



Malignant Transformation of Radicular Cyst/Residual Cyst: A Review of Literature

Bassel Tarakji^{1*}, Ayesha Shireen¹, Ayesha Umair¹,
Saleh Nasser Azzeghaiby¹, Ibrahim Alzoghaibi¹ and Salah Hanouneh¹

¹Department of Oral Maxillofacial Sciences, Al-farabi College of Dentistry and Nursing,
Riyadh, Saudi Arabia.

Authors' contributions

Author BT designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors AS and AU managed the analyses of the study. Authors SNA, BA, and SH managed the literature searches. All authors read and approved the final manuscript.

Review Article

Received 16th February 2014
Accepted 26th April 2014
Published 5th June 2014

ABSTRACT

Aim: The aim of this study is to review the literature concerning malignant transformation of radicular cyst.

Material and Method: A literature search using MEDLINE, accessed via the National Library of Medicine PubMed interface (<http://www.ncbi.nlm.nih.gov/pubmed>), searching for articles relating to the malignant transformation of radicular/residual cyst written in English from 1960-2013.

Results: Our search identified only fourteen studies available to date in English written literature. No randomized controlled trials to assess the possibility of malignant transformation of radicular/residual cyst were in the literature.

Conclusion: The development of malignancy from radicular /residual cysts is rare, however, it should always be considered as a differential diagnosis. The numbers of studied cases in literature are few but small number of case series & case reports are available. Also it is recommended that further work involving large series of tumors arising from radicular /residual cyst to determine the malignancy potential.

Keywords: Odontogenic cyst; radicular cyst; residual cyst; squamous cell carcinoma; odontogenic carcinoma; malignancy.

1. INTRODUCTION

Cysts of the jaws and maxillofacial regions are not new lesions. There is evidence of cystic lesions in the jaws of humans and other animals in the distant past. Lesions of the jaws interpreted as cysts have been found in mummified specimens from the pre dynastic era (c.4500 B.C) and from the 5th dynasty (c.2800 B.C) in Egypt. Early descriptions of cystic lesions of the jaws were written by Aulus Cornelius Celsus (early part of 1st century), Pierre Fauchard (1690–1762) and John Hunter (1729–1793), among others [1].

Kramer [2] has defined a cyst as ‘a pathological cavity having fluid, semifluid or gaseous contents and which is not created by the accumulation of pus’.

Inflammatory jaw cysts comprise a group of lesions that arise as a result of epithelial proliferation within an inflammatory focus due to a number of causes. Radicular cysts are the most common inflammatory cysts and arise from the epithelial residues in the periodontal ligament as a result of periapical periodontitis following death and necrosis of the pulp. Cysts arising in this way are found most commonly at the apices of the involved teeth, but may also be found on the lateral aspects of the roots in relation to lateral accessory root canals. Quite often a radicular cyst remains behind in the jaws after removal of the offending tooth and this is referred to as a residual cyst [3].

Neoplastic changes within simple odontogenic cysts appear to be a rare but definite entity. The tumors associated with epithelial lining of the odontogenic cyst include ameloblastoma, ameloblastic fibroma, calcifying epithelial odontogenic tumor, adenomatoid odontogenic tumor, odontoma, squamous cell carcinoma and mucoepidermoid carcinoma [4]. Among the odontogenic cysts, neoplastic transformation is considered to be highest in keratocyst and dentigerous cyst [5]. The purpose of this study is to review the literature concerning malignant transformation of radicular/residual cyst.

2. MATERIALS AND METHODS

A literature search which was carried out from September – December 2013 using MEDLINE, accessed via the National Library of Medicine PubMed interface (<http://www.ncbi.nlm.nih.gov/pubmed>), searches for articles relating to the malignant transformation of radicular & residual cyst written in english. We used following search string: (Radicular cyst & malignant transformation, residual cyst & squamous cell carcinoma, odontogenic residual cyst & squamous cell carcinoma; oral residual cyst & squamous cell carcinoma) and malignant degeneration of periapical cyst from 1960- 2013. We also used the “Related Articles” feature of PubMed to identify further references of interest within the primary search. These references were obtained, and their bibliographies, pertinent secondary references were also identified and acquired. The process was repeated until no further new articles could be identified. The abstracted literature was reviewed. Several publications were excluded as they did not meet the inclusion criteria and showed inadequate documentation regarding the type of cyst.

Our search retrieved fifty case reports series & case reports. Only fourteen studies were relevant to be included in the study taking into consideration the specific criteria enumerated below:

Inclusion criteria: All the evaluated studies should involve the malignant transformation of only radicular or residual cyst.

Exclusion criteria: All the other cysts like odontogenic keratocyst, dentigerous cyst etc. Were excluded from the study.

3. RESULTS

Between 1960 and 2013, 125 cases of malignant transformation of radicular and residual cysts were reported in the English literature. There were 14 articles with ten case reports, one article with two cases, one case series of 1241 radicular cysts out of which 42 cases showed malignant transformation, one case series of 116 odontogenic cysts out of which 70 cases of radicular cyst showed malignant transformation and one case series of 5 cases (4 dentigerous cyst; 1 lateral radicular cyst). 76 residual cysts and 49 radicular cysts progressed to malignancy with 48 cases of squamous odontogenic tumor-like proliferation and 77 cases of squamous cell carcinoma. Results are summarized in Table 1.

The clinical and histopathological features of radicular cyst have been summarized in Table 2.

4. DISCUSSION

Neoplastic transformation in the epithelial lining of a radicular cyst is a rare but a well-described phenomenon [4].

In the present study literature between 1960 and 2013, 125 cases of malignant transformation of radicular and residual cysts were reported in the English literature with 48 cases of squamous odontogenic tumor-like proliferations (SOTLP) of radicular and residual cysts.

Squamous odontogenic tumor (SOT) is defined as a locally infiltrating neoplasm consisting of islands of well-differentiated squamous epithelium in a fibrous stroma [5]. The SOT must be differentiated from an identical pathologic finding that occurs in odontogenic cysts, which Wright [18] first reported as 'squamous odontogenic tumor-like proliferations (SOTLP)'.

'Squamous odontogenic tumor-like proliferations (SOTLP)' was first described in 1975 by Pullon et al. [21], who published a series of 6 cases. However, two years later Doyle et al [16] described the first case of a SOTLP within the thickness of the membrane of a radicular cyst. Until that time, all published cases had been regarded as latent or incipient neoplasms. Goldblatt et al. [22] disagreed with this view and suggested that the absence of cellular atypia in SOTLP indicates that such lesions are not true neoplasms. The etiology is still not known although some authors consider them to develop from the rests of Serres, or the epithelial rests of Malassez within the periodontal ligament [16,21].

Table 1. Shows all the publications from 1960-2013 for malignant transformation of Radicular cys

Sl.No.	Authors Name	Type of study	Type of cyst	No. of cases	Malignancy
1.	Serge Sala-Perez et al. [6]	Case report	Radicular cyst	1 case	Squamous odontogenic tumor-like proliferation
2.	Parmar RM et al. [7]	Case series	Radicular cyst	42 out of 1241 radicular cysts	42 out of 1241 radicular cyst with squamous odontogenic tumor like proliferation
3.	Bodner et al. [8]	Case series	Residual cyst	70 out of 116 cases	70 cases associated with primary intraosseous squamous cell carcinoma
4.	Muglali M et al. [4]	Case report	Residual cyst	1 case	Squamous cell carcinoma
5.	Chaisuparat R et al. [9]	Case series	2 Odontogenic kercocyst 2 Radicular cyst 2 De novo	2 out of 6 cases	2 cases Primary intraosseous carcinoma
6.	Swinson BD et al. [10]	Case report	Residual cyst	1 case	Squamous cell carcinoma
7.	Oliver JA et al. [11]	Case report	Residual cyst	1case	Squamous odontogenic tumor-like proliferation
8.	Vander Wal KG et al. [12]	Case report	Residual cyst	1case	Squamous cell carcinoma
9.	Schwimmer AM et al. [13]	Case report	Residual cyst	1case	Squamous cell carcinoma
10.	Unal T et al. [14]	Case report	Radicular cyst	1case	Squamous odontogenic tumor-like proliferation
11.	Simon JH [15]	Case report	Radicular cyst	1 case	Squamous odontogenic tumor-like proliferation
12.	Doyle et al. [16]	Case report	Radicular cyst	1 case	Squamous odontogenic tumor-like proliferation
13.	Martinelli C [17]	Case report	Residual cyst	1 case	Squamous cell carcinoma
14.	Wright [18]	Case series	5 cases (4 dentigerous cyst; 1 lateral radicular cyst)	1 case	Squamous odontogenic tumor-like proliferation
Total			76 Residual cyst 49 Radicular cyst	125	48 cases of Squamous odontogenic tumor-like proliferation 77 cases of Squamous cell carcinoma

Table 2. The initial signs of malignant transformation of radicular/residual cyst clinically as well as histopathologically

The initial signs of malignant transformation of radicular/residual cyst	
Clinical signs	Radicular / residual cyst is slow and progressively growing cyst that invades the trabecular bone and can deform and perforate the cortical layers (Central variant) or erode the alveolar crest (Peripheral variant), including mobility of the remaining teeth with swelling and moderate pain of the gums[19] with or without cervical lymphadenopathy[5] Adherence of the cyst lining to the bony cavity, and chronic sinutract [8]. Paresthesia of lip if mental nerve is involved[4]
Histopathological criteria to document malignant transformation of the cyst lining	Transition from the normal lining epithelium to dysplasia and to carcinoma [20]. Squamous odontogenic tumor(SOT) and Squamous odontogenic tumor-like proliferation (SOTLP) are histopathologically very similar with the presence of both cases of aggregates of well-differentiated and non-keratinized squamous odontogenic epithelial cells surrounded by fibrous connective tissue [6]

Opinions on the origin of the SOTLP epithelium in odontogenic cysts are varied. Shear and Speight [3] theorized that the SOTLP epithelium in radicular cysts originates from the rests of Malassez. Unal et al. [14] considered the SOT-like epithelial islands to be 'hamartoid'; however, others have disputed this theory because of the SOTLPs proposed origin from a cystic surface. Philipsen et al. [19] believe that the SOTLPs are a result of a reactive, inflammatory hyperplasia of the epithelial cyst lining. Odell and Morgan (1990) favor a budding type of hyperplasia of the lining epithelium of radicular cysts in response to subsiding inflammation because it usually occurs in areas without inflammation. The SOTLP epithelium in radicular cysts represents a pseudo neoplastic reactive proliferation that mimics the benign, but sometimes locally aggressive SOT [5]. The prevalence for SOTLP in radicular cysts is 3.4%, on the basis of a review of 1241 radicular cysts [7]. The SOTLPs in radicular cysts have a marked predilection for maxillary incisor teeth [5,7]. The findings of Parmar et al. [7] support an origin of the SOTLP to be from the epithelial lining of the cyst. The development of the SOTLPs in radicular cysts is most likely not dependent on the presence of inflammation.

It is important to distinguish between SOT and SOTLP, in part because of differences in their biologic behavior. Of major importance is the fact that the histopathologic features of SOTLPs in odontogenic cysts bear a close resemblance to not only SOT but to acanthomatous ameloblastoma, desmoplastic ameloblastoma, and well-differentiated squamous cell carcinoma. Thus, misinterpretation of the microscopic features of the SOTLPs can result in significant errors in treatment [5].

The SOTLPs in radicular cysts do not represent an early expression of neoplastic transformation. It depicts that the biologic behavior of a radicular cyst with SOTLP is innocuous and shows no apparent potential for recurrence [5].

SOT and SOTLP are histologically very similar, with the presence in both cases of aggregates of well differentiated and non-keratinized squamous odontogenic epithelial cells surrounded by fibrous connective tissue [6].

Radiologically, SOTs are solitary, unilocular and radiotransparent images, though multilocular presentations with involvement of the entire mandibular body are also possible. In some cases displacement of the membrane of the maxillary sinus can be observed. The lesions appear alongside erupted permanent teeth, in edentulous regions, and exceptionally affect the primary dentition [19]. Since SOTLP may have possibly the same origin as SOTs (the epithelial rests of Malassez), it has been suggested that this entity could be the initial expression of the neoplastic form [23] though to date no neoplastic changes or signs of malignancy have been documented.

The odontogenic cysts with the greatest malignancy potential include radicular/residual cysts, lateral periodontal cysts and keratocystic odontogenic tumors – a case of SOT transforming into squamous cell carcinoma has also been reported [24].

Based on the above mentioned information, we consider it essential to carry out a thorough histological study of all lesions removed from the oral tissues. In the presence of a SOTLP, it is very important not to establish a wrong diagnosis of SOT or other conditions such as ameloblastoma or primary intrabony squamous cell carcinoma. The management of this condition comprises enucleation, curettage or local excision of the lesion. To date, there have been no reports of recurrences or malignant changes in the literature relating to odontogenic cysts (radicular cyst) with SOTLP [6].

In our study, 77 cases of Primary intraosseous odontogenic carcinoma (PIOC) arising from radicular and residual cysts were retrieved. Primary intraosseous odontogenic carcinoma (PIOC) is defined as a squamous cell carcinoma arising within the jaw bones; it has no initial connection with the oral mucosa and develops from remnants of odontogenic epithelium [8]. The term PIOC was suggested in 1972 by the World Health Organization (WHO) [25]. Elzay [26] reviewed the literature on PIOC of the jaws and suggested a modification of the WHO classification. Slootweg and Muller [27] presented a slight modification of Elzay's classification, taking into account the various possible origins of PIOC. Waldron and Mustoe later included intraosseous mucoepidermoid carcinoma as an additional type of PIOC [28,29]. Eversole et al. [30] used the term primary intraosseous squamous cell carcinoma (PIOSCC) and further categorized them into three types: type 1 for solid tumors, type 2 for carcinoma arising from odontogenic cysts, and type 3 for carcinoma associated with odontogenic tumors. According to the 2005 WHO Classification of Tumors, there are three subcategories of primary intraosseous squamous cell carcinomas (SCCs): (i) solid tumor that invades marrow spaces and induces osseous resorption, (ii) SCC arising from the lining of an odontogenic cyst, making a subdivision in carcinomas arising in a keratocystic odontogenic tumor (keratocyst) and carcinomas arising in other odontogenic cysts, and (iii) SCC in association with other benign epithelial odontogenic tumors [30].

The definitive diagnosis of PIOSCC is often difficult, as the lesion must be distinguished from alveolar carcinomas that have invaded the bone from the overlying soft tissue, from tumors that have metastasized to the jaw from distant sites, from association with some other odontogenic tumor, and also from tumors of the maxillary sinus [31]. The pathogenesis of PIOSCC is unclear. The malignant transformation of odontogenic cyst epithelium is largely unknown. It has been suggested that the long standing chronic inflammation might be the main predisposing factor for malignant transformation in the cyst epithelium [13,32]. This is based on the observation that the malignant transformation of cyst epithelium was accompanied by chronic infiltration of lymphocytes and plasma cells in the connective tissue of the cyst wall [33].

Chronic inflammation-induced carcinogenesis is a commonly accepted phenomenon [34] including oral cancer [35]. Although the link between inflammation and carcinogenesis has been well established, the specific underlying mechanism remains unclear [36]. There are three main mechanisms by which inflammation can cause cancer, and they appear to involve initiation as well as promotion of carcinogenesis: (i) chronic inflammation is often accompanied by the formation of reactive oxygen and nitrogen species by phagocytes. These have the potential to damage DNA, proteins, and cell membranes, modulate enzyme activities and gene expression, and thereby favor carcinogenesis. The chronic inflammation appears to promote apoptosis of normal cells that leads to a compensatory proliferative response by the remaining cells. This process increases the number of cells that are dividing and therefore are subject to DNA damage and promotes the growth of malignant cells (ii) infectious agents may directly transform cells by inserting active oncogenes into the host genome, inhibiting tumor suppressor or stimulating mitoses (iii) infectious agents may induce immunosuppression with consequent reduced immune surveillance [36,37].

The possibility of a genetic mechanism also exists. The comparison of gene expression between odontogenic carcinoma (OC) and oral mucosal carcinoma revealed numerous upregulated and down regulated genetic events that are unique to OC [38]. OCs often appear at an advanced clinical stage, making it difficult to determine the exact origin of the lesion as de novo or secondary to another pathologic process, such as an odontogenic cyst (Radicular cyst).

Browne and Gough [39] have suggested that keratin metaplasia in long-standing radicular cysts may precede malignant change and examples of epithelial dysplasia are occasionally seen in jaw cysts without any evidence of carcinomatous transformation. There is no evidence, however, that cyst epithelium is at particular risk and there is therefore no justification for regarding cysts as precancerous lesions.

Before the diagnosis of carcinoma arising from a cyst lining can be established, a number of alternative possibilities must be excluded [10,40]. It is possible that cyst and neoplasm may have developed independently adjacent to one another and ultimately fused in some parts. Careful questioning of the patient and clinical examination are necessary to exclude the possibility that the neoplasm arose primarily from the oral mucosa, or that it is a metastatic deposit in the jaw. A further possibility to be considered is that the lesion was initially an epithelial neoplasm which underwent secondary cystic change.

The treatment approach for PIOSCC should be determined by the extent of the carcinoma [41]. If the carcinoma is in situ or located intramural, within the cyst, further surgical intervention should be deferred and the patient closely followed up [42,43]. If the margins of the tumor are positive or there is carcinoma in the surrounding bone, additional therapy is indicated [42,44]. Some combinations of resection with possible grafting, radiation therapy, and chemotherapy should be planned, with neck dissection performed if needed [45,9,46].

5. CONCLUSION

The development of Squamous Cell Carcinoma from radicular /residual cysts is rare, however, it should always be considered in the differential diagnosis. The number of studied cases in literature is limited. Only a small number of case series & case reports are available. We recommend that further work involves large series of tumors arising from radicular/residual cyst to determine the malignancy transformation potential of radicular/residual cyst.

This review clearly demonstrates the importance of clinician awareness of the malignant potential of apparently innocuous cystic lesions. It also underscores the importance of a careful histological examination and the necessity of obtaining biopsy materials from various areas to prevent a misdiagnosis of large-sized cysts.

CONSENT

Not applicable.

ETHICAL APPROVAL

No human or animal subjects were used in the study and the study was approved by the ethical research board of the institution.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Shear M. Cysts of the jaws: Recent Advances. *J Oral Pathol.* 1985;14(1):43-59.
2. Kramer I.R.H. Changing views on oral disease. *Proceedings of the Royal Society of Medicine.* 1974;67:271-76.
3. Mervyn Shear and Paul Speight. *Cysts of oral and maxillofacial regions.* 4th Edition, published 2007 by Blackwell Munksgaard.
4. Muglali M, Sumer AP. Squamous Cell Carcinoma Arising in a Residual Cyst: A Case Report, *J. Contemp Dent. Pract.* 2008;9(6):115-21.
5. Masthan, et al. Neoplasms associated with odontogenic cysts. *J Dent Oral Hyg.* 2011;3(10):123-30.
6. Sala-Pérez S, Marco-Molina V, Gay-Escoda C. Squamous odontogenic tumor-like proliferation in a radicular cyst: A case report. *J Clin Exp Dent.* 2013;5(5):e298-301.
7. Parmar RM, Brannon RB, Fowler CB. Squamous odontogenic tumor-like proliferations in radicular cysts: a clinicopathologic study of forty-two cases. *J Endod.* 2011;37(5):623-6.
8. Bodner L, Manor E, Shear M, van der Waal I. Primary intraosseous squamous cell carcinoma arising in an odontogenic cyst: a clinicopathologic analysis of 116 reported cases. *J Oral Pathol Med.* 2011;40(10):733-8.
9. Chaisuparat R, Coletti D, Kolokythas A, Ord RA, Nikitakis NG. Primary intraosseous odontogenic carcinoma arising in an odontogenic cyst or de novo: a clinicopathologic study of six new cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;101(2):194-200.
10. Swinson BD, Jerjes W, Thomas GJ. Squamous cell carcinoma arising in a residual odontogenic cyst: case report. *J Oral Maxillofac Surg.* 2005;63(8):1231-3.
11. Olivera JA, Costa IM, Loyola AM. Squamous odontogenic tumor-like proliferation in residual cyst: case report. *Braz Dent J.* 1995;6(1):59-64.
12. van der Wal KG, de Visscher JG, Eggink HF. Squamous cell carcinoma arising in a residual cyst. A case report. *Int J Oral Maxillofac Surg.* 1993;22(6):350-2.
13. Schwimmer AM, Aydin F, Morrison SN. Squamous cell carcinoma arising in residual odontogenic cyst. Report of a case and review of literature. *Oral Surg Oral Med Oral Pathol.* 1991;72(2):218-21.
14. Unal T, Gomel M, Gunel O. Squamous odontogenic tumor-like islands in a radicular cyst: report of a case. *J Oral Maxillofac Surg.* 1987;45(4):346-9.
15. Simon Jh, Jensen JL. Squamous odontogenic tumor-like proliferations in periapical cysts. *J Endod.* 1985;11(10):446-8.
16. Doyle JL, Grodjesk JE, Dolinsky HB, Rafel SS. Squamous odontogenic tumor. Report of three cases. *J Oral Surg.* 1977;35:994-6.
17. Martinelli C, Melhado RM, Callestini EA. Squamous-cell carcinoma in a residual mandibular cyst. *Oral Surg Oral Med Oral Pathol.* 1977;44(2):274-8.
18. Wright JM. Squamous odontogenic tumor-like proliferations in odontogenic cysts. *Oral Surg.* 1979;354-358.
19. Philipsen HP, Reichart PA, Zhang KH, Nikai H, Yu QX. Adenomatoid odontogenic tumour: biological profile based on 499 cases. *J. Oral Pathol. Med.* 1991;20:149-58.
20. Bradley N, Thomas DM, Antoniadis K, Anavi Y. Squamous cell carcinoma arising in an odontogenic cyst. *Int J Oral Maxillofac Surg.* 1988;17(4):260-3.
21. Pullon PA, Shafer WG, Elzay RP, Kerr DA, Corio RL. Squamous odontogenic tumor. Report of six cases of a previously undescribed lesion. *Oral Sur Oral Med Oral Pathol.* 1975;40:616-30.
22. Goldblatt LI, Brannon RB, Ellis GL. Squamous odontogenic tumor. Report of five cases and review of the literature. *Oral Sur Oral Med Oral Pathol.* 1982;54:187-96.

23. Stoelinga PJW, Cohen MM, Morgan AF. The origin of keratocysts in the basal cell nevus syndrome. *J Oral Surg*. 1973;33:659-64.
24. Ide F, Shimoyama T, Horie N, Shimizu S. Intraosseous squamous cell carcinoma arising in association with a squamous odontogenic tumor of the mandible. *Oral Oncol*. 1999;35:431-4.
25. Pindborg JJ, Kramer IRH, Torloni H, eds. Histologic typing of odontogenic tumors, jaw cysts and allied diseases. Geneva: World Health Organization. 1972;35-6.
26. Elzay RP. Primary intraosseous carcinoma of the jaws: review and update of odontogenic carcinoma. *Oral Surg Oral Med Oral Pathol* 1982;54:299-303.
27. Sloomweg PJ, Muller H. Malignant ameloblastoma or ameloblastic carcinoma. *Oral Surg*. 1984;57:168-76.
28. Waldron CA, Mustoe TA. Primary intraosseous carcinoma of the mandible with probable origin in an odontogenic cyst. *Oral Surg Oral Med Oral Pathol*. 1989;67(6):716-24.
29. Muller S, Waldron CA. Primary intraosseous squamous carcinoma. Report of two cases. *Int J Oral Maxillofac Surg*. 1991;20:362-5.
30. Eversole LR, Siar CH, van der Waal I. Primary intraosseous squamous cell carcinomas. In: Barnes L, Evson JW, Reichart P, Sidransky D, eds. World Health Organization classification of tumors. Pathology and genetics head and neck tumors. World Health Organization International Agency for Research on Cancer. Lyon: IACR Press. 2005;290-1.
31. Sueti Y, Tanimoto K, Taguchi A, Wada T. Primary intraosseous carcinoma: review of the literature and diagnostic criteria. *J Oral Maxillofac Surg*. 1994;52:580-3.
32. Gardner AF. The odontogenic cyst as a potential carcinoma; a clinico-pathologic appraisal. *J Am Dent Assoc*. 1969;78:746-55.
33. Foley WL, Terry BC, Jacoway JR. Malignant transformation of an odontogenic keratocyst: report of a case. *J Oral Maxillofac Surg*. 1991;49:768-71.
34. Coussens LM, Werb Z. Inflammation and cancer. *Nature*. 2002;420:860-7.
35. Choi S, Myers JN. Molecular pathogenesis of oral squamous cell carcinoma: implication for therapy. *J Dent Res*. 2008;87:14-32.
36. Karin M, Greten FR. NF-kappa B. linking inflammation and immunity to cancer development and progression. *Nat Rev Immunol*. 2005;5:749-59.
37. Hold GL, El-Omar ME. Genetic aspects of inflammation and cancer. *Biochem J*. 2008;410:225-35.
38. Alevizose I, Blaeser B, Gallagher G, Ohyama H, Wong DTW, Todd R. Odontogenic carcinoma: a functional genomic comparison with oral mucosal cell carcinoma. *Oral Oncol*. 2002;38:504-7.
39. Browne RM, Gough NG. Malignant change in the epithelium lining odontogenic cysts. *Cancer*. 1972;29:1199-1207.
40. Kay LW, Kramer IRH. Squamous cell carcinoma arising in a dental cyst. *Oral Surgery, Oral Medicine, Oral Pathology*. 1962;15:910-919.
41. Makowski G, McGuff S, Van Sickels JE. Squamous cell carcinoma in a maxillary odontogenic cyst. *J Oral Maxillofac Surg*. 2001;59:76-80.
42. Fanibunda K, Soames JV. Malignant and premalignant change in odontogenic cysts. *J Oral Maxillofac Surg*. 1995;53:1469-72.
43. McDonald AR, Pogrel MA, Carson J, Regezi J. p53 positivity in squamous cell carcinoma originating from an odontogenic cyst. *J Oral Maxillofac Surg*. 1996;54:216-8.
44. Van der Waal RIF, Buter J, van der Waal I. Oral metastases: report of 24 cases. *Br J Oral Maxillofac Surg*. 2003;41:3-6.

45. Makowski G, McGuff S, Van Sickels JE. Squamous cell carcinoma in a maxillary odontogenic cyst. *J Oral Maxillofac Surg*. 2001;59:76–80.
46. Thomas G, Pandey M, Mathew A, et al. Primary intraosseous carcinoma of the jaws; pooled analysis of world literature and report of two new cases. *Int J Oral Maxillofac Surg*. 2001;30:349–55.

© 2014 Tarakji et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sciencedomain.org/review-history.php?iid=549&id=12&aid=4821>