



Oral Soft Tissue Keratocyst: A Review of Cases from 1975 to 2021

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ABSTRACT

The odontogenic keratocyst be a developmental cyst that's important due to its specific clinical behavior and histopathology. They arise from remnants of the epithelial structures that are related to the event of teeth and occur predominantly intraosseous. However, they occasionally can appear extraosseous in the gingiva as peripheral counterparts. The gingiva is the most common location of peripheral keratocyst, but other sites like mucosal, and intramuscular, epidermal sites have also been reported. The origin of soft tissue OKCs is still under controversy. In this article will be discussing the Oral soft tissue keratocysts reported so far in the literature.

Keywords: Soft Tissue Keratocyst, Odontogenic Keratocyst, Peripheral, Gingiva, Alveolar Mucosa.

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Introduction

The odontogenic keratocyst is a developmental cyst that is important due to its specific histopathologic features and clinical behavior arising from the cell rests of the dental lamina. It can be seen anywhere in the jaw but is most commonly seen in the posterior part of the mandible, whereas they occasionally can appear extraosseous in the gingiva as peripheral counterparts.¹ The gingiva is the common location of peripheral OKC, but other sites like epidermal, mucosal, and intramuscular sites have also been reported. Initially, it was thought of as a gingival cyst of adults but Yih *et al.* demonstrated considerable immunohistochemical differences between soft tissue OKCs and gingiva cysts using markers Ki 67 and p53.² De Oliveira reported the immunopositivity for CK17, CK19, and CK14 which support an odontogenic epithelial origin for oral soft tissue keratocysts. Although, further studies are required in molecular and multicentric approaches to determine the exact origin of soft tissue keratocyst.¹

Clinical Presentation

OKCs may be associated with pain, swelling, or discharge. At times, they experience paraesthesia of the lower lip, this extends in the medullary cavity, and a clinically observable bone expansion occurs later. Dayan *et al.* in 1988 have described the occurrence of OKC in the gingiva, which resembled the gingival cyst of adults

clinically but the histological features were similar to that of an OKC. Two cases with similar features have also been reported, which showed no recurrence after a simple enucleation procedure [Ide *et al.*, 2002]. Authors have suggested the term 'peripheral odontogenic keratocyst' and included it as the histological spectrum of gingival cyst in the adult, which was not a good idea. Chi *et al.* in 2005 have also reported two cases and supported the view that these lesions should be regarded as peripheral OKCs and not as gingival cysts of the adult.² Yih *et al.* [2000] demonstrated substantial immunohistochemical differences between a sample of six gingival cysts in adults and three soft tissue OKCs, which showed moderately positive staining for p53 and strongly positive staining for Ki-67 in the parabasal and basal cells of the epithelial linings of the peripheral OKCs, whereas the six gingival cyst epithelial linings were all completely negative for Ki-67 and p53. The BCL-2 expression was strongly positive in the basal and parabasal cells of the three peripheral keratocyst and showed weak positivity in some of the gingival cysts, this view supported that gingival cyst and peripheral OKC were of distinct entities.²

Histopathology

Oral soft tissue keratocysts, despite their unusual sites, reveal the same pathognomic microscopic features of intraosseous odontogenic keratocysts, hence they can

only be diagnosed histologically due to their unusual sites of clinical presentation. Solid epithelial rests, basal budding, and Satellite micro-cysts, which may be present in intraosseous odontogenic keratocysts, were all absent in oral soft tissue keratocysts.^{3,4}

Source search criteria: The review search is done using the following combinations of keywords peripheral tissue keratocyst, OKC, soft tissue keratocyst, POKC, and keratocyst using the search engine PubMed and google scholar from the year 1975 to 2021 based on the soft tissue presentation of the lesion without any bony involvement.

Cases Review

Stoelinga *et al.* (1975); Buchner and Hansen (1979) reported cases of peripheral keratocyst which had no follow-up.^{5,6} Dayan *et al.* (1988) reported a 42-year-old male patient with a 1cm nodule on the gingival area between the left upper cuspid and the first bicuspid that was treated by enucleation and curettage which showed recurrence when followed up for 10 months.⁵⁻⁷ In 1994 Chegade *et al.* reported six cases, two in maxillary gingiva and four in mandibular gingiva, in which the patient's follow-up was lost in all of them.⁶ In the same year, Fardel and Johannessen reported a case of a 41-year-old female patient with a mandibular and maxillary gingival lesion with histological features of keratocyst, but she was not followed upon.⁶

In 2002, Ide *et al.* reported two cases in female patients- with an asymptomatic left maxillary gingival lesion that has been present for two years in a 38-year-old with no recurrence in 60 months follow-up and an asymptomatic 5mm sessile swelling in the right maxillary gingiva of a 46-year-old patient which was resected, no recurrence was reported in 72 months.^{5,6,8} Chi *et al.* 2004, reported two cases- an asymptomatic 1 cm nodule in the left mandibular gingiva which is fluctuant slightly blue with recurrence after enucleation and curettage in 6 months and a 64-year-old female with an asymptomatic, slowly enlarging 1.5 cm bluish nodule in left maxillary gingiva with no recurrence after enucleation when followed for 21 months.⁵

Chi *et al.*, in 2005, reported two cases in females- one in the left maxillary gingiva with a blue mucosal nodule measuring 1.5 cm in diameter, the lesion was enucleated with no recurrence when followed for 21 months, and another case with submucosal nodule 1 cm in diameter involving the facial attached and unattached gingiva. The lesion was excised, after three months, the patient showed no evidence of disease.^{5,6} In the same year, Preston and Narayana reported a case in maxillary gingiva of an 83-year-old female, and no recurrence was noted when followed up for six months.⁶

In 2008, Ide *et al.* reported a 53-year-old male with left mandibular gingival soft tissue keratocyst with histomorphology consistent with an OKC and no recurrence in 84 months. In the same year, Faustino *et al.* reported a case with a left mandibular gingival lesion

in a 57-year-old female with recurrence in 12 months.⁶ Precheur and Krolls in 2009 reported a case of a 59-year-old male patient with pain and swelling in his left cheek consisting of multiple episodes of swelling and pain with increasing severity over the past 6 months. The histologic diagnosis was consistent with ectopic odontogenic keratocyst when an incisional biopsy was performed.^{3,6,9}

Ide *et al.*, in 2010 reported two cases- a case of painless swelling in the left buccal mucosa posterior to the parotid papilla measuring 3x2x2 cm in a 60-year-old. Histologically, a multilocular cyst with the conventional OKC lining was found, which is diagnosed as soft tissue OKC, and a 16-year-old boy with a 5 mm nodule in the right buccal mucosa. His Microscopic examination revealed a unilocular microcyst (3 mm) and a cyst lining which showed features of conventional OKC.^{5,6,9}

Vij *et al.* 2011 reported a left maxillary gingival soft tissue keratocyst in a 56-year-old male patient.⁶ Grobe *et al.* 2012 reported a 52-year-old male patient with a painless swelling in the right cheek, significantly increasing in size over the previous six months. On the panoramic x-ray, there was no evidence of an odontogenitically-induced process and when mass was excised, the histopathological examination led to the diagnosis of a KCOT, and no recurrence has been reported when followed for four months.^{6,9,10} Kaminagakura *et al.*, 2013 reported a case of a left buccal mucosal lesion in a 37-year-old male with no recurrence reported in 12 months.^{6,9} In the same year, Yamamoto *et al.* reported a 74-year-old male patient with an elastic firm movable mass of 50mm in the right buccal mucosa with no recurrence in 4 months.^{6,9,11}

In 2014 Abe *et al.*, reported a case of a submucosal nodule in the left temporalis muscle in a 46-year-old male measuring 21 mm in diameter, covered with red-colored mucosa with no recurrence was noted in 12 months.^{6,9,12} In the same year Sakamoto *et al.* reported a case of a mandibular gingival lesion in a 24-year-old female with multiple KCOTs removed at ages 10, 12, 14, 15, and 21 from her maxilla and mandible. The present lesion is 3mm, which did not enlarge or diminish in size over four months and it was surgically removed with a 1-mm margin.⁶ Zhu *et al.* also in the same year reported a lesion with solid swelling, non-mobile, measuring 2 cm in diameter in the right buccal mucosa of a 69-year-old male.^{6,9}

Makarla *et al.*, 2015 reported a case in the right buccal mucosa of a 62-year-old male with histological features similar to keratocyst, with no recurrence in 24 months follow-up period.^{6,9} Vazquez-Romero *et al.*, 2017 reported a left maxillary gingival soft tissue OKC in a 32-year-old male with no recurrence reported over 12 months.⁶ In 2018, Witteveen ME reported two cases- a nodule in the right buccal mucosa measuring 2.5 cm in diameter in a 63-year-old male patient in which an excisional biopsy was performed, and a case of a 48-year-old female with a swelling on the inside of the left cheek, which showed a histomorphology consistent with OKC. In both cases, no recurrence was reported.^{6,9}

Bruno-Teixeira-Gonçalves Rodrigues MS, 2020 reported two cases-a single painless well-defined nodular, sessile, non-tender swelling covered by normal oral mucosa, measuring 15 mm in a 48-year-old female, excisional biopsy was performed which showed recurrence in 48 months, and a case of a 63-year-old female with an anterior mandibular gingival lesion with histological features of POKC. The patient recovered in one week and didn't return for follow-up.⁶ In the same year, De Oliveira EM reported a submucosal nodule on the buccal mucosa in a 64-year-old male patient, which is

a painless mid-cheek swelling lasting for about 18 months which is diagnosed as soft tissue keratocyst considering histological features. Beena V T, 2021 reported a case with a well-defined solitary swelling of size 2.5 cm×2.5 cm, firm in consistency, non-tender, slightly compressible nodular mass extending from below the zygoma to the lower border of the lower lip superior-inferiorly. Under general anesthesia, the lesion was excised intraorally and the tissue sections showed features of OKC with no possible recurrence on follow-up for six months.¹³ (Table 1a, b)

Table 1a. Cases reported from 1975- 2021

A	Year	Age	Sex	Site	Clinical Features	Histopathology	Treatment	Recurrence
A1	1975	NS	NS	S1	NS	NS	NS	NS
A2	1979	NS	NS	S2	Reported as the gingival cyst of the adult, keratocyst type	NS	Surgical exploration	NS
A3	1988	42	M	S3	1 cm nodule b/w cuspid & bicuspids	H1	Enucleation & curettage	Recurrence in 10 months
	1994	37	M	S4	Raised, fluctuant 3X3mm, Greyish.	H2	Excision	NS
	1994	66	F	S1	Pale yellow, raised.	H2	Excision	Lost follow-up
	1994	35	F	S4	Mobile nodule, 10 X 10 mm	H2	Excision	Lost follow-up
A4	1994	70	M	S5	White nodule	H2	Excision	Recurrence in 7 years
	1994	57	F	S1	Slowly enlarging, 7 X 5 mm, raised	H2	Excision	Lost follow-up
	1994	42	M	S4	Bone fenestration, saucerization	H2	Excision	Lost follow-up
A5	1994	41	F	S6	Large fibromatous masses in the maxillary molar regions	H3	Incisional biopsy	No follow-up
	2002	38	F	S3	Asymptomatic, present for two years	H4	Enucleation	No recurrence in 60 months
A6	2002	46	F	S7	Asymptomatic 5mm, sessile swelling	H4	Resection	No recurrence in 72 months
A7	2005	64	F	S3	Blue mucosal nodule 1.5 cm in diameter	Keratocystic features	Enucleation	No recurrence in 21 months
	2005	81	F	S1	Submucosal nodule of 1 cm	Keratocystic features	Excised	Recurrence Re-excised, no recurrence in 3 months
A8	2005	83	F	S3	Round yellow nodule on the maxillary gingiva between the left canine and first premolar	Similar Features of OKC	conservative surgical treatment	No recurrence in 6 months
A9	2008	53	M	S5	Fluctuant nodule, measuring 6 mm in diameter.	Similar Features of OKC	-	No recurrence in 84 months
A10	2008	57	F	S5	Asymptomatic small nodule, soft, nonmobile, 5 mm in diameter	Similar Features of OKC	Surgical removal, enucleation	No recurrence in 12 months
A11	2009	59	M	S8	Firm, slightly tender, mobile, 3-4 cm mass	Consistent with OKC	Incisional biopsy	NS
A12	2010	60	M	S9	Painless welling measuring 3*2*2 cm	Multi-locular cyst with conventional OKC lining	Excised	No recurrence
	2010	16	M	S10	5 mm nodule near parotid papilla	Unilocular micro-cyst and cyst lining Features of OKC	-	No follow-up
A13	2011	56	M	S3	swelling was soft in consistency and had well-defined borders measuring. 2.5×2.0 cm	Similar Features of OKC	Excisional biopsy	NS
A14	2012	52	M	S11	Painless swelling over 6 months	Features of OKC	Excision	No recurrence in 4 months
A15	2013	37	M	S9	solitary nodule posterior to the parotid papilla	Similar Features of OKC	Excisional biopsy	No recurrence in 12 months

Table 1b. Cases reported from 1975- 2021

A	Year	Age	Sex	Site	Clinical Features	Histopathology	Treatment	Recurrence
A16	2013	74	M	S10	Elastic, firm movable mass of 50 mm	Similar Features of OKC	Intraorally extirpated under general anaesthesia surgically removed under general anaesthesia.	No recurrence in 4 months
A17	2014	46	M	S12	Submucosal nodule 21 mm in diameter non tender	Similar Features of OKC		No recurrence in 12 months
A18	2014	24	F	S4	3mm lesion which did not enlarge or diminish for 4 months	Similar Features of OKC	Excisional biopsy	NS
A19	2014	69	M	S10	Solid swelling, non-mobile, measuring 2 cm in diameter.	Similar Features of OKC	Extensive resection of the mass & reconstruction with sternocleidomastoid flap	NS
A20	2015	62	M	S10	Asymptomatic swelling with reduced mouth opening, soft to firm measuring 6 × 6 cm in size	Similar Features of OKC	excision	No recurrence in 24 months
A21	2017	32	M	S3	Non painful whitish lump, fluctuant	Similar Features of OKC	A full-thickness incision	No recurrence in 12 months
	2018	63	M	S10	Firm mobile nodule measuring 2.5 cm in diameter.	Consistent with OKC features.	Excision biopsy	No recurrence in 4 years
A22	2018	48	F	S9	Swelling on the inside of the left cheek.	Histomorphology consistent with an OKC.	Incisional biopsy	No recurrence in 1 year
	2020	43	F	S13	Well-defined, sessile, nontender, measuring 15 mm	Similar Features of OKC	Excisional	No recurrence in 48 months
A23	2020	63	F	S14	Asymptomatic, single elevated lesion,tense on palpation with yellowish coloration	Similar Features of OKC	Excisional	No follow-up
A24	2020	64	M	S15	painless mid-cheek swelling lasting for about 18 months swelling was firm in consistency, non-tender,	showed Similar features of OKC	Excision	No recurrence in 10 months
A25	2021	61	M	S16	slightly compressible nodular mass	showed Similar features of OKC	Excision	No recurrence in 6 months

M: Male; F:female; A: Author; A1: Stoelinga et al; A2: Buchner & Hansen; A3: Dayan et al; A4: Chehade et al; A5: Fardel & Johannessen; A6: Ide et al, A7: Chi et al; A8: Preston and Naryana; A9: Ide et al; A10: Faustino et al; A11: Precheur and Krolls; A12: Ide et al; A13: Vij et al; A14: Grobe et al; A15: Kaminagakura et al; A16: Yamamoto et al; A17: Abe et al; A18: Sakamoto et al; A19: Zhu et al; A20: Makarla et al, A21: Vazquez-Romero et al; A22: Witteveen; A23: Bruno-Teixeira-Gonçalves Rodrigues MS; A24: De Oliveira EM; A25: Beena V T; S1: Maxillary gingiva; S2: Buccal mucosa; S3: Left maxillary gingiva; S4: Mandibular gingiva; S5: Left mandibular gingiva; S6: Maxillary & mand gingival lesion; S7: Right Maxillary gingiva; S8: Left cheek; S9: Left buccal mucosa; S10: Right buccal mucosa; S11: Right cheek; S12: Submucosa; S13: Right maxilla; S14: mandibular gingival lesion; S15: Mid cheek; S16: Lower lip region, H1: Features of cystic lining; H2: uniform, thin stratified squamous epithelium with palisading of the basal layer and superficial keratosis; H3: Multiple gingival cysts, some containing keratin. The cyst lumens were filled with fibrin; H4: Stratified squamous epithelium with palisading basal cells & superficial corrugated layer; *NS- not stated

Discussion

OKC being classified as a cyst of odontogenic origin for about five decades, histological character, the pathogenesis, and progress of entity eventually resulted in a transformation from a cyst to an odontogenic tumor in 2005.^{10,14} In the 2017 classification, it was moved back into the cyst category because most of OKC's are documented to completely regress, following decompression, and mutations in OKC are not just limited to the PTCH gene alone.¹⁵

The term Peripheral odontogenic keratocyst was coined by Dayan *et al.* The occurrence of a keratocyst within the oral soft tissues is exceedingly rare. These lesions usually appear as a nodule or a swelling and can occur with or without symptoms. Oral soft tissue

keratocysts can be present with a different clinical profile. They have been suggested to arise from remnants of the dental lamina that become entrapped within the mucosa during embryogenesis.²

Despite its unusual location, oral soft tissue keratocysts reveal an equivalent pathognomic microscopic feature of intraosseous odontogenic keratocysts. Therefore, a histopathological diagnosis should not present any difficulties. Satellite microcysts, solid epithelial rests, and basal budding, which can be present in intraosseous odontogenic keratocysts, were all absent in oral soft tissue keratocysts with some exceptions.²⁻⁴

The differential diagnosis usually includes other odontogenic cysts that could affect this region, especially the gingival cyst of the adult and the peripheral calcifying odontogenic cyst as most POKC are located in the gingiva. Both may produce a painless swelling filled by a bluish-gray or bluish fluid and superficial resorption of cortical bone. The second most common location is the buccal mucosa where other lesions like cystic and cystic-solid salivary gland lesions are considered in the clinical differential diagnosis. Histological analysis is the gold standard for POKC diagnosis. In the extraosseous location, an equivalent histological pattern described for conventional OKC should be present.⁶ keratocysts can be found in other parts of the body, including skin lesions but their origin is not confirmed and requires further clarification.¹

The recurrence rate of POKC is very low. This is not in line with the higher recurrence rate of intraosseous OKCs (up to 62.5%). This could be due to better resectability in soft tissues or the fact that they are two separate entities with different biological behaviors.⁹ In a patient with NBCCS, a higher recurrence rate may be attributed to artificial inflating for a given treatment. OKCs are among the most consistent features of the syndrome along with skeletal anomalies occurring in 65–75%.^{16,17}

Conclusions

The clinical evaluation of soft tissue keratocysts is very difficult, they often present different clinical entities, but they have to be evaluated histopathologically to be diagnosed as keratocyst. The radiographic evaluation to rule out the bony involvement may help in diagnosis. The origin of soft tissue keratocyst is not yet known. The histogenesis and pathogenesis of oral soft tissue keratocysts should be further investigated to clarify whether it represents a type of intraosseous odontogenic keratocyst or whether it is a distinct entity.

Abbreviations

OKC-Odontogenic keratocyst, POKC-Peripheral odontogenic keratocyst, NBCCS-Nevoid basal cell carcinoma syndrome.

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