ORIGINAL ARTICLE

Cytokeratin 14 and cytokeratin 18 expressions in reduced enamel epithelium and dentigerous cyst: Possible role in oncofetal transformation and histogenesis- of follicular type of adenomatoid odontogenic tumor

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ABSTRACT

Introduction: Odontogenic cysts and tumors arise from the structures and remnants associated with tooth development. Cysts and tumors derived from the odontogenic tissues constitute an unusually diverse group of lesions. This diversity reflects the complex development of the dental structures, since all these lesions originate through some alteration from the normal pattern of odontogenesis. Cytokeratin (CK) 14 is the typical intermediary filament of odontogenic epithelium, CK 18 is the major components of the intermediate filaments of simple or single layered epithelial tissue; it is not expressed in stratified squamous epithelium. The present study was undertaken to understand the expression pattern of these cytokeratins in dentigerous cyst, dental follicular tissue, adenomatoid odontogenic tumor (AOT) and unicystic ameloblastoma. **Materials and Methods:** The present study consists of 60 specimens consisting of 20 samples of Dentigerous cyst, 20 samples of Reduced enamel epithelium/dental follicles, 10 samples of Follicular type of AOT, 10 samples of unicystic ameloblastoma. The sections of these specimens were stained for CK 14 and CK 18. The number of cells positive for CK 14 and CK 18 was counted per 100 cells. The cells were counted in four randomly selected high-power fields and the mean was calculated. Scoring of cytokeratin 14 expressions was done using Remmele score. **Results:** The highest expression of cytokeratin 14 was noted in AOT, least was seen in dental follicle/Reduced enamel epithelium (REE). CK18 was negative in all the cases included in the present study. **Conclusion:** In the present study, the expression of CK14 was noted in AOT, Dentigerous cyst (DC), Unicystic Ameloblastoma (UCA) and Dental follicle/REE. The expressions between these lesions were compared. These expression pattern may provide an insight to the histogenesis of AOT.

Key words: Adenomatoid odontogenic tumor, cytokeratin 14, Cytokeratin 18, dentigerous cyst, UnicysticAmeloblastoma, dental follicle, reduced enamel epithelium

INTRODUCTION

Odontogenic cysts and tumors arise from the structures and remnants associated with tooth development. Cysts and tumors derived from the odontogenic tissues constitute an unusually diverse group of lesions. This diversity reflects the complex development of the dental structures, since these lesions all originate through some alteration from the normal pattern of odontogenesis.

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The epithelium associated with odontogenic cysts and tumors is derived from one of the following sources:-

- The pre-functional dental lamina (odontogenic epithelium with ability to produce a tooth), which is more abundant for obvious reasons distal to the lower third molars

- The post functional dental lamina, a concept that covers those epithelial remnants such as cell rests of Serre, located within the fibrous gingival tissue; the epithelial cell rests of Malassez in the periodontal ligament and the REE, which covers the enamel surface until tooth eruption
- The basal cell layer of the gingival epithelium, which originally gave rise to the dental lamina
- The dental papilla, origin of the dental pulp, which has the potential to be induced to produce odontoblasts and synthesize dentin and/or dentinoid material
- The dental follicle
- The periodontal ligament, which has the potential to induce the proliferation of fibrous and cemento-osseous mineralized material.[1]

Odontogenic cysts are one of the most common destructive lesions affecting the jaws. Radicular cysts, dentigerous cysts and odontogenic keratocysts were the most common cystic lesions, accounting for 95.2% of all odontogenic cysts.[2-6]

Adenomatoid odontogenic tumor like many odontogenic tumors, has an interesting history. The earliest irrefutable case that was first found was reported from Norway by Harbitz in 1915 as ''adamantoma''; however, the case reported by James and Forbes from England in 1909 as an ''epithelial odontome'' is almost certainly an AOT.[7]

Like all other odontogenic tumors, the specific stimulus that triggers proliferation of the progenitor cells of AOT is unknown. Because of its exclusive occurrence within the tooth-bearing areas of the jaws and its histologic resemblance to the dental lamina and components of the enamel organ, there is no disagreement that the AOT is of odontogenic origin.[8-11] IHC studies revealed differences between the duct and non-duct forming cells; the non-duct-forming columnar cells expressed amelogenin reactivity, whereas the duct-forming cells showed no reactivity to amelogenin or the other enamel matrix protein (enamelin and sheathlin) antibodies.[12-14]

Dentigerous cyst is one that encloses the crown of an unerupted tooth by expansion of its follicle and is attached to its neck. It has been suggested that dentigerous cysts may be of either extrafollicular or intrafollicular origin and that those of intrafollicular origin may develop by accumulation of fluid either between the REE and the enamel or within the enamel organ itself.

Main in 1970 suggested that the pressure exerted by a potentially erupting tooth on an impacted follicle obstructs the venous outflow and thereby induces rapid transudation of serum across the capillary walls. The increased hydrostatic pressure of this pooling fluid separates the follicle from the crown, with or without reduced enamel epithelium. With time, capillary permeability is altered so as to permit the passage of greater quantities of protein above the low concentration of the pure transudate.[15]

Unicystic ameloblastoma originates within the mandible or maxilla from epithelium that is involved in the formation of teeth. Potential epithelial sources include the enamel organ, odontogenic rests (rests of Malassez, rests of Serres), REE and the epithelial lining of odontogenic cysts, especially dentigerous cysts. The trigger or stimulus for neoplastic transformation of these epithelial residues is totally unknown.[16]

UCA, a variant of ameloblastoma, first described by Robinson and Martinez refers to those cystic lesions that show clinical and radiologic characteristics of an odontogenic cyst but in histologic examination show a typical ameloblastomatous epithelium lining part of the cyst cavity, with or without luminal and/or mural tumor proliferation.[17]

The proposed three pathogenic mechanisms for the evolution of UCA are as follows:

- The reduced enamel epithelium which is associated with a developing tooth undergoes ameloblastic transformation with subsequent cystic development
- Ameloblastomas arise in dentigerous cysts in which the neoplastic ameloblastic epithelium is preceded temporarily by a non-neoplastic stratified squamous epithelial lining
- A solid ameloblastoma undergoes cystic degeneration of the ameloblastic islands, with subsequent fusion of multiple microcysts and develops into unicystic lesions.[18]

Cytokeratins/cytoskeleton is a complex dynamic network of protein filaments that reorganizes continuously and extends throughout the cytoplasm. It is responsible for motility, change in shape, muscle contraction, transport of organelles and segregation of chromosomes.[19,20]

Cytoskeleton depends on three types of proteins:

- **Actin filaments:**
  Also known as microfilaments, are helical polymers of actin andhave a diameter of 5 − 9nm. They are responsible for cell surface movements and maintain polarity of the cell.
- **Microtubules:**
  Are long hollow cylinders made of tubulin and have a diameter of 25mm. They aid in positioning of organelles within the cytoplasm.
- **Intermediate filaments:**
  Are tough rope-like structures and have a diameter of 10nm, in between that of microfilaments and microtubules.[19,20]

Cytokeratins are epithelia-specific intermediate filament proteins responsible for the structural integrity of epithelial cells. Cytokeratins consists of 20 biochemically and antigenically different polypeptides having

molecular weights ranging from 40KDa to 67KDa. All epithelia can be classified based upon cytokeratin protein expression.[19-25]

Hisham *et al*., 2006 showed all cells of the enamel organ were positive for CK 14 and its configuration showed differences related to the stage-specific state of differentiation.[26]

Goa *et al*., 1989 studied cytokeratin expressions in premalignant and malignant lesions and concluded that the keratin expression in oral stratified squamous epithelium is related to the cellular differentiation level. Keratins have a number of distinct advantages for use as marker proteins.[27]

Crivelini *et al*., 2003 showed that all cells of the dental germ were positive for CK 14, except for the preameloblasts and secreting ameloblasts, in which CK 14 was gradually replaced by CK 19.[28]

Crivelini *et al*., 2005 showed that CK 14 labelling indicated differentiation grades for secreting ameloblasts or ameloblasts in the post-secreting stage in the adenomatoid structure of AOT and suggested that the nature of AOT is hamartomatous with histogenesis from the reduced enamel epithelium.[29]

Leon *et al*., 2005 showed the expression of CK 14 in AOT and concluded that the ultrastructural aspects of the AOT tend to support a probable origin in the reduced dental epithelium.[30] [Table 1]

Lopes *et al*., 2005 analyzed the immunohistochemical expression of CKs 7, 8, 10, 13, 14, 18 and 19 in the epithelial components of ameloblastomas and AOT and found that CKs were expressed by several forms of ameloblastomas and AOTs, that are typically expressed by dental germ, which suggested that these tumors have odontogenic epithelial differentiation, whereas it has not evidenced expression of CKs proper of squamous epithelium. Babu *et al*.,2010 in their study observed intense expression of keratin 14 in ameloblastoma by all tumor cells and suggested that they may retain basal cell characteristics with a potential for proliferation.[31]

Lu *et al*.,2007 showed the expression of CK 18 in keratocyst epithelial linings transfers from basal cell layer to spinous layer. The expression of CK 18 immunohistochemical staining and CK 18 mRNA *in situ* hybridization were different, which showed CK 18 might be related to proliferation of OKC epithelial linings. Author has suggested the existence of regulation of CK 18 and CK 18 mRNA expression in these cysts.[32] [Table 2]

Objectives

- To evaluate expression of CK 14, CK 18 in REE/Dental follicle (DF)
- To evaluate expression of CK 14, CK 18 in Dentigerous cyst
- To evaluate expression of CK 14, CK 18 in Follicular type of AOT and to evaluate the possible histogenesis of Follicular type of AOT
- To evaluate expression of CK 14, CK 18 in UCA.

MATERIALS AND METHODS

The study consisted of 20 samples of DC, 20 samples of Dental Follicle/REE, 10 samples of Follicular type of AOT,10 samples of UCA. The expression of CK 14 and CK 18 was determined immunohistochemically using monoclonal antibodies (BiogenexLife Sciences Pvt.Ltd. Hyderabad Telangana) and Biogenex Polymer HRP detection system. Squamous cell carcinoma and breast cancer were used as positive controls. Staining was considered to be positive for CK 14 and CK 18 if only the cytoplasm of the cells were stained. Counting of cells was done at a magnification of x1000 and a total of 100 cells per specimen were counted. The number of CK 14 and CK 18 positive cells per 100 cells was thus determined. The number of positive cells in four randomly selected high power fields were counted and mean was determined. The layer in which CK 14 and CK 18 were expressed was noted. Intensity of CK 14 and CK 18 expression was graded subjectively as positive, strong positive and weak positive. Scoring of CK 14 expression was done using Remmele score.

Table 1: CK 14 expression in AOT, UCA, DC and DF/REE

AOT	DC	DF/REE	UCA	Author
-	Positive/ negative	-	-	Hornia, 1987
-	Positive/ negative	Positive/ negative	-	Goa *et al.*, 1989
-	Positive	-	-	Meara *et al.*, 2000
Positive	-	Positive	Positive	Crevelini *et al.*, 2005
Positive	-	Positive	-	Crevelini *et al.*, 2003
Positive	-	-	-	Esquinche, 2005
Positive	-	-	-	Freidrich *et al.*, 2009

AOT: Adenomatoid odontogenic tumor; UCA: Unicystic Ameloblastoma; DC: Dentigerous cyst; DF: Dental follicle; DEE: Reduced enamel epithelium

Table 2: CK18 expression in AOT, UCA, DC and DF (Dental follicle)/REE

AOT	DC	DF/REE	UCA	Author
-	Positive/ negative	-	Positive	Hornia, 1987
-	Positive/ negative	Positive/ negative	-	Goa *et al.*, 1989
-	Positive	-	Positive/ negative	Meara *et al.*, 2000
Negative	-	Negative	-	Crevelini *et al.*, 2005
-	-	Negative	Negative	Crevelini *et al.*, 2003
-	-	-	Positive	Esquinche, 2005
Positive/ negative	-	-	Negative	Ferreira, 2005

AOT: Adenomatoid odontogenic tumor; UCA: Unicystic Ameloblastoma; DC: Dentigerous cyst; DF: Dental follicle; DEE: Reduced enamel epithelium

RESULTS

The highest expression of cytokeratin 14 was noted in AOT [Figure 1], moderate in DC [Figure 2], UCA [Figure 3] and least was seen in dental follicle/Reduced enamel epithelium[Figure 4]. Cytokeratin 18 was negative in all the cases included in the present study [Figure 5-8].

The mean percentage of CK 14 positive cells in different groups was evaluated by one-way ANOVA statistics. Highest mean percentage with 3.90 was seen in AOT and least positivity of CK 14 expression was seen in DF/REE with 3.0526 which were not statistically significant [Tables 3 and 4].

Statistical analysis was done using SPSS software, T-test between AOT, Dentigerous cyst and UCAwith respect to percentage, positivity, intensity and Remmeles score of CK 14 expressions was determined. Results showed statistically significant differences between AOT and dentigerous cyst/UCAwith AOTshowing more percentage, positivity, intensity and Remmele score for CK 14 expression as compared to dentigerous cyst and UCA.

DISCUSSION

AOT is an odontogenic tumor whose origin is still controversial. Some, but not all of the follicular types of AOT may be derived from the odontogenic epithelium of a dentigerous cyst. Dental lamina remnants likely represent progenitor cells for the peripheral type of this benign odontogenic tumor. Following entrapment, these epithelial remnants proliferate in response to an unknown stimulus, giving rise to the lesion. Furthermore, Malassez remnants found in the periodontal ligament may possibly give origin to an extrafollicular AOT.[30,33,34]

The study analyzed cytokeratin expression in the epithelium of odontogenic neoplasms. The typical intermediate filament of odontogenic epithelium is CK 14. All cells of the REE and

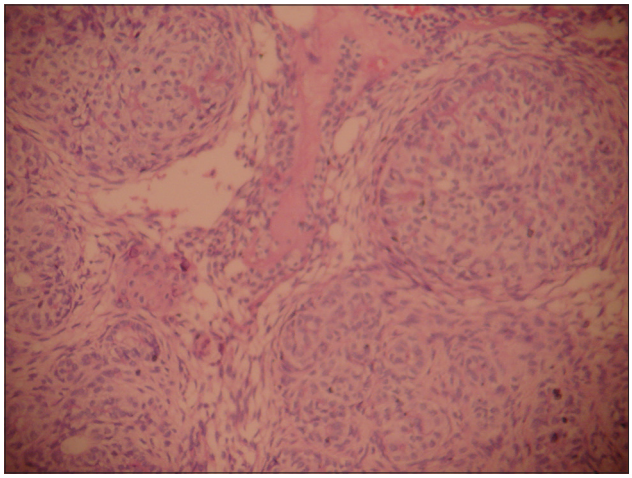

Figure 1: Photomicrograph showing rosettes and ducal pattern of adenomatoid odontogenic tumor (AOT). (H&E stain, x100)

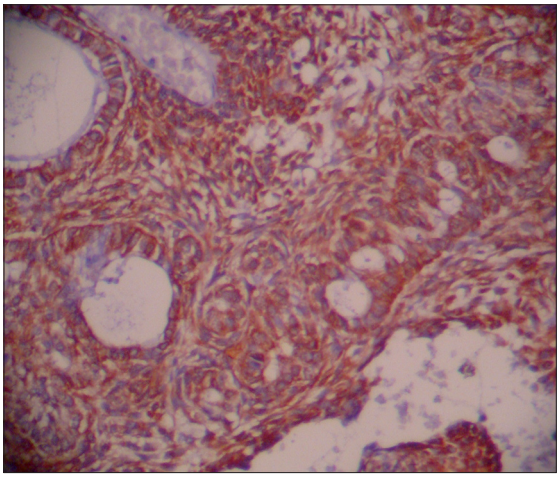

Figure 2: Photomicrograph showing AOT stained with CK 14. (IHC stain, x100)

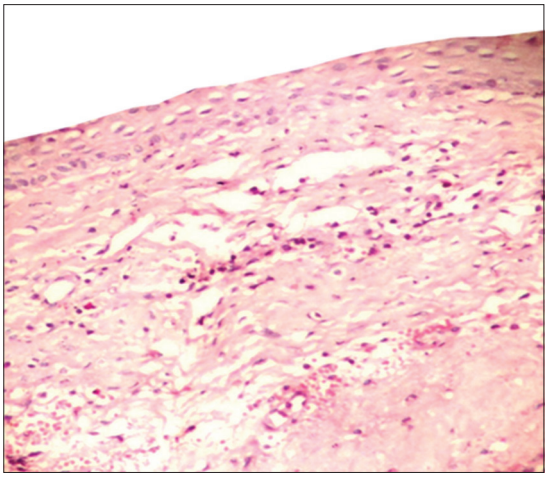

Figure 3: Photomicrograph showing cystic cavity lined by 2-4 layered squmaous epithelium with underlying fi brocellular connective tissue of dentigerous cyst (DC) (H&E stain, x100)

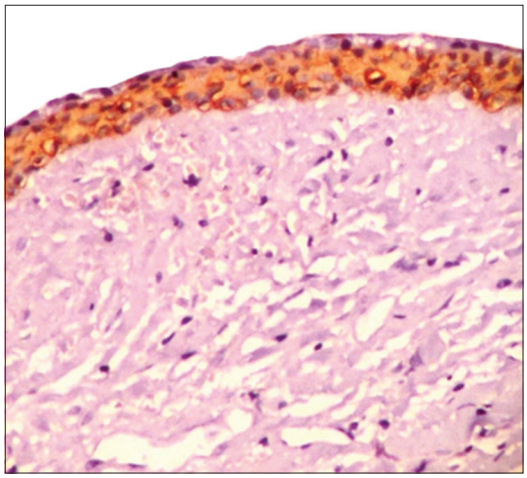

Figure 4: Photomicrograph showing DC stained with CK 14. (IHC stain, x100)

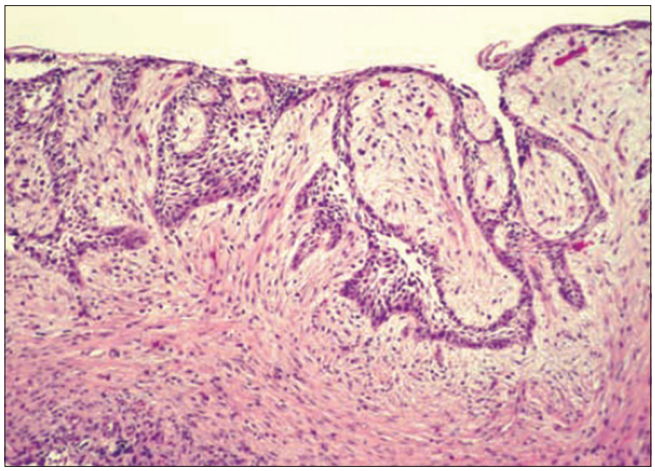

Figure 5: Photomicrograph of unicystic ameloblastoma (UCA) showing cystic cavity lined by stratifi ed squamous epithelium with basal columnar cells and superfi cial stellate reticulum like cells. (H&E stain, x40)

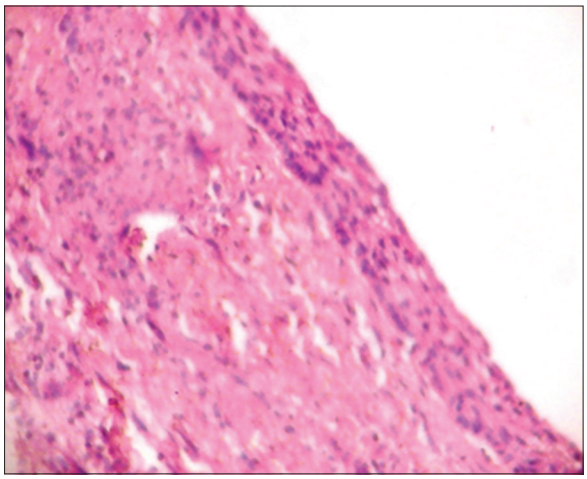

Figure 7: Photomicrograph showing Dental follicle (DF)/Reduced enamel epithelium (REE). (H&E stain, x100)

Table 3: Expression of CK 14 in study groups

Groups	Positive expression (%)	Negative expression (%)
Adenomatoidodontogenic tumor	10 (100)	Nil (0)
Unicysticameloblastoma	10 (100)	Nil (0)
Dentigerous cyst	20 (100)	Nil (0)
Dental follicles/REE	15 (75)	5 (25)

REE: Reduced enamel epithelium

Table 4: Mean percentage of CK 14 expression in study groups

Groups	Number	Mean	Std. deviation
AOT	10	3.900	0.56135
UCA	10	3.5000	0.70711
DC	20	3.4500	0.94451
DF/REE	20	3.0526	1.47097
Total	60	3.4542	1.11097

AOT: Adenomatoid odontogenic tumor; UCA: Unicystic Ameloblastoma; DC: Dentigerous cyst; DF: Dental follicle; DEE: Reduced enamel epithelium

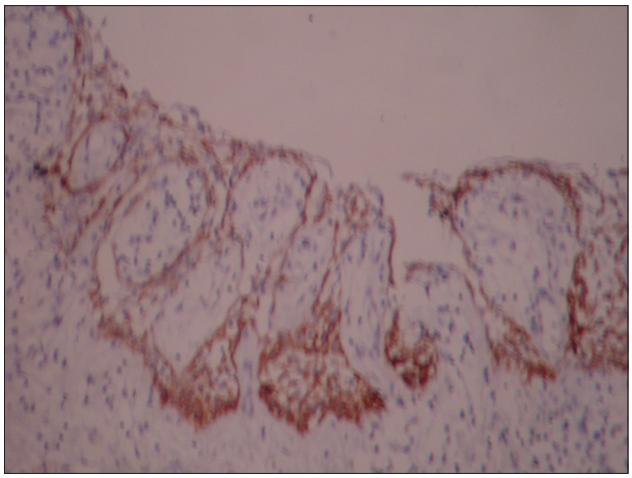

Figure 6: Photomicrograph showing UCA stained with CK 14. (IHC stain, x100)

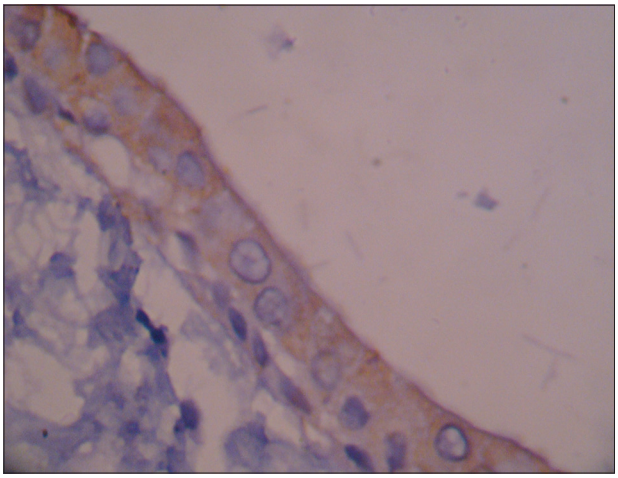

Figure 8: Photomicrograph showing DF/REE stained with CK 14. (IHC stain, x200)

AOT exhibited CK 14 and thus it was hypothesized that AOT arises from REE.[28]

Our study findings correlate with the above-mentioned study, as CK 14 expression was seen in AOT and DF/REE.

Meara JG *et al*. studied the pattern of cytokeratin 18 expression in Odontogenic keratocyst (OKC) and DC. DC showed intense staining as compared to OKC.[35] Positive expression of CK 18 and CK 14 is seen DF/REE and DC, suggesting that the possible source of DC could be REE.[27]

Hormia *et al*., 1987 suggested that DC arose between the REE and the enamel, or by the spilt in the enamel organ itself. Author proposed that their results suggested that two histogenic entities could occur that could not be distinguished by routine histological examination.[36]

It has been quoted that the cytokeratin 18 positive cells could have a specific histogenic origin and could, consequently, have

distinct functional characteristics. Another possibility is that the expression of cytokeratin polypeptide No. 18 in follicular cysts is a sign of oncofetal transformation in these lesions. This implication is supported by the finding that dermal keratinocytes, which in normal adult skin are devoid of cytokeratin polypeptide No. 18, do express this polypeptide in fetal skin and after oncogenic transformation. It remains to be elucidated whether the presence of cytokeratin polypeptide No. 18 in follicular cyst epithelium could be associated with the development of ameloblastomatous changes in the cyst wall.[37,38]

With reference to aforementioned data, the present study showed negative expression of CK 18 in DC, AOT, UCA and DF/REE. So we are unable to correlate the CK 18 expression in any of the lesions included in our study for their oncofetal transformation.

Results from our study showed CK 14 is positive with AOT, DC, DF/REE and UCA, whereas CK 18 was negative in all these cases. Cases which were positive for CK 14 and CK 18 were supposed to be evaluated for expression of calretinin. But none of the cases in our study were positive for both CK 14 and CK 18 hence calretinin was not analyzed as quoted. The expression of CK 14 in all the lesions in the present study was compared between the groups.

In AOTs, immunopositivity for CK 14 was detected in all cases. The CKs was expressed by ameloblastomas and AOTs, that have shown typical CKs of dental germ suggesting that these tumors have odontogenic epitheilial differentiation, whereas it has not evinced proper CKs of squamous epithelium.[39,40]

Neoplasms related to the odontogenic apparatus may be composed only of epithelial tissue or epithelial tissue associated with odontogenic ectomesenchyme. The immunohistochemical detection of different cytokeratin polypeptides has made it easier to explain the histogenesis of many epithelial diseases. The expression of CK 14 in the REE probably indicates that AOT originates from REE, which is in consistence with the findings of research work done by various authors. Despite advances in the field of epigenetic alteration, origin of AOT is still controversial. However, additional studies with a larger sample size are necessary to prove this hypothesis.

REFERENCES

1. Mosqueda-Taylor A.New findings and controversies in odontogenic tumors. Med Oral Patol Oral Cir Bucal 2008;13:E555-8.
2. de Souza LB, Gordón-Núñez MA, Nonaka CF, de Medeiros MC, Torres TF, Emiliano GB.Odontogenic cysts: Demographic profile in a Brazilian population over a 38-year period. Med Oral Patol Oral Cir Bucal 2010;15:e583-90.
3. Ledesma Montes C, Hernandez GuerreroJC, Garces Ortiz M. Clinicopathologic study of odontogenic cysts in a Mexican sample population. Arch Med Res 2000;31:373-6.
4. Avelar RA, Antunes AA, Carvalho RW, Bezerra PG, Oliveira Neto PJ, Andrade ES. Odontogenic cysts: A Clinicopathological study of 507 cases. J Oral Sci 2009;51:581-6.
5. Ochsenius G, Escobar E, Godoy L, Penafiel C. Odontogenic cysts: Analysis of 2,944 cases in Chile. Med Oral Patol Oral Cir Bucal 2007;12:E85-91.
6. Rao K, Smitha, Umadevi HS, Priya NS. Clinicopathological study of 100 Odontogenic cysts reported at V S Dental College- A Retrospective Study. JAdv Dent Res 2011;II: 51-8.
7. James W, Forbes JG. An epithelial odontome. Proc R Soc Med 1909;2:166-75.
8. Smith RR, Olson JL, Hutchins GM, Crawley WA, Levin LS. Adenomatoid odontogenic tumor: Ultra-structural demonstration of two cell types and amyloid. Cancer 1979;43:505-11.
9. Schlosnagle DC, SomerenA. The ultrastructure of the adenomatoid odontogenic tumor. Oral Surg Oral Med Oral Pathol 1981;52:154-61.
10. Yamamoto H, Kozawa Y, Hirai G, Hagiwara T, Nakamura T. Adenomatoid odontogenic tumor: Light and electron microscopic study. Int J Oral Surg 1981;10:272-8.
11. Poulson TC, Greer RO Jr. Adenomatoid odontogenic tumor: Clinicopathologic and ultrastructural concepts. J Oral MaxillofacSurg 1983;41:818-24.
12. Takata T, Zhao M, Uchida T, Kudo Y, Sato S, Nikai H. Immunohistochemical demonstration of an enamel sheath protein, sheathlin in odontogenic tumors. Virchows Arch 2000;436:324-9.
13. Mori M, Yamada K, Kasai T, Yamada T, Shimokawa H, Sasaki S. Immunohistochemical expression of amelogenins in odontogenic epithelial tumours and cysts. Virchows Arch A PatholAnatHistopathol 1991;418:319-25.
14. Saku T, Okabe H, Shimokawa H. Immunohistochemical demonstration of enamel proteins in odontogenic tumors. J Oral Pathol Med 1992;21:113-9.
15. Main DM. The enlargement of epithelial jaw cysts. Odontol Revy 1970;21:29-49.
16. Regezi JA. Odontogenic tumor In: Regezi JA.Text book of Oral Pathology. 4th ed. Missouri: Elsevier publications; 2003. p. 267-288
17. Takahashi K, Miyauchi K, Sato K. Treatment of ameloblastoma in children. Br J Oral MaxillofacSurg 1998;36:453-6.
18. Leider AS, Eversole LR, Barkin ME. Cystic ameloblastoma. A clinicopathologic analysis. Oral Surg Oral Med Oral Pathol 1985;60:624-30.
19. Fuchs E, Weber K. Intermediate Filaments: Structure, dynamics, function and disease. Annu RevBiochem 1994;63:345-82.
20. Chu PG, Weiss LM. Keratin expression in human tissue and neoplasm. Histopathology 2002;40:403-39.
21. Stigbrand T. The versatility of cytokeratins as Tumor Markers. Tumor Biol 2001;22:1-3.
22. Moll R, Franke WW, Schiller DL. The cataloge of human cytokeratins: Patterns of expression in normal epithelia, tumors and cultured cells. Cell 1982;31:11-24.
23. Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclatures and classification of potentially malignant disorders of the oral mucosa. J Oral PatholMed2007;36:575-80.
24. Van der Velden LA, Manni JJ, Ramaekers FC, Kuijpers W. Expression of intermediate filaments proteins in benign lesions of the oral mucosa. Eur Arch Otorhinolaryngol 1999;256:514-9.
25. Vaidya MM, Sawant SS, Borges AM, Ogale SB, Bhisey AN.

Cytokeratin expression in precancerous lesions of human oral cavity. Oral Oncol 1998;34:261-4.
26. Osman HI. Immunohistochemical Detection of CK 14 in Developing Enamel Organ of Rat Molars. Egypt Dent J 2006;52:1399-407.
27. Gao Z, Mackenzie IC, Cruchley AT, Williams DM, Leigh I, Lane EB. Cytokeratin expression of the odontogenic epithelia in dental follicles and developmental cysts. J Oral Pathol Med 1989;18:63-7.
28. Crivelini MM, de Araújo VC, de Sousa SO, de Araújo NS. Cytokeratins in epithelia of odontogenic neoplasms. Oral Dis 2003;9:1-6.
29. Crivelini MM, Soubhia AM, Felipini RC. Study on the origin and nature of the adenomatoid odontogenic tumor by immunohistochemistry. J Appl Oral Sci 2005;13:406-12.
30. Leon JE, Mata GM, Fregnani ER, Carlos-Bregni R, de Almeida OP, Mosqueda-Taylor A, *et al*.Clinicopathological and immunohistochemical study of 39 cases of adenomatoidod ontogenictumour: A multicentric study. Oral Oncol2005;41:835-42.
31. Babu NC, Dawra G, Sindura CS. Immunohistochemical evaluation of Bcl2 and CK 14 and CK 19 in Ameloblastoma. JContemp Dent2010;1:36-9.
32. Lu DP, Xing RD, Shu P, Tang XF, Zhang M. Cytokeratin 18 and their gene expression in jaw odontogenic keratocyst epithelial lining. Hua Xi Kou Qiang Yi XueZaZhi2007;25:106-10.
33. Lee JK, Lee KB, Hwang BN.Adenomatoid odontogenic tumor: Acase report. J Oral MaxillofacSurg 2000;58:1161-4.
34. MotamediMH, ShafeieHA, AziziT. Salvage of an impacted canine associated with an adenomatoido dontogenic tumour: A case report.Br Dent J 2005;199:89-90.
35. Meara JG, Pilch BZ, Shah SS, Cunningham MJ. Cytokeratin expression in the odontogenic keratocyst. J Oral MaxillofacSurg 2000;58:862-5.
36. Hormia M, Ylipaavalniemi P, Nagle RB, Virtanen I. Expression of cytokeratins in odontogenie jaw cysts: Monoclonal antibodies reveal distinct variation between different cyst types. J Oral Pathol 1987;16:338-46.
37. Quinlan RA, Schiller DL, Hatzfekl M, Achtstätter T, Moll R, Jorcano JL, *et al*. Patterns of expression and organization of cytokeratin intermediate filaments. Ann NY AcadSci 1985;455:282-306.
38. Morris A. Steinberg ML, Defendi V. Keratin gene expression in simian virus 40 Tranrforrmed human keratinocytes. ProcNatlAcadSci USA 1985;82:8498-502.
39. Lopes FF. Immunohistochemical analysis of cytokeratins in ameloblastoma and adenomatoid odontogenic tumor. J Bras Patol Med Lab 2005;41:425-30.
40. Araujo VC, Sousa, Nunes FD, Araujo NS. Immunohistochemical analysis of 89 benign salivary gland tumors. Rev Odontol USP1991;5:1-6.

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