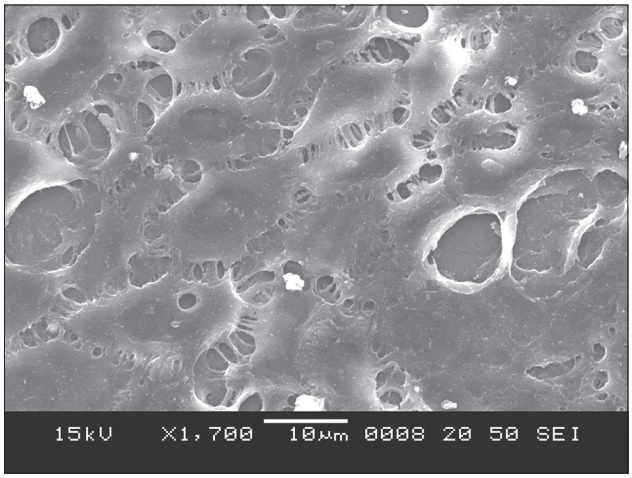

Figure 3: Scanning electron microscopy (SEM) image of normal mucosa showing normal desmosomal junctions. (x1700)

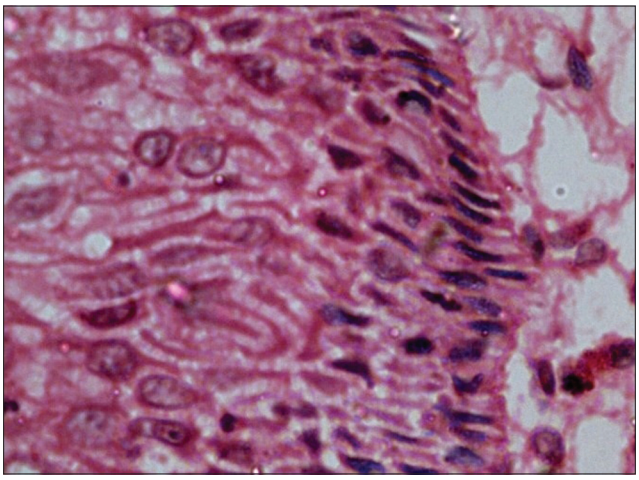

Figure 4: Fragile desmosomes in Odontogenic keratocyst (OKC) (H&E stain, x1000))

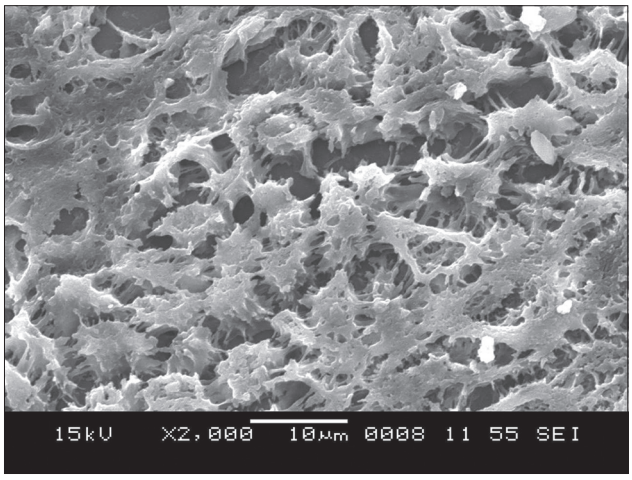

Figure 5: SEM image of odontogenic keratocyst (x2000)

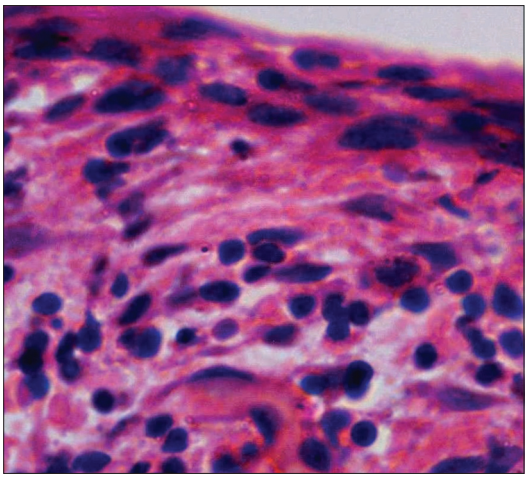

Figure 6: Very few desmosomes in dentigerous cyst (H&E stain, x1000)

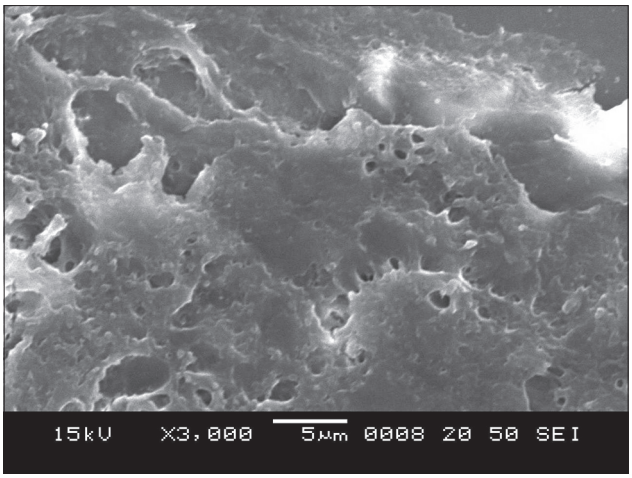

Figure 7: SEM image of dentigerous cyst (x3000)

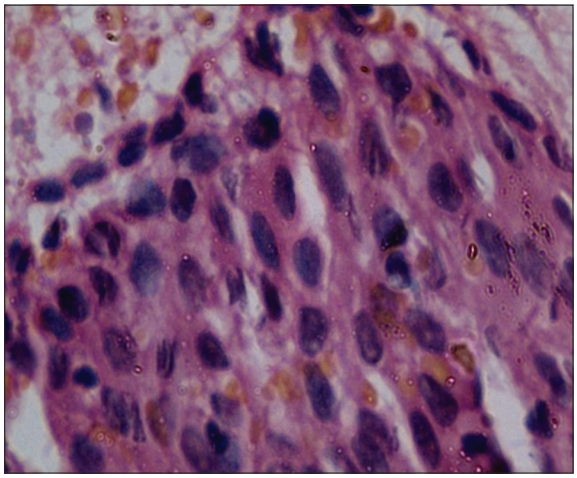

Figure 8: Desmosomes as seen in radicular cyst (H&E stain, x1000)

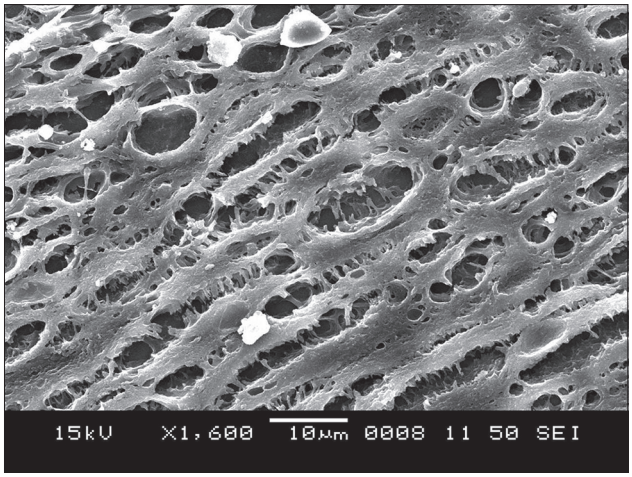

Figure 9: SEM image of desmosomes in radicular cyst (x1600)

many places. This structural damage may attribute to the fragility of the epithelium which many a times is evident even at the light microscopic level in the form of splits; especially at the basal and the suprabasilar levels. It has already been documented that these basal and the suprabasilar cells have the highest proliferative activity. This is one of the reasons for the recurrent behavior of OKCs. Loss of either desmocollin 1 (Dsc 1), desmoglein 3 (Dsg3), or desmoglein 4 (Dsg4) produces blistering phenotypes in mice due to loss of adhesion. In the case of Dsc1 and Dsg4, blistering is accompanied by increased proliferation and alterations in differentiation. The increased proliferation and alteration can be attributed to Dsc1 and Dsg4 in cases of OKC.[12-14] Misexpression of either Dsg3 or Dsc3 in suprabasal layers of the epidermis, driven by the keratin 1 promoter, results in increased cell proliferation and altered differentiation.[15,16]

Whether these changes in desmosomes in OKC are a result of defective adhesion or are a consequence of altered desmosomal cadherin ratios in the cyst is uncertain. Thus, we put forth the hypothesis that the loss of structural integrity could be the reason for fragility of epithelium in OKC, which in turn leads to recurrence and aggressive clinical behavior of the cyst.

CONCLUSION

Desmosomes have evolved in parts to enable tissues like the heart, the skin and its appendages (e.g. hair) to withstand mechanical stress. Consequently, when desmosomal adhesion is compromised through gene mutations these tissues are primarily affected. As more research is conducted on desmosomes, we are bound to further understand not only the physical nature of these junctions but also their prospective roles as signaling centers during development, homeostasis and disease. In our literature search we did not come across any studies focusing on the relationship of desmosomal junctions and odontogenic cysts. Through this study, we have tried to analyze the desmosomes in various odontogenic cysts. The study revealed that there was an increase in number and prominent desmosomes observed in case of OKC. However, the associated damage to the desmosomes seen helped us in postulating the theory that the structural damage may be

responsible for friability and subsequent recurrence nature demonstrated by OKC.

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