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FORTUITOUS SEBACEOUS GLANDS IN ORTHOKERATINIZED ODONTOGENIC CYST (OOC): A CASE REPORT AND REVIEW OF LITERATURE

[1]Kavitha L, [2]Kavitha B, [3]Sivapathasundharam B

[1]Reader, Department of Oral and Maxillofacial Pathology, Ragas Dental College, Chennai, India
[2]Professor, Department of Oral and Maxillofacial Pathology, Meenakshi Academy of Higher Education and Research, Faculty of Dentistry, Meenakshi Ammal Denatl Collge, Chennai, India
[3]Professor and Head, Department of Oral and Maxillofacial Pathology, Meenakshi Academy of Higher Education and Research, Faculty of Dentistry, Meenakshi Ammal Denatl Collge, Chennai, India

ABSTRACT: Sebaceous glands are exocrine glands that constitute an integral part of the skin. Ectopic sebaceous glands commonly seen in the buccal mucosa and the lateral part of the vermillion border of the lips in the oral cavity are called fordyce granules and are observed in 80% of the population. Sebaceous elements in odontogenic cysts are relatively rare. Pluripotency of odontogenic epithelium explains the concurrent occurrence of sebaceous glands with odontogenic cystic lesions. A case report of orthokeratinized odontogenic cyst with sebaceous differentiation in a 24-year-old male patient is discussed in this article with emphasis on histogenesis, literature review and differential diagnosis.

Keywords: Sebaceous Glands, Orthokeratinized, OOC, odontogenic cyst, case report

INTRODUCTION

Sebaceous glands in otherwise healthy oral mucosa are seen at various sites in the oral cavity namely buccal mucosa, labial mucosa, commissures, and retromolar areas. Their presence is not considered pathologic, rather they are ectopic and are termed Fordyce granules or Fordyce spots.[1,2] They are described as choristomas occurring in oral cavity. Many sebaceous glands of the oral cavity, unlike the sebaceous glands of the scalp, are not associated with hair follicles and are thus called free" sebaceous glands.[3]Apart from the oral cavity, their ectopic presence is encountered in normal mucosa of gastrointestinal tract, eye lids (Meibonian glands), penis (Tyson glands), salivary glands,and nipples (Montgomery tubercules) and are not associated with hair follicles.[4,5]Sebaceous differentiation in pathological conditions like odontogenic cysts, soft tissue (non-odontogenic cysts/ fissural) cysts, salivary gland neoplasm, oral cavity carcinomas have been documented in literature [6-11], but their relation to the production and growth of these lesions is not apparent.

Sebaceous glands are composed of lobules of centrally placed lipid filled, pale staining cells and peripherally placed flattened basaloid germinative cells. The peripheral germinative cells on maturation, accumulate lipids, become foamy and give rise to centrally placed lipid filled cells.

The sebaceous glands along with hair follicles form a pilosebaceous unit.[5] The secretions of sebaceous glands are sebum which in Latin means 'fat'. The sebum is composed of triglycerides, wax esters and squalene. The sebum has insulatory, emollient and protective role. They inhibit the growth of fungi and bacteria and are considered as pheromones too. They are constant in number but their size and number can increase with age. Hormones (androgens) and inflammatory conditions enhance the function of sebaceous glands.[4,5]

In the spectrum of cystic lesions of oral cavity, sebaceous glands are seen in entities like dermoid cyst (soft tissue and intraosseous counterparts), dentigerous cyst, odontogenic keratocyst and radicular cyst.[6,7,9-11]A case of a jaw cyst infected with sebaceous glands is reported here because of its rarity.

CASE REPORT

A 24-year-old male patient registered a pain problem for two weeks in his left cheek area. The pain was mild, intermittent, and non-radiating type. Extraorally there was no swelling. On intraoral examination, inflammed operculum was seen covering the distal cusps of 38. The involved tooth was partially impacted with its mesial cusps exposed to the oral cavity. The status of the remaining dentition was normal.

A unilocular radiolucent lesion on the left side of the mandible stretching from the distal root surface of 37 to the center of the anterior-posterior ramus and from the sigmoid notch affecting the coronary process to the lower boundary of the supero-inferior mandibular ramus was found during radiography [Figure 1]. The radiolucency had scalloped and sclerotic margins. The lesion arises in the anterior part of the condyle-sparing ramus of the mandible and the posterior half of the ramus. The apices of 37, 38 and the distal part of 38 are included above. It stretches inferiorly until the lower boundary of the mandible affecting the lower alveolar canal. The orthopantamogram also shows an unerupted 28 and horizontally impacted 48. Based on the presence of unilocular radiolucency with scalloped and sclerotic border in relation to partially impacted third molar, radiographic diagnosis as odontogenic keratocyst, unicystic ameloblastoma or dentigerous cyst was considered.

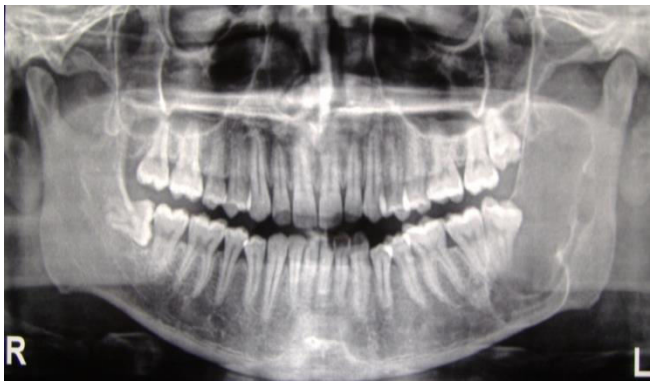

Figure 1. Orthopantamogram

The Figure 1 Orthopantamogram showing unilocular radiolucency on the left side of the mandible extending from the distal root surface of 37 to the middle of the ramus antero-posteriorly and from the sigmoid notch involving the coronoid process to the lower border of the mandibular ramus supero-inferiorly.

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The lesion was excised surgically. On gross examination, the lesion was cystic measuring about 4.5 x 2 cm. The entire tissue was grossed and subjected to histopathological examination.
Microscopically, a cystic lining epithelium surrounding a lumen was seen. The lumen showed amorphous and laminated flakes of eosinophilic keratinaceous material. The lining epithelium was folded and was of varied thickness. The epithelium-connective tissue interface was flat with few areas exhibiting peg shaped rete ridges and a split in the epithelial connective tissue interface. The stratified squamous epithelium exhibited areas of orthokeratinization predominantly and focal areas of parakeratinization. Prominent granular layer with few areas of basal cell palisading was evident. [Figure 2]. Numerous discrete sebaceous lobules were seen in close association with the epithelium [Figure3]. Sebaceous elements were distributed both within the epithelium and juxta-epithelially. The acinar lobules exhibited central zone of lipid filled pale staining cells containing abundant foamy cytoplasm with centrally placed nucleus surrounded by a peripheral layer of basaloid germinative cells. The cystic stromawas made up of fibrovascular connective tissue with diffuse chronic inflammatory cells subepithelially. Inflammatory cells seen were predominantly lymphocytes and plasma cells. Numerous Russell bodies were also seen. Inflammatory cell exocytosis was observed in certain areas. The whole tissue was subjected for serial sectioning and consecutive sections revealed sebaceous elements without any other adnexal structures like hair follicles or sweat glands. With the clinicopathological correlation, a final diagnosis of orthokeratinized odontogenic cyst (OOC) with sebaceous differentiation was given.

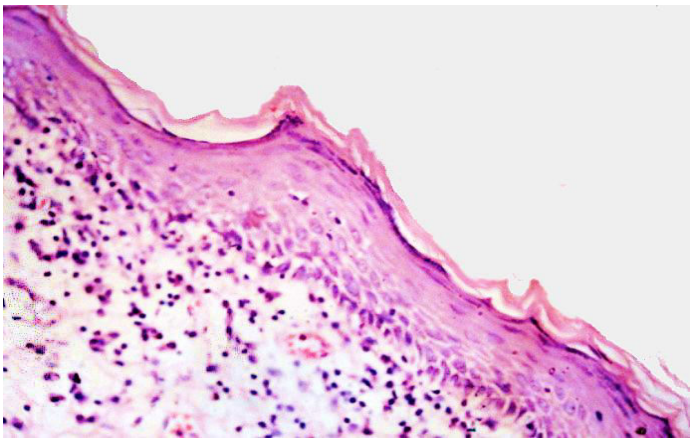

Figure 2. Orthokeratinized stratified squamous cystic lining epithelium with well-developed granular cell layer.

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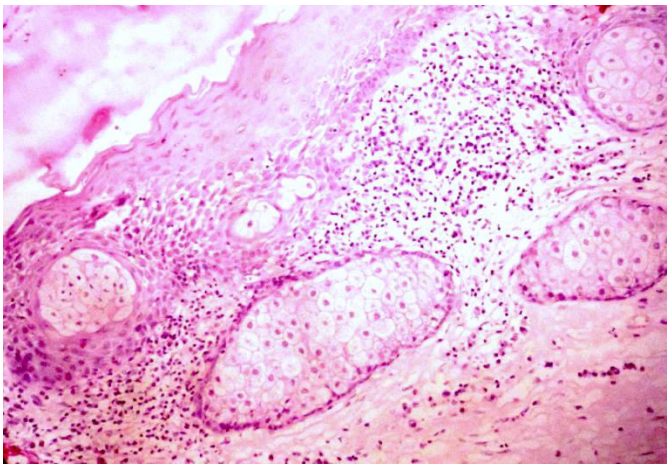

Figure 3: Stratified squamous cystic lining epithelium with sebaceous differentiation. Intraepithelial and subepithelial acinar lobules of sebaceous glands show central zone of lipid filled pale staining cells containing abundant foamy cytoplasm with centrally placed nucleus a peripheral layer of basaloid germinative cells surrounds it.

DISCUSSION

Sebaceous glands are holocrine glands that grow out of the outer root sheath of hair follicles as lateral protrusions. With the release of the cells' lipid content called sebum, the secretions depend on the degeneration of the acini. The secretions flow into the sebaceous duct, which at the infundibulum level enters the hair follicle. However the lack of hair follicles in the oral cavity does not facilitate intra-oral sebum secretion and the sebaceous lobules exist as ectopic structures.[4] While 80% of the population experiences heterotopic array of sebaceous glands in the oral cavity, its fortuitous occurrence with odontogenic pathologies is comparatively uncommon.[1] The presence of sebaceous differentiation in orthokeratinized odontogenic cyst needs differentiation from similar presentation in other jaw cysts (odontogenic and soft tissue counterparts).

Dermoid cysts develop mostly at locations where fusion of embryonic sections occurs. They appear most commonly in the periorbital area in the head and neck region, while 6.5% of dermoid cysts in this region are located in the oral cavity.[12] Most intraoral dermoid cysts are contained in the floor of the mouth as midline clusters, preceded by the submandibular and sublingual region. Apart from the lines of fusion they are less frequently reported in the antero-lateral aspect of tongue, buccal mucosa and lower lip. In both the intraosseous dermoid cyst and the orthokeratinized odontogenic cyst with sebaceous components, the typical keratinizing epithelium with a conspicuous granular cell layer is shown, differentiation between these two lesions becomes significant in diagnosing and treatment planning.

Jawbone dermoid cysts are extremely rare. In English language literature, only 20 cases have been reported to date.[13] Dermoid cysts are lined with epidermis-like, keratinized stratified squamous epithelium, i.e., basal layer, spinous cell layer, granular cell layer, and keratin layer. Dermoid cyst exhibits adnexal structures like sebaceous glands and hair follicles.[14,15] In the present case, though the cystic lining epithelium is associated with sebaceous glands, serial sections did not reveal the presence of associated hair follicles or sweat glands. Therefore, intra-osseous dermoid cyst was excluded from the diagnosis.

Epidermoid cysts also have a stratified squamous keratinized lining epithelium with a basal layer, but unlike the dermoid cyst they do not exhibit adnexal structures like sebaceous glands

and hair follicles. Allard (1982) hypothesized that certain so-called dermoid cysts are in fact epidermoid cysts with the fortuitous inclusion of foresight spots in the wall, considering the ubiquity of sebaceous glands in the oral cavity (Fordyce granules).[15] However, epidermoid and dermoid cyst are postulated to occur in the lines of fusion and are not aggressive and expansile as odontogenic cysts as seen in the present case. Radicular cysts in relation to maxillary central incisors with sebaceous differentiation has been reported by Kumar et al.[11] In the present case, absence of caries and periodontal pathology rules out the diagnosis of inflammatory cyst.

The first documented report of sebaceous glands in the wall of a dentigerous cyst associated with an impacted third molar was described by Hofrath in 1930.[16] Gorlin in 1957 and Spouge in 1966 also described dentigerous cyst with sebaceous differentiation.[6,17] Histological inspection typically reveals a thin layer of non-keratinized stratified squamous epithelium connective tissue wall lining the lumen.1 The epithelial lining, which is essentially a reduced enamel epithelium, consists of 2-4 smooth or cuboidal cell layers of cells. In the present case, the epithelial lining shows no resemblance to reduced enamel epithelium and predominantly exhibits keratinized squamous epithelium unlike dentigerous cyst which is non-keratinized.[6,16,17]

The odontogenic keratocyst (OKC) is the third most widespread odontogenic cyst (after radicular and dentigerous cysts) and constitutes around 12% of all maxillofacial cysts.[15] It is distinguished by a thin normal coating of corrugated parakeratinized stratified squamous epithelium with palisaded hyperchromatic basal cells. The elevated rate of recurrence, permeative growth trend and satellite cyst involvement that contributes to the "aggressive" behaviour of OKC unlike OOC that exhibits lamellations of orthokeratin with prominent granular cell layer histologically and has a indolent behaviour as observed in the present case.[19] OKC with sebaceous acinar structures have also been reported in literature.[10,20,21] It is important to differentiate between OKC and OOC as the latter is non-aggressive and may require a conservative surgical approach unlike OKC which necessitates complete enucleation with radical surgery and regular monitoring for recurrence.

The present case shows orthokeratinized epithelium predominantly and focal areas of parakeratinized epithelium with well-developed granular cell layer and few areas of palisaded basal layer suggestive of orthokeratinized odontogenic cysts (OOC) with sebaceous differentiation. The present case exhibits similar histological presentation to the three cases of OOC with sebaceous differentiation reported by Chi AC et al.[9] OOC is a separate entity by itself and not a variant of OKC as it was designated earlier.[18,19] Moreover, radiographic presentation of radiolucent lesion in relation to mandibular molar region with scalloped and well corticated border is coherent with the histopathological diagnosis of OOC. [7,9,20]

Table 1: Review of cases of Orthokeratinized odontogenic cyst with sebaceous differentiation

Reference	Age	Gender	Site involved	Diagnosis Given
Christensen RE et al., 1982[7]	20 years	Female	Mandibular second and third molar region	Orthokeratinized variant of odontogenic keratocyst (OKC) with sebaceous differentiation
Vuhahula E et al., 1993[22]	21 years	Male	Maxillary second premolar region	Orthokeratinized variant of odontogenic keratocyst (OKC)
Chi AC et al., 2007[9] (report of 5 cases)	44 years	Female	Mandibular third molar	Orthokeratinized odontogenic cyst (OOC); (predominantly orthokeratinized, focally parakeratinized)
	28 years	Female	Mandibular third molar region	Orthokeratinized odontogenic cyst (OOC)

	20 years	Male	Maxillary third molar region, into maxillary sinus	Orthokeratinized odontogenic cyst (OOC); (predominantly orthokeratinized, focally parakeratinized)
	24 years	Male	Mandibular third molar region	Orthokeratinized odontogenic cyst (OOC); (orthokeratotic stratified squamous epithelium)
	13 years	Male	Mandibular premolar region	Orthokeratinized odontogenic cyst (OOC); (predominantly orthokeratinized, focally parakeratinized)
Aksakallı N et al., 2019[20] (report of 4 cases)*	One case-second decade, Two cases-third decade and One case-sixth decade.	Two males and two females	All cases were in the mandible. Three cases in mandibular molar region. Once case between the canine and first molar region.	Two cases - Keratocystic odontogenic tumor (KCOT) Two cases - Orthokeratinized odontogenic cyst (OOC)
The present case (2020)	24 years	male	Mandibular molar region	Orthokeratinized odontogenic cyst (OOC);(predominantly orthokeratinized, focally parakeratinized)
* Only abstract was available				

The presence of sebaceous glands in orthokeratinized odontogenic cyst is unique as the review of literature reveals only 10 reported cases of orthokeratinized odontogenic cysts with sebaceous differentiation till now. Of the 10 reported cases, 2 were reported in the maxilla and 8 in the mandible. Out of the 8 cases in the mandible, one in the premolar region and seven were in third molar region. The present case falls in the third molar region similar to its occurrence in majority of the previous cases.[9,20,21] Orthokeratinized odontogenic cyst is characterized by stratified squamous cystic epithelium with cuboidal or flat basal cells, prominent granular cell layer and orthokeratin towards the lumen. The predominant presence of orthokeratinized epithelium in our case was suggestive of orthokeratinized odontogenic cyst.[1,2]

The histogenesis of jaw cysts with sebaceous elements still needs concrete substantiation. Proposed theories to explain the occurrence of aberrant or ectopic sebaceous glands are proposed in connection with different types of jaw cysts (1) Odontogenic epithelium pluripotentiality, which has the ability to differentiate into sebaceous, mucous, respiratory and other cell types.(2) In order to produce a wide range of structures, oral mesenchyma can interact with the epithelium (3) Sebaceous glands located deeper within the cyst wall may be caused by sequestered epithelial cell metaplasia. (4) Migration by fistula or following marsupialization of the oral epithelium into the bone.[10, 14,17]

CONCLUSION

To conclude, it is certainly apparent that much greater understanding of the jaw cysts with adnexal differentiation is needed, to consider odontogenic cysts with seabaceous differentiation as a separate entity and the role of these adnexal structures in the development and aggressiveness of these lesions is to be further investigated.

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