Original Article

Assessment of expression of podoplanin in odontogenic tumors and cysts—An immunohistochemical study

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Abstract

Aim: The present study was conducted to determine the podoplanin expression in odontogenic tumors and cysts. **Materials and Methods:** It consisted of 12 cases of the keratocystic odontogenic tumor (KCOT), 10 cases of ameloblastoma, 8 cases of dentigerous cysts (DC), 8 cases of radicular cysts (RC) and 8 dental follicles (DF) as controls which were immunohistochemically evaluated using an antibody against podoplanin. **Results:** Immunostaining intensity, % of PPC and total score of ameloblastoma was higher than DC and DF but less than KCOT (t- 1.48). When DC was compared with KCOT and RC, the podoplanin expression was significantly higher with DC ($P < 0.05$). The podoplanin expression was comparatively higher with KCOT as compared to RC and DC. OT (t-4.40) revealed higher podoplanin expression as compared to OC and DF (t-5.54). **Conclusion:** There was significantly higher expression of podoplanin in cases of ameloblastoma and KCOT as compared to the RC, DC and DF. Podoplanin may be considered as a useful marker to delineate the aggressiveness of ameloblastoma and KCOT.

Keywords: Ameloblastoma, keratocystic odontogenic tumor, podoplanin

Introduction

The occurrence of odontogenic tumors and cysts are not an uncommon phenomenon. These entities constitute major pathology for which the patient seeks treatment. The most common odontogenic tumor is ameloblastoma and the mandibular posterior tooth region is the favorite site for its occurrence. A keratocystic odontogenic tumor (KCOT) which was previously known as odontogenic keratocyst (OKC) has been considered as a neoplastic in nature. KCOT shows destruction and has a high recurrence rate.[1] Clinically, both lesions provide sufficient clues for the diagnosis. The occurrence site, nature of the lesion is a few diagnostic points. Both show the expansion of jaws in anteroposterior and buccolingual direction. Histopathologically, several genes and proteins show expression which depicts the invasive nature of these lesions.[2]

Podoplanin is a proteinaceous transmembrane marker for the detection of oral squamous cell carcinoma (OSCC). Apart from its role in SCC, its expression in KCOT and ameloblastoma has been established.[3] The classification of odontogenic tumors depending upon immunostaining according to the podoplanin distribution may be fruitful for the oral pathologists.[4] The present study was conducted to determine the podoplanin expression in ameloblastoma and KCOT and its comparison with the radicular and dentigerous cyst (DC).

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Materials and Methods

The present study was conducted in the department of oral pathology. It consisted of 12 cases of KCOT, 10 cases of ameloblastoma, 8 cases of DCs, 8 cases of radicular cysts (RC) and 8 specimens of dental follicles (DF) which were considered as control. Specimens were paraffin-embedded which were retrieved from the record room of the department. Institutional clearance was obtained from the ethical committee prior to the study.

0.01 M citrate buffer was used for immersing sections which were first heated for 6 min and then 15 min so as to obtain the antigen. Subsequently, peroxide block was used for immersing the tissues and later on covered with power block reagent for 20 min. Anti-podoplanin antibody was spread to all sections for 1 h following which slides were covered for 15 minutes with a post-primary block. Later on, the second antibody was applied to all sections. Substrate chromogen was applied to all sections for 3 min and Mayer's hematoxylin staining was done.

Based on the expression of podoplanin in epithelial odontogenic cells, scoring was given for immunostaining (I) which revealed either absent- 0, weak- 1, moderate- 2, strong- 3, and very strong- 4. Similarly, odontogenic cells which showed podoplanin were labeled as podoplanin positive cells (PPC) (II) were labeled as 0 with 0% PPC cells, 1-<25% PPC, 2- 25–50% PPC, 3-50–75% PPC, 4- >75% PPC. Final score (I + II) with 0 showed absent, 1–4 showed weak and 5–8 showed strong.

Results thus obtained were subjected to statistical analysis using the Chi-square test and T-test. A *P* value of less than 0.05 was considered significant.

Results

The percentage of PPC and total score of ameloblastoma was more than DC (t- 4.21) and DF (t- 4.92). The podoplanin expression was comparatively higher with KCOT as compared to RC and DC. Similarly, it was found that the total score was higher in RC (t- 4.45) as compared to DF. When DC was compared with KCOT (t- 5.17) and RC (2.72), the podoplanin expression was significantly higher with DC ($P < 0.05$) [Table 1]. It was seen that immunostaining intensity (I), % of PPC (II) and the total score (I + II) was higher with OT (t- 4.40) as compared to OC and DF (t- 5.54). Similarly, it was higher with DF (t- 2.05) when it was compared with DC [Table 2].

Table 1: Comparison of Immunostaining (I), % of PPC (II) and total score (I + II) in study cases

Groups	Immunostaining (I)		% of PPC (II)		Total score (I + II)	
	t	*P*	*t*	*P*	*t*	*P*
Amelo vs DC	3.50	0.01	3.84	0.01	4.21	0.01
Amelo vs KCOT	0.34	0.06	1.62	0.06	1.48	0.06
Amelo vs RC	1.82	0.07	1.70	0.07	1.83	0.07
Amelo vs DF	3.80	0.02	5.24	0.02	4.92	0.02
DC vs KCOT	4.96	0.01	3.64	0.01	5.17	0.01
DC vs RC	2.72	0.03	2.63	0.03	2.72	0.03
DC vs DF	0.001	0.5	1.52	0.5	0.74	0.5
KCOT vs RC	2.87	0.01	0.75	0.4	2.47	0.01
KCOT vs DC	4.90	0.01	3.84	0.01	5.32	0.01
RC vs DF	4.01	0.02	4.35	0.02	4.45	00.02

Table 2: Comparison of Immunostaining between odontogenic tumors (OT), odontogenic cysts (OC) and dental follicle (DF)

Groups	Immunostaining (I)		% of PPC (II)		Total score (I+II)	
	t	*P*	*t*	*P*	*t*	*P*
OT vs OC	4.21	0.01	3.56	0.01	4.40	0.01
OT vs DF	4.45	0.04	5.31	0.04	5.54	0.04
OC vs DF	1.34	0.5	2.57	0.5	2.05	0.5

Discussion

Ameloblastoma occurring in the tooth-bearing area is a true neoplasm of enamel organ which is considered to be non- functional, unicentric, clinically persistent, and anatomical benign. This is the most commonly and persistently occurring OT.[5]

There are several histological variants of ameloblastoma such as unicystic, plexiform, desmoplastic, acanthomatous, follicular, etc. Sometimes, the clinical features of lesions are so identical, making diagnosis difficult. Thus markers like podoplanin play an essential and vital role.[6]

Podoplanin was initially found in puromycin-induced nephrosis on the surface of rat podocytes and hence the name podoplanin. It is made up of 162 amino acids is a transmembrane sialomucin like glycoprotein also called T1 alpha-2, Aggrus, and Gp36. Its expression is seen in normal and neoplastic sites such as the uterus, lungs, esophagus, bone, and oral cavity.[7] Gupta *et al.* concluded that Podoplanin expression in OKC is potentially associated with the moderate invasive nature of the neighboring structures.[8]

The present study evaluated the podoplanin expression in various OTs like ameloblastoma and KCOT as well as in OCs such as DC, RCs and its comparison with the normal DF. In this study, we found that immunostaining intensity, % of PPC and total score of ameloblastoma was significantly higher than DC and DF.

A KCOT is commonly seen in posterior mandibular region, angle, and ramus and causes significant swelling, pain, and expansion of cortical plates and subsequent paresthesia of the involved area depending on the involvement of nerve such as an inferior alveolar nerve. We found that podoplanin expression in KCOT found to be higher as compared to ameloblastoma, DC and RC. There was a basal and suprabasal expression of podoplanin in cases of KCOT.[9]

Etemad-Moghadam S and Alaeddini M found an association of podoplanin with OTs.[10] Tijoe *et al.*[11] in their study concluded that podoplanin is associated with the proliferative activity of ameloblastoma and there is a considerable expression that makes this marker a suitable indicator.

Freidrich *et al.*[12] suggested the role of podoplanin in enhancing the proliferative activity of the lining epithelium of KCOT. We found that podoplanin expression in OTs was significantly higher than OCs such as radicular and DCs.

RC also is known as periapical cyst arises from epithelial rest of Malassezia in the periodontal ligament, which is a cyst seen in apex of nonvital teeth which show well defined asymptomatic swelling in the region. It is an inflammatory cyst. It is mostly observed in the maxillary anterior region and can show pain in case it is infected.[13]

DC is a developmental cyst seen with impacted or partially erupted teeth especially mandibular third molar or canines. It is considered to be enlargement of follicular space more than 5mm. It is frequently encountered in children. It is also known as a follicular cyst.[14] In our study, we found that podoplanin expression was less with radicular and DC as compared to KCOT and ameloblastoma.

In the present study, we compared the podoplanin expression in OCs and DF it was seen that the difference was non- significant. Its expression was found to be higher in DFs as compared to OCs. Quintanilla *et al.* in their review stated the role of podoplanin in the diagnosis of various conditions such as inflammation and cancer.[15]

Conclusion

There was significantly higher expression of podoplanin in cases of ameloblastoma and KCOT as compared to a RC, DC and DF. Podoplanin increases the proliferative activity of odontogenic epithelial cells of ameloblastoma and KCOT and hence enhances its aggressiveness and invasive nature. Podoplanin may be considered as a useful marker to delineate the aggressiveness of ameloblastoma and KCOT.

Podoplanin has a role in the diagnosis of various cysts, OT, inflammation, and cancer cells. Hence, it can be used in the practice of primary care for identification and management of such cases.

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Conflicts of interest

There are no conflicts of interest.

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