Original Article

Role of mast cells and angiogenesis in different histological types of ameloblastoma

Ali Tahir, Abdul Hannan Nagi, Ehsan Ullah

Department of Morbid Anatomy and Histopathology, University of Health Sciences, Lahore, Pakistan

Objective: To study the role of mast cells and angiogenesis in different histological types of ameloblastoma.

Methodology: In this prospective study, 28 biopsies of different histological types of ameloblastoma were evaluated. Microvessels were stained with CD-34 and mast cells were counted using Toluidine blue stain.

Results: Mean age of patients was 29.71±2.544 (95% CI: 24.4934.93). The most common histological type was plexiform followed by follicular type. Mandible was more commonly involved (89.3%) than maxilla (10.7%). Mean mast cell count in all 28 cases was 6.39±0.915 and was significantly higher than normal oral mucosa (p=0.000). Mean microvessel count was 12.75±1.234 but it was not significantly higher than mean MVD of normal oral mucosa (p=0.242). The mast cell count differed significantly among different histological types of ameloblastoma

Conclusion: The mast cell density was significantly increased in ameloblastoma but the increase in mast cells did not correlate with angiogenesis in and around the tumour tissue. (Rawal Med J 2014;39: 395-398).

Key words: Mast cells, angiogenesis, ameloblastoma, microvascular density.

INTRODUCTION

Ameloblastoma is a benign but locally aggressive neoplasm of jaws derived from odontogenic epithelium. It is the most common neoplasm of jaws and this slowly growing tumor can cause large facial deformities.[1] It has three clinical types i.e. (i) Polycystic (common) ameloblastoma (ii) Unicystic ameloblastoma and (iii) Peripheral (extra-osseous) ameloblastoma.[2] This is the most common odontogenic tumor in India showing a peak occurrence in third decade.[3] It shows a predilection for mandible. A total of 22.8% of the ameloblastomas involve the whole length of one half of the mandible and some extending to the opposite side showing the aggressiveness of this tumor.[3] The ameloblastoma of posterior maxilla is most dangerous because of its proximity to vital structures and its intra-cranial extension can be lethal.[4] The duration of symptoms until first diagnosis in Asians is 3.1 years. Average size of tumor in developing countries is much larger than developed countries and females present with larger lesions than men.[5]

Mast cells are well known to be involved in allergic, inflammatory and immune reactions. In addition, they are also involved in pain, tissue damage as well as repair. More recently, they have been related to cancer and mediate their effect through release of many cytokines and chemokines, pro-angiogenic factors and via heparin release.[6,7] Their role has been studied in many malignancies such as adenomatous polyps,[8] colorectal cancers,[9] malignant melanoma,[10] oral squamous cell carcinoma,[11-14] skin dysplasias,[15] multiple myeloma[16] and many other tumors. An increased mast cell count may be the result of tumor invasiveness; on the other hand; these mast cells may elicit tumor progression.[7] The aim of this study was to evaluate mean mast cells and angiogenesis count in ameloblastoma.

METHODOLOGY

Sample size was calculated by using P.A.S.S 2008 (Power analysis and sample size software) and twenty-eight (28) formalin-fixed oral biopsies of ameloblastoma were obtained. After gross examination, paraffin embedded tissue sections were made. Patients who were immune-compromised or on radio/chemo-therapy or

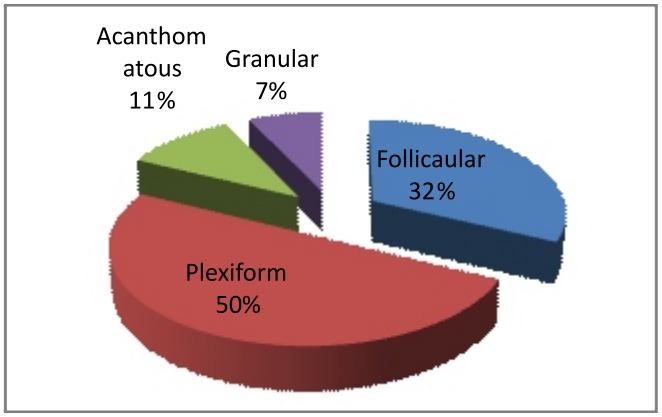
undergoing any treatment that affects mast cells were excluded. Normal tissues were obtained from non-inflamed sub-gingiva of patients undergoing minor oral surgeries with patients' consent.

The recorded clinical data included age, gender, location of tumour, clinical presentation and type of biopsy performed histopathologic data included the histological type of tumour, involvement of margins and soft tissue invasion. Following Haematoxilyn & Eosin based diagnosis, microvessel density (MVD) was assessed by using monoclonal anti-human CD-34 class II antibody. The numerical mast cell density was determined by staining the tissue slides with toluidine blue. From each paraffin block, three tissue sections each 4µm thick were cut on three different slides for haematoxylin and eosin stain, CD-34 antibody and toluidine blue stain, respectively.

RESULTS

Mean age of patients was 29.71±2.544 (95% CI: 24.49-34.93). The mean age of males with was 32.21±3.425 (95% CI: 25.02-39.41) and mean age of females was 24.44±2.67 (95% CI: 18.2830.61) (p=0.158). The most common histological type was plexiform followed by follicular type (Fig.1). Mandible was more commonly involved (89.3%) than maxilla (10.7%).

Fig. 1. Various histological types of ameloblastoma seen.



Although, the mean age of patients having acanthomatous and granular types was 23 and 41 years respectively, the difference was not statistically significant (p=0.553) (Table 1).

Table 1. Mean age among various histological types of ameloblastoma.

Histological type of ameloblastoma	Mean	N	Std. Error of Mean
Follicular	29.67	9	5.627
Plexiform	29.43	14	3.321
Acanthomatous	23.33	3	3.180
Granular	41.50	2	8.500
Total	29.71	28	2.544

Mean mast cell count was 6.39±0.915 and it was significantly higher than normal oral mucosa (p=0.000). Mean microvessel count was 12.75±1.234 but it was not significantly higher than mean MVD of normal oral mucosa (p=0.242).

Table 2. Mean MVD and Mast cell count in various histological types of ameloblastoma.

Histological type of ameloblastoma		MVD	Mast Cell Count
Follicular	Mean	12.33	4.33
	Std. Error of Mean	1.922	1.000
	No. of cases	9	9
Plexiform	Mean	13.50	6.50
	Std. Error of Mean	2.137	.930
	No. of cases	14	14
Acanthomatous	Mean	13.00	6.33
	Std. Error of Mean	1.528	1.667
	No. of cases	3	3
Granular	Mean	9.00	15.00
	Std. Error of Mean	1.000	10.000
	N	2	2
Total	Mean	12.75	6.39
	Std. Error of Mean	1.234	.915
	N	28	28

The mast cell count and MVD were not significantly correlated with each other (r=0.035, p=0.860). However, mast cell count differed significantly among different histological types of ameloblastoma (p=0.036) but MVD did not significantly differ in various histological types of ameloblastoma (p=0.846) (Table 2).

DISCUSSION

The role of inflammatory cells in malignancies has been a focus of several researchers in recent years. Mast cells exert their tumorigenic effect through

four mechanisms; (1) immunosupression (2) angiogenesis (3) degradation of extracellular matrix and (4) mitogenesis.[10] Among these, angiogenesis plays a vital role in tumor growth. In order to outgrow the size of 2mm,[3] solid tumors need oxygen supply[17] and angiogenesis is necessary to remove waste products and to provide nutrition and immune cells to the growing tumor.[18] Angiogenesis is an early event in tumorigenesis and is found in many premalignant conditions such as gastric dysplasia, carcinoma in situ of breast, atypical adenoma of colon[19] and oral leukoplakia with dysplasia.[12]

Mast cells are highly granulated cells and secrete many pro-angiogenic factors such as angiopoitin-1,[20] vascular endothelial growth factor (VEGF), bFGF,[21] MCP-4 [chymase][22] and histamine.[23] There is impressive evidence of pro-angiogenic and thus pro-tumor role of mast cells.[7] VEGF has been shown to be significantly increased in premalignant and invasive oral lesions.[24] However, in some tumors such as breast cancer, mast cells seem to play anti-tumor effects and represent a favourable prognosis,[25] whereas, in some tumours, such as non-small cell lung carcinoma (NSCLC), oral squamous cell carcinoma and basal cell carcinoma, the role of mast cells is still controversial.

Ameloblastoma arises from odontogenic epithelium and is characterised by intra-osseous growth except for the peripheral type.[26] It mimics a malignancy by its habit of invasion into the trabeculae of surrounding cancellous bone of jaws that results in its recurrence if not carefully excised beyond its radiological margin.[4] Pathogenesis of its cause and mode of expansion are still poorly understood. Little or no study has been done on the role of inflammatory mediators and angiogenesis in the expansion and invasion of this tumor.

To evaluate the role of mast cells, MVD and mast cell density were calculated in 28 cases of ameloblastoma. Our study showed a mean mast cell density of 6.39±0.915. Mast cells were significantly higher in the granular type of ameloblastoma (p=0.036). The mean MVD was 12.75±1.234. On applying spearman correlation test, it was found that mean MCD and MVD were not significantly correlated to each other. However, when compared with MCD and MVD of normal oral mucosa, it was shown that mast cells are significantly increased in ameloblastoma (p=0.020) but no such significance was seen in angiogenesis (p=0.242). It can be said that the process of neo-angiogenesis is not significantly increased in this tumor and new blood vessels formation takes place at a normal rate as in any growing tissue of the body. Mast cells certainly do not seem to cause angiogenesis in this tumor and may have invaded as inflammatory cells around the pathological tissue. Further studies with larger sample size and greater number of immune-markers are required to assert these findings.

CONCLUSION

Mast cell density was increased in ameloblastoma and was correlated with histological type of ameloblastoma. Microvessel density was not increased and mast cell density and microvessel density were not correlated with each other.

Author contributions:
Conception and design: AT, AHN, EU
Collection and assembly of data: AT
Analysis and interpretation of the data: EU, AT
Drafting of the article: AT
Critical revision of the article for important intellectual content: AHN
Statistical expertise: EU
Final approval and guarantor of the article: AHN, AT
Corresponding Author email: Ali Tahir. alitahir@live.com
Conflict of Interest: None declared
Rec. Date: Feb 5, 2014 Accept Date: Aug 4, 2014

REFERENCES

1. Cawson RA, Odell EW. Odontogenic tumours and tumour-like lesions of the jaws. In: Cawson's essentials of oral pathology and oral medicine 2008; 8th ed. Philadephia.
2. Sapp JP, Eversole LR, Wysocki GP. Odontogenic tumours. In: Contemporary Oral and Maxillofacial Pathology. 2nd ed. London, UK: Mosby; 2004
3. Sriram G, Shetty RP. Odontogenic tumour: a study of 250 cases in an Indian teaching hospital. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:14-21.
4. Gardner DG. Some current concepts on the pathology of ameloblastomas. Oral Surg Oral Med Oral Pathol 1996;82:660-9.
5. Reichart PA, Philipsen HP, Sonner S. Ameloblastoma: biological profile of 3677 cases. Eur J Cancer 1995;31:86-99.
6. Metcalfe DD. Mast cell and mastocytosis. Blood 2008;112:946-55.
7. Galinsky DST, Nechushtan H. Mast cells and cancer-no longer just basic science. Crit Rev Oncol Hematol

2008;68:115-30.
8. Gounaris E, Erdman SE, Restaino C, Gurish MF, Friend DS, Gounarin F, et al. Mast cells are an essential hematopoietic component for polyp development, Proc Natl Acad Sci U. S. A 2007;104:19977-82.
9. Fisher ER, Paik SM, Rockette H, Jones J, Caplan R, Fisher B. Prognostic significance of eosinophils and mast cells in rectal cancer: findings from the National Surgical Adjuvant Breast and Bowel Project (protocol R-01). Human Pathol 1989;20:159-63.
10. Ch'ng S, Wallis RA, Yuan L, Davis PF, Tan ST. Mast cells and cutaneous malignancies. Modern Pathol 2006;19:149-59.
11. Iamaroon A, Pongsiriwet S, Jittidecharaks S, Pattanaporn K, Prapayasatok S, Wanachantararak S. Increase of mast cells and tumor angiogenesis in oral squamous cell carcinoma. J Oral Pathol Med 2003;32:195-9.
12. Michailidou EZ, Markopoulos AK, and Antoniades DZ. Mast Cells and Angiogenesis in Oral Malignant and Premalignant Lesions. Open Dentistry J 2008;2:126-32.
13. Kalra M, Rao N, Nanda K, Rehman F, Girish KL, Tippu S, et al. The role of mast cells on angiogenesis in oral squamous cell carcinoma. Medicina Oral Patologia Oral y Cirugia Bucal 2012;17:190-6.
14. Oliveira-Neto HH, Leite AF, Costa NL, Alencar RC, Lara VS, Silva TA, et al. Decrease in mast cells in oral squamous cell carcinoma: Possible failure in the migration of these cells. Oral Oncol 2007;43:484-90.
15. Grimbaldeston MA, Finlay-Jones JJ, Hart PH. Mast cells in photodamaged skin: what is their role in skin cancer? Photochem Photobiol Sci 2006;5:177-83.
16. Ribatti D, Vacca A, Nico B, Quondamatteo F, Ria R, Minischetti M, et al. Bone marrow angiogenesis and mast cell density increase simultaneously with progression of human multiple myeloma. Br J Cancer 1999;79(34):451-5.
17. Folkman J. Tumor angiogenesis. In: Cancer Medicine 2000;5th ed:13-52.
18. Makrilia N, Lappa T, Xyla V, Nikolaidis I, Syrigos K. The role of angiogenesis in solid tumours: An overview. Eur J Intern Med 2009;20:663-71.
19. Raica M, Cimpean AM, Ribatti D. Angiogenesis in pre-malignant conditions. Eur J Cancer 2009;45:1924-34.
20. Nakayama T, Yao L, Tosato G. Mast cell-derived angiopoietin-1 plays a critical role in the growth of plasma cell tumors. J Clin Invest 2004;114:131725.
21. Esposito I, Menicagli M, Funel N, Bergmann F, Boggi U,Mosca F, et al. Inflammatory cells contribute to the generation of an angiogenic phenotype in pancreatic ductal adenocarcinoma. J Clin Pathol 2004;57:630-6.
22. Muramatsu M, Katada J, Hattori M, Hayashi I, Majima M. Chymase mediates mast cell-induced angiogenesis in hamster sponge granulomas. Eur J Pharmacol 2000;402:181-91.
23. Sorbo J, Jakobsson A, Norrby K. Mast cell histamine is angiogenic through receptors for histamine1 and histamine 2. Int J Exp Pathol 1994;75:43-50.
24. Johnstone S, Logan RM. Expression of vascular endothelial growth factor (VEGF) in normal oral mucosa, oral dysplasia and oral squamous cell carcinoma. Int J Oral Maxillofac Surg 2007;36:263-6.
25. Rajput AB, Turbin DA, Cheang MC. Stromal Mast cells in invasive breast cancer are a marker of favourable prognosis: a study of 4,444 cases. Breast Cancer Res Treat 2008;107:249-57.
26. Kramer IRH, Pindborg JJ, Shear M. Histological typing of odontogenic tumours. The World Health Organization: Histological typing of odontogenic tumors: an introduction to the second edition. J Dent Assoc S Afr 1992;47:208-10.