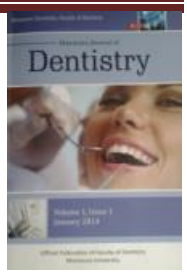


Immunohistochemical assessment of Matrix Metalloproteinase-1 in Ameloblastoma

Ahmed Mohamed, Mahmoud F Elsherbeny, Mohamed I. Mourad

Abstract:

Background: Ameloblastoma (AM) is a benign odontogenic epithelium but it has aggressive and invasive behavior and high rate of recurrence. Matrix metalloproteinase-1 (MMP-1) is a member of the matrix metalloproteinases family, and its aberrant expression is implicated in tumor invasion and metastasis.

The aim of this study was to compare the immunoexpression of Matrix Metalloproteinase-1 (MMP-1) in different types ofAmeloblastomas (AMs) and to correlate the clinical, radiographic and histological features of AMs in relation to MMP-1 expression.

Material and Methods: A total of 25 formalin fixed paraffin embedded tissues previously diagnosed as AM was utilized. Diagnosis was confirmed by H&E stain. Tissue sections were prepared and stained with MMP-1. Statistical analysis was performed using SPSS version 26.0.

Results: There was astatistical significant difference between conventional and unicystic AM cases in age, size, x-ray and MMP-1 expression. Moreover, there was a significant difference between old & young age cases, as well as between unilocular&multilocular cases and between small& large cases regarding expression of MMP-1.

Conclusions: MMP-1 could be considered as a reliable marker or indicator for the local invasion, expansion and progression of AM. In addition, Stromal cells of AM are involved with the neoplastic cells in the regulation of tumor progression and expansion due to their role in degradation of matrix components.

Key words: MMP-1, AMs, UA.

Introduction

Ameloblastoma (AM) is an odontogenic tumor of ectodermal origin characterized by proliferation of the odontogenic epithelium without the ectomesenchymal tissue.[1] It is a benign neoplasm, that is locally invasive with highly destructive behavior and risk of recurrence. [2]

It represents approximately 1% of oral tumors. About 80% of AMs occur in the mandible and the remaining 20% in the upper jaw. A slight male predilection and major occurrence in the mandibular molar-ramus area were elicited. [3]

According to the the classification of tumors of the World Health Organization (WHO), the variants of AMs are the conventional, the extraosseous AM, the desmoplastic and the unicystic type.[4] The microscopic subtypes most commonly seen in conventional AM are the follicular and plexiform type. [3]

Effort has been made to identify the underlying mechanisms of its local invasiveness on both the gene and protein levels, including cell population proliferation,apoptosis, matrix degradation and relevant oncogenes and antioncogenes. [5] Multi-gene abnormalities were identified in the genesis and development of tumors. [6]

Matrix metalloproteinases (MMPs), also called matrixns, are zinc and calcium-dependent endopeptidases, that are the major proteases involved in extracellular matrix (ECM) degradation. [7] These enzymes play central roles in the regulation of the ECM during embryonic development and tissue remodeling. [8, 9]They are capable of degrading a wide range of extracellular molecules and a number of bioactive molecules. MMPs activity is regulated by two major endogenous inhibitors: alpha2-macroglobulin and tissue inhibitors of metalloproteinase (TIMPs). [8, 9]

The present study was conducted to evaluate the expression of MMP-1 in AM in an attempt to explain its role in local invasiveness and growth behavior.[10]

Material and Methods

The present study will be carried out on twenty- five formalin- fixed, paraffin embedded tissues blocks of AM which will be retrieved from archival files of Oral Pathology Department, Faculty of Dentistry, Mansoura University.Demographic characterization of patients (age, gender, size and site), clinical features and radiographic pictures were collected from the files of each patient. “old” and “young” subsets based on a cut-point of 60 years; however, > old age and ≤ young age. Lesions were classified as large and small on the basis of a cut-point of 5 cm. Large is more than 5 cm and ≤ 5 cm were detected as small.

Serial sections of 3µm-thickness were cut from each paraffin-embedded tissue block, placed on glass slides and were stained with

routinehematoxyline and eosin (H&E). Tissue sections of 3µm thickness were cut from the paraffin blocks, placed on Silanized (positively charged) slides, and used for immuno-histochemical staining.

The immunohistochemical staining was performed using the labeled Strept-Avidin-Biotin-Peroxidase complex system (LSAB), following manufacturer's kit manual instructions.

Tissue sections were deparaffinized in xylene for 10 minutes, rehydrated in graded series of ethanol and washed twice in phosphate-buffered saline (PBS) for 5 minutes. All sections were micro-waved with citrate buffer (pH 6.0) for 20 minutes, the slides were then left to cool at room temperature for 20 minutes. Non-specific protein binding was blocked with 10 minute exposure to 10% non-immune goat serum at room temperature. The sections were incubated with monoclonal antibody MMP-1 (anti-MMP-1 antibody, diluted 1:50) for 30 minutes at room temperature in a humid chamber. They were then rinsed 4 times with PBS. Biotinylated Goat Anti-polyvalent secondary antibody (linking reagent) was applied to each section for 10 minutes at room temperature. Subsequently sections were incubated with Streptavidin-biotin-peroxidase conjugate for another 30 minutes at room temperature. Tissue sections were washed between incubations by PBS solution 4 times. The 0.02% diaminobenzidine hydrochloride (DAB) was used as chromogen to visualize the peroxidase activity.The tissue sections were finally washed with water, counterstained by Mayer´s haematoxyline and cover slipped. Negative control slides were applied by the procedures (run parallel) with replacement of the primary antibodies by plain PBS.

The positivity of immunohistochemical staining was determined in 10 fields at 400 time magnifications for each slide and recorded. Then, the mean was calculated to determine the percentage of positive cells for each slide.

Data were tabulated, coded then analyzed using the computer program SPSS (Statistical package for social science) version 26.0 to obtain. Inter-group comparison of categorical data was performed by Fisher exact test for table (2x2) or Monte-Carlo for table (>2x2). P value < 0.05 was considered statistically significant.

Results

The age of the studied cases was ranged from 16 to 76 years, with a mean age of 31.64±11.88. However, majority of cases were demonstrated at age ranged from 25 to 40 years. Most of the studied cases were in young age (64%). The cases exhibited a slight male predilection. Cases of the present study showed a great tendency for occurance in mandible (88%) especially at posterior region (60%). The size of 15 cases (60%) was large (> 5 cm) while the remaining cases were small (≤ 5 cm).

The studied cases presented as painless swelling with buccolingual expansion leading to facial asymmetry. Few cases (2 cases) complanied from mild pain and numbness and associated with impacted third molar.

The radiographic picture of the studied cases appeared as unilocular or multilocular radiolucent lesions. Twelve cases were unilocularradiolucencies with well defined borders. Five cases of the unilocular lesions were associated with unerupted third molar, resembling dentigerous cyst. While the other 13 cases were presented as multilocularradiolucencies with soap bubble or honey comb appearance.

13 cases were conventional and 12 were unicystic. The conventional type was more frequent than the unicysic type. The most common histological variant was the follicular form (64%).The examined specimens of follicular AM showed islands of odontogenic epithelium. The follicles contained a layer of tall columnar ameloblast- like cells with reverse polarity and a central core of loosely arranged stellate reticulum- like cells. The stroma was highly collagenous in the most of cases (fig. 1). The examined specimens of plexiform AM exhibited anastomosing strands of odontogenic epithelium. These strands showed peripheral tall columnar ameloblastic- like cells with palisaded and polarized nuclei and central stellate reticulum- like cells. The examined unicystic AM cases showed ameloblastomatous proliferation confined to the cyst lining (luminal type) or at connective tissue of the cyst wall (mural type) (figs. 2). The mural type was the most frequent unicystic type (58.3%).

Statistically, Monte-Carlo test revealed a significant difference between conventional and unicystic AM cases regarding age, size, x-ray and MMP-1. Studied conventional cases were larger than unicystic cases and occasionally encountered at older age than unicystic type. Also, all conventional cases were multilocular. Conventional cases expressed MMP-1 more than unicystic. Meanwhile, there was a non significant difference betweenthem regarding gender and site (table. 1).

In the present study, MMP-1 was expressed as brownish cytoplasmic discoloration in the lesional and in the stromal cells. The reaction was moderate to intense in most of cases (80%). Conventional AM cases revealed intense immunopositive reaction to MMP-1 in both neoplastic and stromal cells (fig. 3). The unicystic luminal AM cases showed mild reaction to MMP-1detected in the odontogenic epithelial confined to the cystic lining and stromal cells in the cystic fibrous capsule (fig.4). The unicystic mural type showed moderate reaction to MMP-1 in both epithelial lining of the cyst wall and follicles of AM in fibrous capsule in addition to stromal cells.

Statistically, there was a significant difference between old & young age cases, as well as between unilocular&multilocular cases and between small& large cases regarding expression to MMP-1. The expression of MMP-1 was more prominent in old age cases, multilocular cases and large size lesions. Meanwhile, there was a non significant difference at gender and site portions.

Table (1): Association between unicystic and multicystic AMs

		Unicystic		Conventional		Total		P
		No	%	No	%	No	%	
Age	**Old**	**0**	**0.0%**	**4**	**30.8%**	**4**	**16.0%**	**<0.001***
	Young	**12**	**100.0%**	**9**	**69.2%**	**21**	**84.0%**	
Sex	**Male**	**7**	**58.3%**	**6**	**46.2%**	**13**	**52.0%**	**0.54**
	Female	**5**	**41.7%**	**7**	**53.8%**	**12**	**48.0%**	
Site	**Anterior mandible**	**4**	**33.3%**	**3**	**23.1%**	**7**	**28.0%**	**0.32**
	Posterior mandible	**8**	**66.7%**	**7**	**53.8%**	**15**	**60.0%**	
	Posterior maxilla	**0**	**0.0%**	**3**	**23.1%**	**3**	**12.0%**	
Size	**Large**	**2**	**16.7%**	**13**	**100.0%**	**15**	**60.0%**	**<0.001***
	Small	**10**	**83.3%**	**0**	**0.0%**	**10**	**40.0%**	
X-Ray	**Unilocular**	**12**	**100.0%**	**0**	**0.0%**	**12**	**48.0%**	**<0.001***
	Multilocular	**0**	**0.0%**	**13**	**100.0%**	**13**	**52.0%**	
MMP-1	**Mild**	**5**	**41.7%**	**0**	**0.0%**	**5**	**20.0%**	**<0.001***
	Moderate	**7**	**58.3%**	**0**	**0.0%**	**7**	**28.0%**	
	Intense	**0**	**0.0%**	**13**	**100.0%**	**13**	**52.0%**	

Data expressed as frequency (Number-percent)
P: Probability *: significance <0.05
Test used: Fisher exact or Monte-Carlo

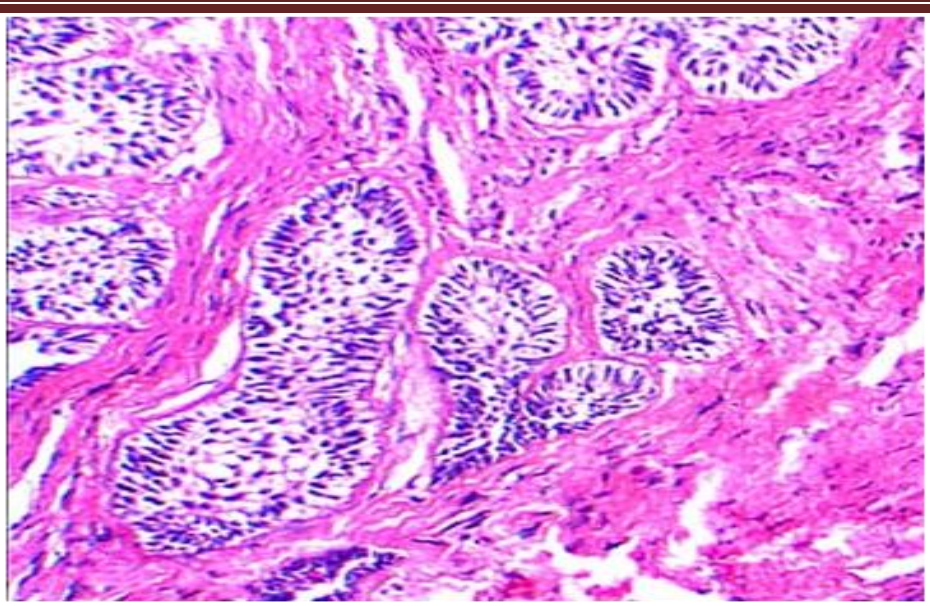


Fig. (1): Follicular AM shows peripheral arrangement of ameloblast-like cells with reverse polarity and central located stellate reticulium-like cells.

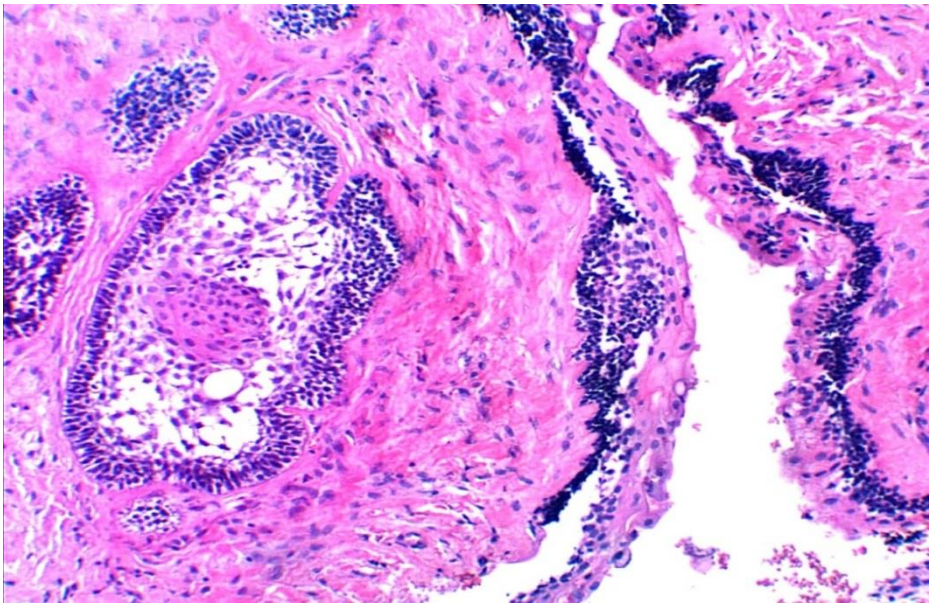


Fig. (2): Mural unicystic AM shows follicles of AM infilterated into the fibrous connective tissue capsule of cyst.

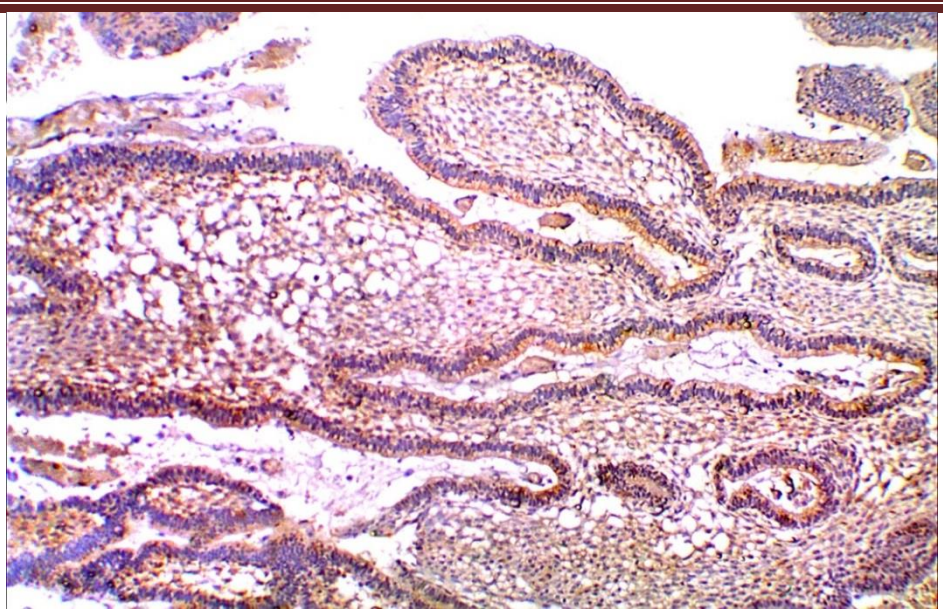


Fig. (3): Plexiform AM with large blood filled spaces shows intense immune reaction to MMP-1 within odontogenic epithelium and mild stromal elements **(LSAB-DAB).**

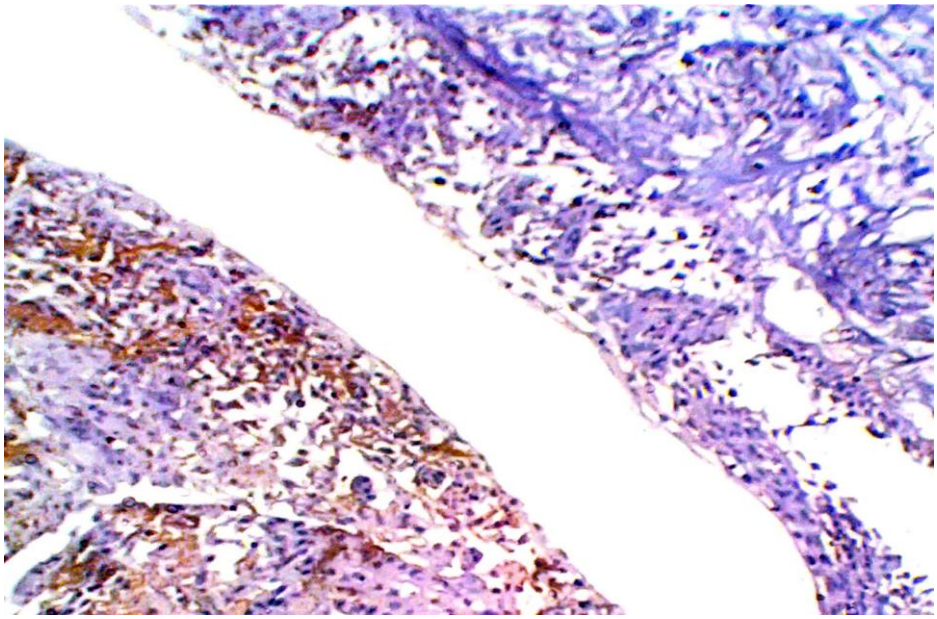


Fig. (4): Unicystic AM (luminal type) shows mild immune reaction to MMP-1 in the cytoplasm of odontogenic epithelial cells **(LSAB-DAB)**.

Discussion

Ameloblastoma among benign tumors holds a unique position by its locally destructive and invasive nature. Tumors that originate from the odontogenic apparatus or its remnants in the jaws show diverse clinical presentations, behavior and histologic patterns. [11]

In the present study, majority of cases were demonstrated at age ranged from 25 to 40 years. This coincides partially with Hertog et al., [12]Oomens et al.,[13]Yang et al. [14] and Hendra et al. [15] who reported the 3rd to 6th decades as the most affected age among their studies AM cases. This wide variation in age range of AM could be explained by FaqiNurdiansyahHendra et al. [15] who indicated that AM tends to occur at young age in developing countries. The peak incidence of AM among

their African and South American cases was in the 3rd decade, while it was the 5th and 6th decades among their European and North American cases. The diversity of age range might be due to socioeconomic factors, [15]ethnic background [16] and accelerated aging as a result of poor nutrition and reduced access to the health care system. [15] The conventional AM occurred in 3rd to 4th decades while unicystic AM affect younger age group, mainly 2nd decade of life. These findings are in agreement with Kim and Jang.,[17]Vohra et al. [18] and Rastogi. S. 2010. [19] who repoted that unicystic AMs are more commonly seen in younger patients, with 50% of cases being diagnosed during the second decade of life.

There was a slight male predilection among the cases of the present study. This is in accordance with Rastogi. S., [19]More et al.,[20]Chawla et al.,[21]Siar et al. [22] and Hendra et al. [15] Meanwhile, Costa et al. [23] reported female predominance among their studied AM cases. On the other hand, Saforaet al.[24]and Oomens et al.[13]reported higher male predilection among their cases. Furthermore, Hertog et al. [12] and Saghravanian et al. [25] reported equal male and female frequencies among their studied AM cases. No proper explanation can be provided for this variation. But, Reichart PA et al. [26]and Dhanutai K et al.[27] in their large review of 2280 cases and multicentric international study of 1289 cases, respectively, observed an almost equal male- female ratio. Hence, the variation in gender predilection among between the different studies might be attributed to the dissimilarity of the studied series. Moreover, Simon EN et al.[28] recorded variable tendancies for gender predilection among their different ethnic populations such as black and white people.

Being similar to McClary et al., [29] Yang et al., [14]Ruslin et al. [30] and Hendra et al. [15], majority of the studied AM cases were located in the mandible (88%), especially the molar-ramus area followed by maxilla (12%). In the current work, 60% of the tumors were in the posterior region and 28% in the anterior region of the mandible. This agrees with Filizzola et al. [31] and Saghravanian et al. [25] who reported that the posterior region of the mandible, was the most involved region with AMs.

The available clinical data of the present studied AM cases from their reports revealed hard bony swelling, facial asymmetry and mild pain. Most of the studied AM cases were large (> 5 cm). This is in similar to Siar et al., [32]Milman et al., [33]Saghravanian et al. [25]andIntapa C. [34] who reported that progressive and expansive growth, swelling and pain are important behavioral characteristics of AMs, causing patients to suffer from asymptomatic facial asymmetries at more advanced stages of the lesion. In contrast, Laborde.[35]reported most cases were small. This is might be due to reduced access to health care system in developing countries, AM cases might be left untreated. Therefore, large sizes causing facial disfiguration and functional problems could be reached. [36, 37]Pain could be reffered to pressure on inferior alveolar nerve. [29]

In the current study, conventional AM, radiographically, revealed multilocular radiolucency with a “soap bubble” or “honeycomb” appearance. This is at the same line with Ghandhi et al., [38]Hertog et al., [12]Milman et al. [33]and Ruslin M et al. [30] who detected classical “soap bubble” or “honeycomb” appearance.Like Kim JD et al. [39] and Hertog and Van der Wall., [40] some studied conventional AMs were associated with unerupted third molar resembling dentiderous cysts or odontogenickeratocysts. The present studied unicystic AMs presented as unilocularradiolucencies with well defined borders and some of them were associated with unerupted third molar, resembling dentigerous cyst which matches with Jwayoung Kim et al. [41] and Dave PM et al. [42] who revealed that unicystic AM is a well-defined, unilocular radiolucencyassociated with the crown of an unerupted tooth, usually a mandibular third molar resembling dentigerous cyst. On the other hand, Nigel R. Figueiredo.[43] reported multilocular radiolucent unicystic AM. This may be due to LaurèneAvril et al. [44] who explained that the radiographic pictures of such lesions varied from a unilocular to multilocular radiolucency according to the tumor type (conventional or unicystic AMs). Buccal and lingual cortical expansion with thinning of the cortical plate, irregular scalloping margins of these radiolucent lesions related to resorption of the roots of teeth adjacent to the tumor were reported which is accordant withWorth HM., [45]LaurèneAvril et al.[44] and Nigel R. Figueiredo et al. [43] who showed that radiolucency with a corticated border, and margins, which usually show irregular scalloping with root resorption. This partially agrees with Philipsen HP et al., [46]More et al. [20] and Filizzola et al. [31]Philipsen HP et al. [46] who repoted that root resorption was seen in 70% cases, with displacement of teeth also noted in 70% of our cases. Moreover, More et al. [20] using a combination of panoramic, periapical and CT radiographs found the probability of root resorption adjacent to AMs to be closer to 78.5%.In addition, Filizzola et al. [31] found root resorption present in 56% of the tumors located in close proximity with the adjacent teeth.

Statistical analysis of finding of the present study revealed a significant difference between conventional and unicystic AM cases regarding age, size and x-ray. Meanwhile, there was a non significant difference between them regarding gender and site. This is in partial agreement with Hertog et al. [12] who found that no statistically significant differences between unicystic and conventional AMs with regard to age, gender and site.

Similar to Milman et al., [33]Laborde.[35] and Nalabolu et al., [47] the histopathologic patterns of the studied AM cases were follicular and plexiform with the follicular type being more common than the plexiform type. Meanwhile, Siar et al. [22] reported that the plexiform AM was the most common type. For these authors, the quantity of tissue available for analysis has a relevant impact on the predominant histological type of ameloblastomas. Thus, it is possible that the differences seen between the present study and those by Reichart et al. [26] and Kim and Jang. [17] are, in part, associated with the quantity of material

available for microscopic evaluation. [48] Most cases of unicystic AM in the present study were mural subtype. This agrees with Hertog et al. [49] and Filizzola et al. [31] In contrast, Chawla et al. [21] and Saghravanian et al. [25] reported that most of unicystic AM cases were luminal subtype. This due tothe extent to which ameloblastomatous epithelium proliferates and penetrates the connective tissue wall of the cyst.Therefore, the scientific argument that should be investigated is whether luminal type should be considered as odontogenic cysts in future WHO classifications. [50]

The current work revealed that all the studied AM cases were MMP-1 positive. The expression of MMP-1 was observed in ameloblast and stellate reticulum- like cells and surrounding stromal cells. This resembles Medeiros.,[51]Pinherio et al., [52]Ribeiro et al., [53]Kessenbrock K et al., [54]Shen LC et al. [10] and Dutra KL et al. [55] who denoted the same results in their studies with AMs. All these authors suggested that expression of MMP-1in the tumor cells and/or surrounding stromal cells has been associated with regulation of tumor progression in ameloblastic tumors. Unlike our study, Kumamoto et al. [56] mentioned that MMP-1 was found only in stromal cells of the AMs and not in the tumor cells. Also, Ribeiro et al. [53] demonstrated MMP-1 at columnar cells on the periphery of cells of AM. These different results could be interpreted by Ribeiro et al. [53] who pointed to the temporal expression of MMP-1 depending on the needs of tumor development. Moreover, they attributed this difference to the possibility of using different clones. In addition, detection of MMP-1 in central portions of AM nests may be due to the presence of tenascin which is a substrate for MMP-1 in stellate reticulum- like cells. [51]

Our study revealed intense immunopositive reaction to MMP-1 in both neoplastic and stromal cells of conventional AMs. This is in accordance with Pinherio et al. [52] and Ribeiro et al. [53]Who reported that the expression of active forms of MMP-1in conventional AMs and suggested that these enzymes could release mitogenic factors present in bone matrix, thus increasing cell proliferation and contributing to the local invasiveness of the tumor. [52] This partially agrees with Shen LC et al. [10] who reported intense, moderate and mild immunopositive reaction to MMP-1 in both neoplastic and stromal cells. This disagrees withKumamoto et al. [56] who mentioned that the MMP-1 was expressed only in mesenchymal cells of AM demonstrating that these proteins are associated with AM tumor behavior.

In the current work, the unicystic luminal AM cases showed mild reaction to MMP-1detected in the cystic lining and stromal cells in the cystic fibrous capsule. The unicystic mural type showed moderate reaction to MMP-1 in both epithelial lining of the cyst wall and follicles of AM in fibrous capsule in addition to stromal cells. Meanwhile,Dutra KL et al. [55] reported that MMP-1 intense immunoexpression was found in unicysticAM variants which is dissimilar to our findings.

In the present study, there was higher expression of MMP-1 among conventional AMs when compared with unicystic AMs. This is in agreement with Shen LC et al. [10] who observed the same result. Meanwhile, Dutra KL et al. [55] mentioned that there was lower expression among conventional AMs when compared with unicystic type.

Conclusions: Metalloproteinase-1 (MMP-1) could be considered as a reliable marker or indicator for the local invasion, expansion and progression of AM. In addition, Stromal cells of AM are involved with the neoplastic cells in the regulation of tumor progression and expansion due to their role in degradation of matrix components. Furthermore, surgical excision of unicystic AM is more conservative than conventional AM.

gland tumors form approximately 2-5% of head and neck tumors [1,2] . Nearly 80% of salivary gland tumors occur in parotid glands. Parotid gland neoplasms include a various group subtypes [3]. Precise distinction among neoplastic and benignity is significant in planning therapeutic strategy and estimation of condition prognosis [4].

It is also significant to assure if neoplasm is intra or extra glandular and also superficial or deep to determine operative lines; so, by radiological methods aim not only in determining surgery but help in assessing additional probable relapses and catastrophes [5].

There are many radiological methods like ultrasound , computed tomography, magnetic resonance imaging and SPECT for assessment of salivary gland neoplasms[6]. MRI is the most dependable tool to determine if tumors are benign or neoplastic. MRI also still the most favorable radiological method for staging salivary gland neoplasm due to its precious soft tissue contrast& its excellent representation at different planes and superior anatomic presentation. represents the key for evaluation of neoplasm site[7] .

High-resolution multiplanar turbo spin-echo (TSE) T1, T2 and post contrast (Gadolinium) images with fat

saturation (FS) represents the key for evaluation of neoplasm site[8].

MATERIALS AND METHODS

We prospectively estimated MRI features of twenty four patients having pain and swelling in the region of

parotid , with an age ranged from twenty nine to sixty three years with an average age of fourty six year. There were fifteen females and nine males. All patients were subjected to conventional MRI examination.

Our Neck MRI exam included the following sequences: Axial T1 turbo spin echo (TSE) without Fat suppression, Axial T2 Turbo-spin echo without fat suppression, and Coronal T2 sequence with fat suppression.

The MRI features included (lesion margin well defined or ill defined, signal intensity hypo intense or hyperintense on T1, T2, homogeneity of tumors , infiltration into surrounding tissue and enhancement of the neoplasm) .

Lesion with major dimension was selected for analysis. Image analysis was done via two radiologists (reader one : with seven years; reader two: two years of experience in Head &Neck radiology) that are unaware of pathological report and research design.

Statistical Analysis: the resulting data will be statistically analysed by using x^2 test. The significance level will be set at P value less than 0.05.

RESULTS

This prospective study was conducted on 24 patients complaining of parotid tumors. Patients were referred Oncology Center of Mansoura University and Mansoura University Hospitals. Those patients underwent conventional weighted MRI examination of the parotid masses and MRI charitеria were evaluated for all cases. Two radiologists evaluated the MRI features to establish a consensus

Table (1): The different pathologic groups of the parotid tumors of the studied patients.

	Histopathology	No. of Patient 24	% 100
I)Benign Tumors	No.19		79.1%
	Pleomorphic adenoma	11	45.8%
	Warthin tumor	7	29.1%
	oncocytoma	1	4.1%
II)Malignant tumors	No. 5		20.8%
	Mucoepidermoid carcinoma	3	12.5%
	Adenoid cystic carcinoma	2	8.3%
Total No.		24	100%

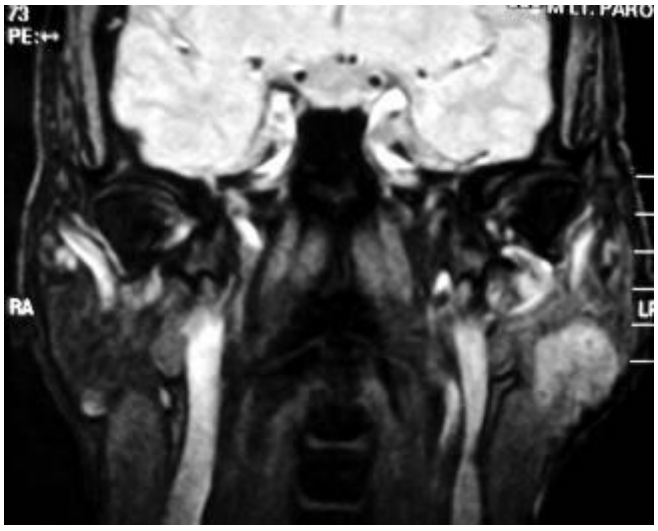
Table 2 Comparison between benign and malignant tumors regarding conventional MRI findings

MRI characters	Benign n=19	malignant n=5	Significance
Margin definition of MRI			
• Well defined	19(100%)	1(20%)	P<**0.02***
• Ill defined	0	4(80%)	

T2 intensity on MRI			
• high	16(84.2%)	0	P< **0.03***
• mixed	3(15.7%)	1(20%)	
• low	0	4(80%)	
Infiltration of surrounding			
• +ve	0	5(100%)	P<**0.001***
• -ve	19(100%)	0	

Regarding T2, signal intensity sixteen out of ninteen benign lesions showed high SI with the remaining three lesions showed mixed SI and from five malignant lesions, four lesions showed low SI, only one lesion showed mixed SI. There was statistically significant difference between benign and malignant lesions with P< 0.03.

Case 1 Female aged 63 year with LT parotid mass …. Pathological assessment show PA



DISCUSSION:-

Parotid neoplasms involve different varieties of benign and malignant subtypes. Precise discrepancy among malignancy and benignity is essential in planning of management processes and estimation of disorder outcome [9].

MRI is essential within diagnosis and assessment of different disorders within clinical practice due to benefits of many soft-tissue contrasts and nonexistence of ionizing radiation.in parotid neoplasms, MRI can identify tumor site and spread, and relation among neoplasm and CNVII [10].

The present study included twenty four patients who were classified into ninteen benign parotid tumors (representing 79.1%) and five malignant tumors (representing 20.8%) and this was in agreement with **Zajkowski, (2000**) who stated that 70-80% of tumors of salivary glands are benign[11].

In the present study, all ninteen benign lesions in our study had well defined margin and four out of five malignant lesions had ill-defined margin. There was statistically significant difference between benign and malignant lesions regarding signal intensity on T2 and margin definition. These results were in agreement with **Christe et al., (2011) and** Xu **et al., (2013)** who strongly suggested that a sharp margin was associated with a benign tumor [12,13]. Similar results reported by **Ikeda et al., (2004)** who found 11 out of 17 malignant tumors showed partially unclear or invasive margins on all MR images [14]. Our

results were in contrast to **Freling et al. (1992)** who reported that signal intensity and tumor margin were not valuable factors to predict benign or malignant disease [15].

Infiltration into deep structures was observed only in patients with malignant tumors. None of the benign tumors had infiltrative margins. Our study revealed statistically significant difference between benign and malignant tumors regarding tumor infiltration into surrounding tissues.

CONCLUSIONS:-

Therefore, it can be concluded that, MRI is the best imaging diagnostic modality for characterization of the parotid tumors.

References

1. Assili S, Fathi Kazerooni A, Aghaghazvini L, Saligheh Rad HR, Pirayesh Islamian J. Dynamic Contrast Magnetic Resonance Imaging (DCE-MRI) and Diffusion Weighted MR Imaging (DWI) for Differentiation between Benign and Malignant Salivary Gland Tumors. J Biomed Phys Eng, 2015; 5: 157–68.

2. Lee WH, Tseng TM, Hsu HT, Lee FP, Hung SH,Chen PY. Salivary gland tumors: A 20-year review of clinical diagnostic accuracy at a single center. Oncol Lett, 2014; **7**:583-7.

3. El-Naggar AK. WHO classification of tumors of salivary glands. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (eds) WHO classification of head and neck tumours, 4th edn. IARC, Lyon, 2017; p 160.

4. Takumi K, Fukukura Y, Hakamada H, Ideue J, Kumagae Y, Yoshiura T.Value of diffusion tensor imaging in differentiating malignant from benign parotid gland tumors. Eur J Radiol, 2017; 95:249–256.

5. Behrooz Davachi , **Mahrokh Imanimoghaddam, Mohamad Reza Majidi** , **Ahmad Sahebalam, Masoomeh Johari, Adineh Javadian Langaroodi etal.** Imaging Findings of Salivary Gland Tumors. J Dent Res Dent Clin Dent Prospect, 2014; 8(4) 246- 251.

6. Abdel Razek AA, Ashmalla GA, Gaballa G, Nada N. Pilot study of ultrasound. Parotid Imaging Reporting and Data System (PIRADS): inter-observer agreement. Eur J Radiol, 2015; 84:2533- 2538.

7. Celebi I, Mahmutoglu AS. Early results of real-time qualitative sono elastography in the evaluation of parotid gland masses: a study with histopathological correlation. Acta Radiol, 2013; 54:35- 41.

8. Kato H, Kanematsu M, Watanabe H, Mizuta K, Aoki M. Salivary gland tumors of the parotid gland: CT and MRI imaging findings with emphasis on intratumoral cystic components. Neuroradiology, 2014; 56:789–95.

9. Antony J, Gopalan V, Smith RA, Lam AK. Carcinoma ex pleomorphic adenoma: a comprehensive review of clinical, pathological and molecular data. Antony J Head and Neck Pathol, 2012.

10. Yerli H, Aydin E, Haberal N, Harman A, Kaskati T, Alibek S. Diagnosing common parotid tumours with magnetic resonance imaging including diffusion-weighted imaging vs fine-needle aspiration cytology: a comparative study. Dentomaxillofac Radiol, 2010; 39: 349-55.

11. Zajkowski P, Jakubowski W, Bialek EJ, Wysocki M, Osmólski A, Serafin-Król M. Pleomorphic Adenoma and Adenolymphoma in Ultrasonography. Eur J Ultrasound, 2000; 12(1): 23-29.

12. Christe A, Waldherr C, Hallett R, et al. Imaging of Parotid Tumors: Typical Lesion Characteristics in MR Imaging Improve Discrimination between Benign and Malignant Disease. Am J Neuroradiol, 2011; 32:1202-1207.

13. Xu ZF, Yong F, Yu T, et al. Different histological subtypes of parotid gland tumors: CT findings and diagnostic strategy. *World J Radiol* 2013; 5: 313-320.

14. Ikeda M, Motoori K, Hanazawa T, et al. Warthin tumor of the parotid gland: diagnostic value of MR imaging with histopathologic correlation. AJNR Am J Neuroradiol, 2004;25:1256–1262.

15. Freling NJ, Molenaar WM, Vermey A, et al. Malignant parotid tumors: clinical use of MR imaging and histologic correlation. Radiology , 1992; 185: 691-696.