EXPRESSION OF CD 10 IN DENTIGEROUS CYSTS AND AMELOBLASTOMAS – A RELIABLE PROGNOSTICATOR

[1]RABIA ANJUM
[2]NADIA NASEEM
[3]RABIYA SAIF
[4]AH NAGI

ABSTRACT

CD 10, a surface glycoprotein, depicts the proliferation potential, differentiation and prognosis of neoplastic cells. Dentigerous Cyst (DC) is the most common developmental odontogenic cyst having high proliferative index thus related with epithelial dysplasia and neoplasms. Ameloblastoma is an uncommon, benign and locally aggressive odontogenic neoplasm with high rate of recurrence after surgery. This study was therefore designed to determine the expression of CD10 in DCs and ameloblastomas. Twenty-five patients presenting with DCs (n=12) and ameloblastomas (n=13) were selected. Relevant clinical and radiographical findings were recorded and biopsies were submitted for histological diagnosis. CD 10 immunopositivity was assessed by immunohistochemistry in four microscopic high power fields showing maximum number of immunopositive cells.

Mean age was 26.5 ± 11.24 years and 42.07 ± 9.24 years while male to female ratio was 7:5 and 7:6 for DCs and ameloblastomas respectively. Most of the patients (58.3%) of DCs presented asymptomatically while 41.6% patients reported with painful swelling. Comparing, all patients with ameloblastomas presented with painless swelling. Radiographically, all DCs and 46.2% of ameloblastomas were unicystic while 53.8% were multicystic radiolucent lesions. Histologically, epithelial atypia was seen in 50% and 23% of DCs and ameloblastomas respectively. High CD 10 cytoplasmic & membranous immunoreactivity was observed in the superficial epithelial lining of the DCs and the neoplastic epithelial cells of ameloblastomas while the stellate reticulum like cells showed only cytoplasmic immunopositivity. CD 10 expression may indicate neoplastic disposition of DCs while locally invasive and recurrence potential in ameloblastomas.

Key Words: *Dentigerous cyst, Ameloblastoma, CD10.*

INTRODUCTION

Dentigerous cyst (DC) is the most common developmental cyst present in the oral cavity, accounting approximately for 20% of the developmental cysts of the jaws, and is almost always related with the crown of a tooth attached to the cemento-enamel junction. It is believed to develop as a result of accumulation of fluid between the reduced enamel epithelium and the tooth crown, thus leading to the expansion of the follicle beyond the 3mm normal diameter and hence is usually associated with impacted or unerupted teeth.[1]

[1] Dr Rabia Anjum, BDS, M.Phil, (Oral Pathology), Research Fellow, (University of Health Sciences, Lahore)
[2] Dr Nadia Naseem, MBBS, M.Phil, (Histopathology), Assistant Professor, (University of Health Sciences, Lahore)
[3] Dr Rabiya Saif, BDS, M.Phil, (Oral Pathology), Demonstrator, (de,Montmorency College of Dentistry)
[4] Prof AH Nagi, MB PhD, FCPS, FCPP, FRC Path, Head of Pathology Department, (University of Health Sciences, Lahore)

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Ameloblastoma is an uncommon benign, locally aggressive odontogenic neoplasm that accounts for 10% of all tumours present in the mandible and maxilla.[2] Although the aetiology is unknown, it is believed to arise from various sources of odontogenic epithelium like dental follicle.[3]

CD 10 is a single-chain, 90-110-kDa cell surface zinc dependent metalloprotease inactivating various bioactive neuropeptides.[4] CD 10 protein regulates cell growth and apoptosis thorough signal transduction pathways. As CD 10 has structural similarity to the matrix metalloproteases in the stroma, so it is believed that it affects invasion and metastatic potential of tumor cells by altering the cellular microenvironment.[5] It is expressed by a variety of normal cell types, including lymphoid precursor cells, germinal center B lymphocytes and some epithelial cells like gastric mucosa.[6] CD 10 may suggest apoptosis or proliferation of cancer cells.[7] Initially, CD 10 was reported in lymphoid neoplasms but it can also be seen in malignant epithelial neoplasm and melanoma.[8] Both the neoplastic cells

and stroma show positive immunostaining thus indicating it is involved in carcinogenesis and might be a novel prognostic factor in some malignant tumors.[6] In intratumoural stromal cells it may also contribute to tumour progression.[5]

High CD 10 expression indicates poor prognosis in various tumours like breast carcinoma[5], malignant melanoma[9], cutaneous basal cell and squamous cell carcinoma[10] and oral squamous cell carcinoma.[11] In dentigerous cyst, cytoplasmic and membranous immunoreactivity is seen mainly in the superficial layers of the epithelial lining. In ameloblastoma, the stellate reticulum like cells shows cytoplasmic reaction while the neoplastic epithelial cells show both cytoplasmic and membranous immunostaining.[12]

High CD 10 expression in dentigerous cyst may indicate its neoplastic potential while in ameloblastoma it may recognize areas having locally invasive behavior and high risk of recurrence.

METHODOLOGY

Twenty-five cases including both dentigerous cyst (n=12) and ameloblastoma (n=13) were taken from Oral and Maxillofacial surgery Department of de,montmorency College of Dentistry, Lahore thorough convenient sampling. The duration of study was six months. Data including the patient's age, gender, site, laterality as well as radiological findings were noted. Samples were taken in the form of small curetting's, incisional and true cut biopsies. After detailed gross examination of specimens paraffin embedded blocks were prepared. Twelve cases were diagnosed as dentigerous cyst, while rest of the cases diagnosed as ameloblastoma. To confirm the diagnosis 5 µm thick sections were cut and mounted on glass slides, sections were stained with haematoxylin and eosin stain and examined by light microscope.

IMMUNOHISTOCHEMISTRY

About 4 µm thick sections were cut from all paraffin blocks and mounted on poly L _lysine coated glass slides. Sections were deparaffinized in xylene and rehydrated in graded ethyl alcohol, followed by immersion in citrate buffer solution of pH 4.8 and were put in the microwave oven before staining procedures. For immuno staining, Universal kit (Lab Vision) employing the streptavidin biotin system was used to carry out the peroxidase anti-peroxidase method of immunohistochemical staining. Sections were then incubated with a primary monoclonal anti CD 10 antibody (DAKO) and DAB chromogen was applied to the sections followed by counter staining with hematoxylin. For each positive section, four microscopic high power fields showing maximum number of immunopositivite cells were selected.

RESULTS

Male predominance was seen both for DCs and ameloblastomas (Table 1). Regarding site, lesions were seen mostly in the posterior region of mandible while very few were found in the anterior region of both mandible and maxilla. Among n=25 cases, n=13 were present on the right side, n=7 on the left side and only n=3 cases in the anterior region. Clinically, among n=12 cases of dentigerous cyst n=9 patients presented with the pain in mandible or maxilla while n=3 patients were asymptomatic. All patients n=13 of ameloblastoma reported with painless swelling. Radiographic examination revealed unicystic radiolucent lesion in all cases of dentigerous cyst. While in ameloblastoma n=7 cases (53.8%) were multicystic and n=6 cases (46.15%) were unicystc radiolucent lesions.

Microscopically, n=12 cases revealed stratified squamous epithelial lining with underlying connective tissue surrounding a cystic cavity thus diagnosed as dentigerous cyst (Fig 1). Mild to moderate degree of chronic inflammation was seen in connective tissue of n=10 (83.3%) cases of dentigerous cyst while n=2 (16.67%) cases showed severe degree of inflammation. Among n=12 cases of dentigerous cysts, basal layer atypia characterized by pleomorphism, altered nuclear cytoplasmic ratio and increased stratification was seen in n=6 (50%) cases.

As regards ameloblastomas, n=2 follicular (15.38%), n=5 plexiform (38.46%) and n=6 unicystic (46.15%) variants were found on microscopy (Fig 2). Out of n=13 cases only n=3 (23%) showed basal layer atypia. The reason for increase atypia in dentigerous cyst comparing to ameloblastoma is dense chronic inflammatory infiltrate present in underlying connective tissue. The chronic inflammation leads to chronic irritation thus stimulating proliferation of epithelial cells resulting in epithelial hyperplasia or metaplasia.[13]

Positive CD 10 was seen in all cases examined in the present study. The positive sections showed a homogenous and brownish cytoplasmic and membranous immunoreactivity in the superficial layers of the epithelial lining of dentigerous cyst (Fig: 3) In the ameloblastoma, the neoplastic epithelial cells showed cytoplasmic and membranous immunopositivity while the stellate reticulum like cells showed only cytoplasmic reaction (Fig 4)

DISCUSSION

Inflammation present in the connective tissue increases the number and surface area of immunopos-

TABLE 1: THIS TABLE SHOWS THE GENDER DISTRIBUTION AND MEAN AGE AMONG THE PATIENTS WITH DENTIGEROUS CYST AND AMELOBLASTOMA. THERE IS A MALE PREDOMINANCE WHEREAS MEAN AGE <45YEARS

Sr. No.	Male	Female	Total	Mean age
Dentigerous cyst	7	5	12	26.5
Ameloblatoma	7	6	13	42.07

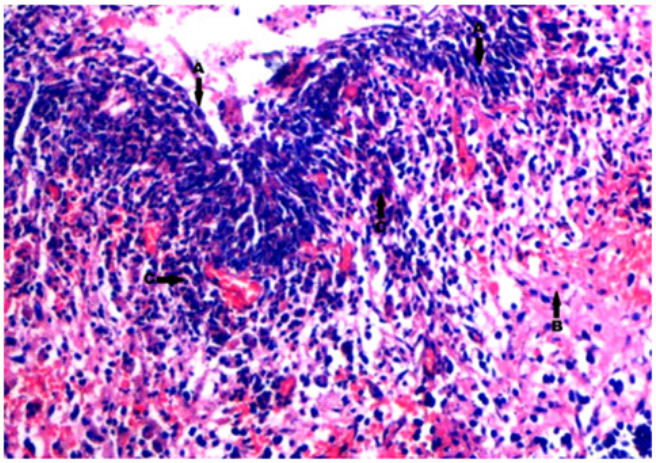

Fig 1: This figure shows the dentigerous cyst with epithelial lining (A), edematous connective tissue (B) and inflammatory infiltrate encroaching the epithelium (C). (H&E,40X)

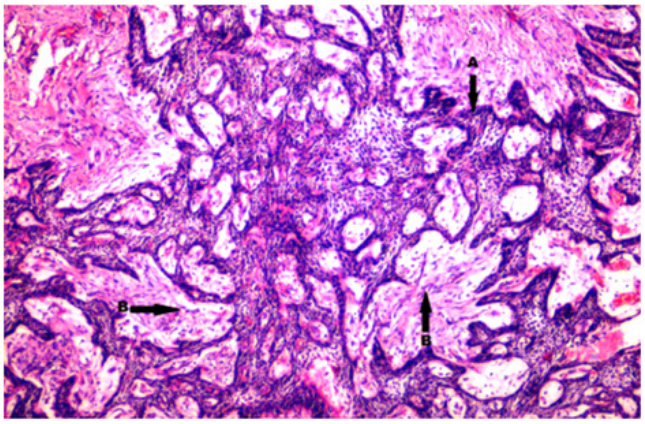

Fig 2: This figure shows the plexiform variant of ameloblastoma with neoplastic epithelial cells showing reverse polarization (A) and star shaped cells in stellate reticulum (B). (H&E, 20X)

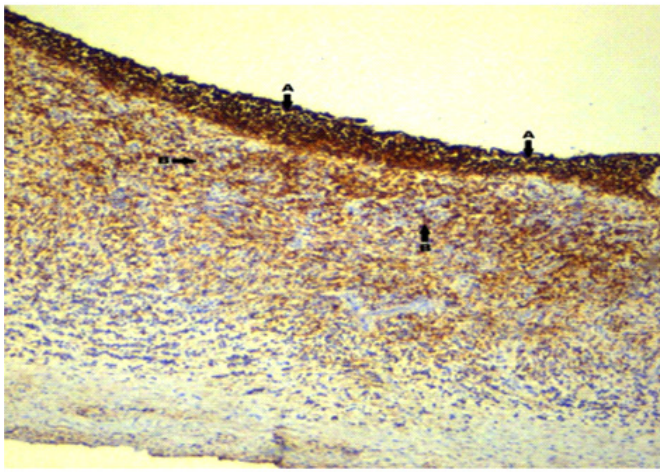

Fig 3: This figure shows the dentigerous cyst with intense brown CD 10 immunostaining in the epithelial lining (A) and the inflammatory cells of connective tissue (B). (H&E,10X)

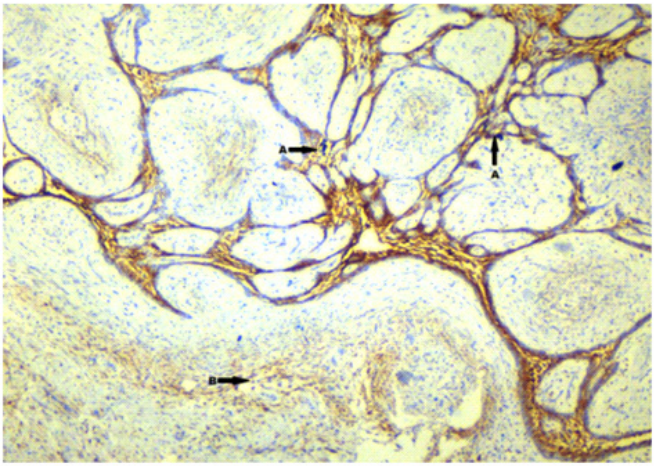

Fig 4: This figure shows ameloblastoma with intense brown CD 10 immunostaining in neoplastic epithelial cells (A) and star shaped cells of stellate reticulum(B). (H&E, 10X)

itive cells. This could be explained on the assumption that chronic inflammation can stimulate epithelial proliferation.[14] CD 10 is related with differentiation and growth of neoplastic cells, and its expression is found to be increased with the increase of tumor dysplasia.[15] Dentigerous cysts are the most prevalent non inflammatory odontogenic cysts. They develop within the normal dental follicle around an unerupted tooth as a result of fluid accumulation between the follicular epithelium and the crown of the tooth.[16]

The histopathological features of a cyst, a continue thin stratified squamous epithelial lining surrounding a cavity and a connective capsule of variable density reported in present study are similar with Godoy et al criteria.[17] Occasionally this cyst is related with ameloblastoma, epithelial dysplasia, squamous cell carcinoma or mucoepidermoid carcinoma.[1]

Positive CD 10 staining was seen in all dentigerous cyst chrarcterised by homogenous and brown staining. Masloub et al who conducted his study by using n=26 paraffin embedded blocks reported the similar findings as homogenous brown staining in dentigerous cyst thus concluding high CD 10 expression might predict the neoplastic potentiality of the epithelial lining of this cyst.[12] Liapatas et al who did his study on periapical granulomas and cysts also observed the same features.[18]

Ameloblastomas may arise from different sources of odontogenic epithelium, including dental follicle epithelial lining. Approximately 50% of ameloblastomas tend to develop from the epithelial lining of a dentigerous cyst.[16] Although ameloblastomas are benign neoplasm but they behave aggressively and infiltrative.[19] Multicystic ameloblastomas are likely to be more aggressive and have a higher risk of recurrence than unicystic and peripheral ameloblastomas.[20] In the present study neoplastic cells of ameloblastoma showed membranous as well as cytoplasmic staining. Strong and intense CD 10 positivity was seen in multicystic

variants while comparing with unicystic ameloblastoma. Similar findings were reported by Lezzi et al who conducted his study on n=45 cases of ameloblastoma, solid variants exhibited a uniformly strong and intense CD 10 positivity in the areas of infiltrating odontogenic epithelium while focal CD 10 stromal positivity was present in unicystic ameloblastoma.[21] The similar findings were also observed in other study by Masloub et al.[12] Thus these studies explain the argument of Ogawa et al who stated that CD 10 was associated with the differentiation and growth of neoplastic cells. So this marker could function to assist the neoplastic transformation of dentigerous cyst and the locally invasive behavior of ameloblastoma.[15]

CONCLUSION

Based upon the results of the present study, it might be concluded that high CD 10 expression in dentigerous cyst may predict the neoplastic potential within epithelial lining of this cyst. Also, in unicystic and multicystic ameloblastoma, high CD 10 expression might be helpful to identify areas with biological progression towards local invasion and recurrences. Hence appropriate surgical measures may be adapted for the excision of ameloblastomas and larger DCs after initial diagnosis.

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CONTRIBUTION BY AUTHORS

1 Rabia Anjum:	Title selection, design planning, methodology, analysis.
2 Nadia Naseem:	Interpretation, analysis & discussion.
3 Rabiya Saif:	Article participation in methodology.
4 AH Nagi:	Supervisor.