

ORIGINAL ARTICLE

Histological Pattern of Ameloblastoma in Affiliated Hospitals of Oral and Maxillofacial Surgery Department Faculty of Dental Medicine Airlangga University

Widhi Satrio Nugroho¹, Stanley Santosa Kamadjaja¹, Coen Pramono², David Buntoro Kamadjaja²

¹ Oral Maxillofacial Surgery Program, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia

² Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Introduction: Ameloblastoma is a benign tumor. Clinically there are no distinct differences from the types of ameloblastoma. The correlation of clinical, radiological, and histological features is expected to provide a better understanding of this disease. This study to describe the distribution of the histopathological type of mandibular ameloblastoma in patients post mandibular resection. **Methods:** This study was a retrospective study with a descriptive method using total sampling of the medical records of mandibular ameloblastoma patients who had undergone mandibular resection and with viable postoperative histopathological data in the hospital network of the Department of Oral and Maxillofacial Surgery, Airlangga University, Surabaya in 2015-2019. **Results:** 22 data samples were obtained. The histopathological examination of all subtypes, the most common type of pattern was 14 cases with mixed type histological patterns, the most common combination was follicular & plexiform type in the third decade of life, and the single histology subtype most commonly found was the follicular type. No statistically significant differences were found between the histopathological subtypes, mixed type of ameloblastomas and the demographical and clinical parameters, but significant results were found between mixed type and tumor location **Conclusion:** The most common histologic type is mixed type with a combination of follicular and plexiform types, but it is recommended to use immunohistochemistry examination to provide a better understanding.

Keywords: Ameloblastoma, Mandibular Resection, Histopathology, SDG3 Good Health and Well-Being

Corresponding Author:

Widhi Satrio Nugroho, PhD

Email: widhi.satrio.nugroho-2017@fkg.unair.ac.id

INTRODUCTION

Various theories about the growth etiology of ameloblastoma have been proposed (6), stated the possible pathogenesis of ameloblastoma growth could be from (a) remaining cells of the enamel organ, either from the remaining dental lamina or sheath of Hertwig, (b) developing enamel organs, (c) basal cells from the forming jaw epithelium, (d) heterotropic epithelium from other parts of the body, especially the pituitary gland, (e) epithelium from cysts, especially dentigerous cysts, (f) Rest of Serres epithelial cells in the gingiva, (g) basal cells from the oral mucosa, the results of basal cell epithelium invagination to the developing jaw bone (6). Based on WHO classification of ameloblastoma histological subtype (2017) ameloblastoma is divided into 6 subtypes (a) Follicular type, (b) Plexiform type, (c) Acanthomatous type, (d) Basal cell ameloblastoma, (e) Granular cell ameloblastoma, (f) Desmoplastic type. The most common histological features found are the follicular and plexiform patterns (11).

Clinical symptoms and radiological features of ameloblastoma do not show specific features, whereas a correct diagnosis is important before performing any surgical procedures (9,10). The most common problem encountered in treating patients with ameloblastoma is the determination of the appropriate and adequate therapy and reconstruction after mandibular resection. The success of therapy also depends on the outcome of the histopathological examination to confirm the appropriate follow-up and its evaluation.

Up to recently, no data exists regarding the histopathological type of mandibular ameloblastoma post resection in Surabaya hospitals with no oral and maxillofacial surgery specialist services and education. Thus research on the distribution of ameloblastoma types is needed to determine the distribution of these data and their relationship with other factors.

MATERIALS AND METHODS

This study used a retrospective study with a cross sectional study design by examining the medical records and histopathological readings of ameloblastoma patients who had undergone mandibular resection

at network hospitals in 2015-2019. The data of the patients studied consisted of age, gender, duration of tumor growth, patient complaints, previous surgery history, tumor location, radiological features, definitive therapy, and postoperative histopathology results. The data was then processed and presented descriptively and the results were statistically analysed using the SPSS 16.0, Chi square test.

This study was approved by Research Ethics Committee, Universitas Airlangga Faculty of Dental Medicine No. 732/HRECCFODM/XI/2019.

RESULTS

Table I showed that there were 22 patients with equal percentage of sex between men and women (50%), and the average age was 34.5 years old. The patients all presented with a complaint of 100% enlargement of the jaw and 13 patients (59.09%) complained of tooth mobility in the area involved with the tumor.

Tumor growth was 2 years or less in 16 patients (72.73%). The history of treatment before the appearance of the

tumor was extraction of teeth in 2 patients (9.09%) that were involved with the tumor and removal of cysts in 2 patients (9.09%). As a general rule, unless removal is contraindicated, all impacted teeth should be extracted by means of a process known as odontectomy (13). Radiologically, 14 patients (68.18%) presented a multilocular appearance and 8 patients (31.82%) with unilocular appearance of the mandible. Meanwhile, 2 patients (14.29%) had a honeycomb appearance and 12 patients (85.71%) had a soap bubble appearance. The location of the tumor was highest in the right mandible in 10 patients (45.45%), and involving the mandible corpus in 20 patients (90.91%). Hemimandibulectomy was the most common case found in 15 patients (68.18%) along with reconstruction with or without grafts. Autografts are the best substitute for bone with defects, although there are several weaknesses of autograft (11).

The results of histopathological examination revealed that the most common type was mixed type ameloblastoma in 14 patients (63.64%) with various combinations, the highest combination being follicular & plexiform type in 9 patients (64.29%) in the third decade, while the single type most commonly found was follicular

Table I: Characteristic Patient

Patient Characteristic	n	%	Patient Characteristic	n	%
Genders			Tumor site		
• Males	11	50	• Mandible dextra	10	45.45
• Females	11	50	• Mandible sinistra	9	40.91
Ages			• Anterior mandible	3	13.46
• <20- years	4	18.18	Anatomical tumor site		
• 21-30 years	4	18.18	• Corpus	20	90.91
• 31-40 years	8	36.36	• Angle	13	59.09
• 41-50 years	2	9.09	• Ramus	12	54.55
• 51-60 years	3	13.64	• Symphysial	6	27.27
• > 60 years	1	4.55	Surgical intervention		
Onset			• Hemimandibulectomi	15	68.18
• < 2 years	16	72.73	• Segmental resection	6	27.27
• > 2 years	6	27.27	• Marginal resection	1	4.55
Clinical features			Reconstruction plate		
• Swelling	22	100	• Plate rconstruction	17	77.27
• Mobility tooth	13	59.09	• Mini plate	4	18.18
• Parastesia	3	13.64	• Combination	1	4.55
Previous treatment history			Autogenous graft (non vascularized bone graft)		
• Tooth extraction	2	9.09	• Costochondral	9	40.91
• dredging	1	4.55	• Costae	4	18.18
• Drainage incision	1	4.55	• Crista illaca	5	22.73
• Cyst removal	2	9.09	Histopathological type		
• No treatment	15	68.18	• Follicular type	4	18.18
Radiographic appreance			• Plexiform type	3	13.64
• Multilocular	14	63.63	• Mixed type	14	63.64
• Unilokular	8	36.36	• Ameloblastic carcinoma	1	4.55
Radiographic multilocular appreance			Mixed type distribution		
• Soapbubble	12	85.71	• Folicular+Plexiform+Acanthomatous	2	15.38
• Honeycomb	8	14.29	• Folicular+Plexiform	9	64.29
			• Desmoplastix+Acanthomatous	1	7.69
			• Plexiformed+Desmoplastic	1	7.69
			• Plexiformed+Acanthomatous	1	7.69

type. The complete data can be seen in Table I. The histology subtype ameloblastoma was then observed in distribution by age and genders group with the most cases was mixed type in the third decade age group of 5 patients, and the same number of men and women in the mixed type. No statistically significant differences were found between subtype ameloblastomas with regard to age and gender ($p=0.643$ and $p=0.187$) (Table II). The most common combination was follicular-plexiform in 3 patients in the second and third decade age groups and most commonly found in men, as many as 5 patients. No statistically significant differences were found between mixed type ameloblastomas with regard to age and gender ($p=0.313$ and $p=0.539$) (Table III). Based on the location of the classification modification Sriram and Shetty (2008) discovered the highest positions on the side of class 6 as much as 6 patients (40.90%), besides that mixed types were found the most in class 6, with statistically significant between mixed type ameloblastomas and tumor location ($p=0.040$) (Table IV).

Table II: Histological review correlation with patients ages dan genders

	Histological Review				P Value
	Follicular N(4)/%	Plexiform N(3)/%	Mixed N(14)/%	Ameloblastic carcinoma N(1)/%	
Ages					0.643
<20- years	0/0	2/66.6	3/21.4	0/0	
21-30 years	2/50	1/33.3	3/21.4	0/0	
31-40 years	1/25	0/0	5/35.7	1/100	
41-50 years	1/25	0/0	1/7.14	0/0	
51-60 years	0/0	0/0	2/14.2	0/0	
> 60 years	1/25	0/0	0/0	0/0	
Genders					0.187
Male	1/25	2/66.6	7/50	1/100	
Female	3/75	1/33.3	7/50	0/0	

Table III: Histological mixed type review correlation with patients ages dan genders

	Histological Review					P Value
	Follicular Plexiform Acanthomatous N(2)/%	Follicular Plexiform N(9)/%	Desmoplastic Acanthomatous N(1)/%	Plexiform Desmoplastic N(1)/%	Plexiform Acanthomatous N(1)/%	
Agess						0.313
<20- years	0/0	2/22.2	0/0	1/100	0/0	
21-30 years	0/0	3/33.3	0/0	0/0	0/0	
31-40 years	1/50	3/33.3	0/0	0/0	1/100	
41-50 years	1/50	0/0	0/0	0/0	0/0	
51-60 years	0/0	1/11.1	1/100	0/0	0/0	
> 60 years	0/0	0/0	0/0	0/0	0/0	
Genders						0.539
Male	1/50	5/55.5	0/0	0/0	1/100	
Female	1/50	4/44.4	1/100	1/100	0/0	

Table IV: Shriram and shetty classification (2008) correlation with histological review pattern

	Tumor Location. Sriram and Shetty (2008)						P Value
	Class 1 N(3)/%	Class 2 N(5)/%	Class 3 N(0)/%	Class 4 N(1)/%	Class 5 N(4)%	Class 6 N(9)%	
Histological review							
Mixed Type	2/66,6	2/40	1/100	1/100	3/75	6/66,6	0.040
Single Type	1/33,3	3/60	0/0	0/0	1/25	3/33,3	0.524

DISCUSSION

Ameloblastoma is an odontogenic epithelial neoplasm, particularly originating from enamel organ type which has not yet evolved into hard tissue form (5). The classification of ameloblastoma was divided into two main categories based on WHO in 2017 into: clinical features which were classified into 4 major types: (a) conventional, (b) peripheral, (c) unicystic, (d) metastasizing ameloblastomas; 6 histopathological types, such as: (a) follicular, (b) plexiform, (c) acanthomatous, (d) basal cell ameloblastomas, (e) desmoplastic, and (f) granular cell (12).

According to this study, there were 22 patients with mandibular ameloblastoma who received mandible resection therapies with or without grafts. The amount of patients in each gender is equal, with 11 patients of each gender (50%), in contrast with Ruslin et al. (2017) which stated that demographically, the prevalence of ameloblastoma in females was higher than males in Indonesia, with 35 (62.5%) and 21 (37.5%) patients, respectively. Ameloblastoma was also found frequently in the elderly, particularly in 3rd and 4th decades of life. In our patients, there were 8 patients in the 3rd decades of life and 14 patients above 30 years old. This finding was consistent with a previous study by Reichert et al. in 1995 and Olusanya (7).

This investigation classified patients based on histological subtypes of: (a) follicular, (b) plexiform, (c) acanthomatous, (d) basal cell, (e) granular cell, (f) desmoplastic, (g) mixed, and (h) ameloblastic carcinoma. Our study discovered that most of cases were the subtype mixed type consisting of 14 patients (63.64%) with the most combination being the follicular-plexiform type, with total of 9 patients (64.29%). Mixed type ameloblastoma with follicular-plexiform combination form is categorized into the histological description of solid/multicystic ameloblastoma being one of most common combination. Effiom (1), stated that both histological patterns may arise along with multicystic ameloblastoma and based on age predilection, it was consistent with the finding that the tumor started to present clinical signs and symptoms thus the patient started to be aware and seek for treatment starting 36 years old of age.

Based on mandibular anatomy, the most common location was found in mandible corpus with 20 patients (90.91%). According to the tumor distribution which was based on location on the mandible using Modification of Sriram and Shetty Classification (2008), we found that the most common case was Class 6 with 9 patients (40.90%). Histologically, of 14 patients with mixed-type subtype, Class 6 was the most common, followed by Class 5, with follicular-plexiform-acanthomatous type with 6 and 3 cases, respectively, also statistically significant. This finding is in accordance with Hendra (2) that these patient datas matches with global demographic data, the incidence of ameloblastoma, which is mostly found in the posterior segment of the mandible and the ascending ramus, and lesser in the medial part.

In the mixed type of desmoplastic-acanthomatous combination subtypes, plexiform-desmoplastic is included in the hybrid ameloblastoma category because of a combination of one or more histological patterns of ameloblastoma involving the desmoplastic subtype. These tumors are relatively rare and only comprise of 4–13% of the total number of ameloblastomas. The type of ameloblastoma that is commonly found is the conventional type (follicular and plexiform types), about 91% of all ameloblastoma cases (1).

Li (3) stated that in their research to examine the proliferative ability and prognosis of ameloblastoma based on radiographic limits using IHC examination, ameloblastoma with radiographic borders that are not clear, presents a high expression of Ki-67 which can be one of the parameters that can relate prognosis to radiographs and IHC.

This research can be continued with the examination of tumor markers using immunohistochemical methods to obtain the character of ameloblastoma aggressiveness which has the potential to be used as a basis for making recommendations for standard operating procedures

(SOP) in patients with mandibular ameloblastoma in the field of Oral & Maxillofacial Surgery.

CONCLUSION

From the result of the study it is found that the tumors are most prevalent at fourth decade, equally found in both sexes, the most common histology is mixed type with combined follicular - plexiform type being the most prevalent, and that the follicular type being the most common single type lesions. It is also found that the results of our study are in accordance with many similar studies. Molecular study is expected to provide a better understanding of the biological characteristics of ameloblastoma as a means for diagnosis confirmation and treatment monitoring

REFERENCES

1. Effiom, O. A., Ogundana, O. M., Akinshipo, A. O., Akintoye, S. O. Ameloblastoma: Current etiopathological concepts and management. *Oral Diseases* 2018, 24(3), 307–316.
2. Hendra FN, Van Cann EM, Helder MN, Ruslin M, de Visccher JG, Forouzanfar T, et al. Global incidence and profile of ameloblastoma: a systematic review and meta-analysis. *Wiley Oral Diseases* 2019: 1-10.
3. Li Y, Han B, Li LJ. Prognostic and proliferative evaluation of ameloblastoma based on radiographic boundary. *Int J Oral Sci* 2012; 4: 30– 33.
4. Eko Wicaksono Subagio, David B. Kamadjaja, Dianiza Afikaningtyas, ZefryZainal Abidin, Pratiwi Soesilowati, Coen Pramono D. Early healing phase in rat's calvarial critical-size defect after implantation of bovine cortical membrane. 2018.
5. Nakamura N, Mitsuyasu T, Higuchi Y, Sandra F, Ohishi M. Growth characteristics of ameloblastoma involving the inferior alveolar nerve: A clinical and histopathologic study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001;91:557–62.
6. Neville, BW, Damm, Douglas D, dkk. *Oral and Maxillofacial Surgery.* 2nd ed. Philadelphia; W.B. Saunders Company; 2002: p. 611-619
7. Olusanya AA, Adisa AO, Lawal AO, Arotiba JT (2013). Gross surgical features and treatment outcome of ameloblastoma at a Nigerian tertiary hospital. *Afr J Med Med Sci* 42:59–64.
8. Sriram G, Shetty RP: Odontogenic tumors: a study of 250 cases in an Indian teaching hospital. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; 105: e14
9. Saka Winias. The potential combination of PLDSCs with acemannan in chitosan-composites scaffold for regeneration in defect Ameloblastoma. *Biochemical and Cellular Archives.* 2020.
10. Saka Winias. Combination of dental follicle stem cells and nanocomposite fibrous scaffold for regeneration of post operative bone defect

Ameloblastoma. *Biochemical and Cellular Archives*. 2020

11. Scheper MA, Duarte EC, Intapa C, Zhang M, Nascimento LM, Almeida TP, et al. Expression of midkine in ameloblastomas and its correlation with clinicopathologic parameters. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;114:497- 502.
12. Humidat, A. K. M., Kamadjaja, D. B., Bianto, C., Rasyida, A. Z., Purwati, & Harijadi, A. Effect of freeze-dried bovine bone xenograft on tumor necrosis factor-alpha secretion in human peripheral blood mononuclear cells. *Asian Journal of Microbiology, Biotechnology and Environmental Sciences* 2018, 20(December), S88–S92.
13. Wright JM, Vered M. Update from the 4th edition of the World Health Organization classification of head and neck Tumours: odontogenic and maxillofacial bone tumors. *Head Neck Pathol* 2017; 11:68–7.
14. Rasyida, A. Z., Rizqiawan, A. Considerations in performing odontectomy under general anesthesia: case series. *Dental Journal (Majalah Kedokteran Gigi)* 2018, 51(4): 185.