Original Article

Intraosseous jaw lesions: A 25-year experience

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Abstract

Context: Jaw bones can be afflicted by to a diverse group of lesions ranging from developmental, reactive/inflammatory, cystic lesions to tumors and tumor-like lesions

Objectives: The objective of this study is to determine the relative frequency, demographic and pathologic profiles of patients with intraosseous jaw lesions from Thailand.

Subjects and Methods: Biopsy records from 1995 to 2019 were reviewed. Age, gender and location of the lesions were collected from the biopsy records. Data were analyzed by appropriate statistics using the IBM SPSS software version 22.0.

Results: From 23,344 accessioned cases, 7382 cases (31.62%) were encountered within the jaw bones. Age of the participants ranged from 1 to 96 years with the mean ± standard deviation = 36.05 ± 17.80 years. Pediatric participants (aged ≤16 years) comprised 13.80% of all the participants, whereas the geriatric ones (aged ≥65 years) accounted for 7.55%. The male-to-female ratio was 0.89:1. The majority of lesions were observed in the mandible. The most prevalent intra-osseous jaw lesion was radicular cyst followed by dentigerous cyst and ameloblastoma. The most common malignant tumor was osteosarcoma followed by ameloblastic carcinoma and lymphoma. Among the pediatric participants, dentigerous cyst was the most prevalent jaw lesion, while that in the geriatric participants was radicular cyst.

Conclusions: This is the largest study on intra-osseous jaw lesions encompassing several pathological entities ever conducted from Thailand. It thus provides an invaluable database for clinicians to formulate a differential diagnosis as well as for the pathologists to render the final diagnosis. The results of this study are in accordance with previous studies in general.

Keywords: Demographic, intra-osseous jaw lesions, pathological, relative frequency, Thailand

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INTRODUCTION

Maxilla and mandible constitute major bones of the oral cavity with important structural, protective, masticatory as well as esthetic functions. These bones can be afflicted by a diverse group of lesions ranging from developmental, reactive/inflammatory, cystic lesions to tumors, and tumor-like (TTL) lesions. Some of these lesions are unique in that they arise exclusively within this anatomical region and not encountered anywhere else in the body such as odontogenic cysts and odontogenic tumors.[1]

Since the first histological typing of odontogenic tumors, jaw cysts and allied lesions published in 1971, there have been several modifications in 1992, 2005 and the latest one

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in 2017 due to the better understanding of the nature and biologic behavior of these jaw lesions. In the 4th Edition of the World Health Organization Classification of Head and Neck tumors, odontogenic keratocyst and calcifying odontogenic cyst were reclassified as a cyst. In addition, orthokeratinized odontogenic cyst was also recognised as a separate entity rather than being regarded as a variant of the odontogenic keratocyst. New entities such as sclerosing odontogenic carcinoma and primordial odontogenic tumor were added. On the contrary, ameloblastic fibro-dentinoma, ameloblastic fibro-odontoma and odontoameloblastoma were removed. Ossifying fibroma and osseous dysplasia were renamed cemento-ossifying fibroma and cemento-osseous dysplasia, respectively.[2,3]

There have been numerous studies on the intra-osseous jaw lesions, but most of them focused on the specific groups of lesions such as odontogenic or nonodontogenic cysts,[1,4-10] odontogenic or nonodontogenic tumors[11-14] or individual cyst[15] and tumor,[16] while others are based upon specific groups such as pediatric patients[17-19] or patients in the specific geographical areas.[5-7,20-24] The relative frequency of the intra-osseous jaw lesions differs since demographic, cultural, ethnic and geographical differences do exist. The most prevalent pathologic entity in a particular region may not hold true in another region. Thus, extraporating data from other geographical regions may not be applicable to a particular region. There has been limited number of studies encompassing all pathological entities within the jaw bones from Thailand. The objectives of the present study were to determine the relative frequency, demographic and pathologic profiles of the patients with intra-osseous jaw lesions from Thailand.

SUBJECTS AND METHODS

This retrospective study was approved by the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University (No. 058/2019 approved on July 05, 2019). Biopsy records of the Department of Oral Pathology, Faculty of Dentistry, Chulalongkorn University during 1995–2019 were reviewed.

Inclusion criteria

All lesions from the maxilla and the mandible diagnosed within the aforementioned period.

Exclusion criteria

Soft-tissue lesions causing bone erosion were excluded from this study.

Age and gender of the participants were retrieved from the biopsy records. Pediatric participants were defined as individuals aged 16 and below, whereas geriatric participants were defined as those aged 65 years and above. Regarding the location of the lesions, each jaw was divided into four regions, namely anterior, anterior-posterior, posterior regions and maxilla or mandible not otherwise specified and a combination of maxilla and mandible. Specimens taken from maxilla or mandible without specific anatomical location were designated as maxilla or mandible not otherwise specified. In the context of incisional biopsies and surgical specimens as well as the recurrent lesions, only one diagnosis was collected into this study. Lesions were reclassified according to the 4th Edition of the World Health Organization Classification of Head and Neck Tumors.[3] Lesions were divided into three groups. Groups I: Developmental/reactive/inflammatory (DRI) group, Group II: Cystic group and Group III: TTL group. Due to the lack of sufficient clinical history and radiographic data for some of the fibro-osseous lesions, some of these lesions were diagnosed with just fibro-osseous lesions. Similarly, any cyst which lacked sufficient clinical, radiographic information or pathognomonic histopathological features was classified as cyst not otherwise specified.

Statistical analysis

Data analysis was conducted by the descriptive statistics. The categorical data were presented in frequencies and percentage. The continuous data were presented in means and standard deviation (SD). The associations between lesion groups and each categorical independent variable (age range, sex and locations) were analyzed using the Chi-square test, whereas associations between lesion groups and continuous independent variable (age) were analyzed using Welch one-way analysis of variance followed by Games Howell *post hoc* analysis. All analyses were performed using SPSS Software version 22.0 (IBM Inc., Chicago, IL, USA). $P < 0.05$ indicated statistically significant difference.

RESULTS

Of the total of 23,344 accessioned cases, 7382 cases (31.62%) were encountered within the jaw bones. The age of the participants ranged from 1 to 96 years with the mean ± SD = 36.05 ± 17.80 years. The majority of the participants (73.33%) were in the 2nd to the 5th decades of life. Pediatric participants aged 16 and below accounted for 13.80% of all the participants, whereas geriatric participants aged 65 years and above accounted for 7.55% of all the participants. Three thousand eight hundred and ninety-six participants (52.78%) were female, whereas 3,486

participants (47.22%) were male. The male: female ratio was 0.89:1. In the pediatric participants, male participants slightly outnumbered female participants with the male: female ratio = 1.14:1. In the geriatric participants, female participants slightly outnumbered male participants with a male: female ratio = 0.94:1.

Regarding the anatomical distribution of the lesions, the majority of the lesions were discovered in the mandible (59.04%), especially the posterior part, angle, ascending ramus and condyle (44.09%), whereas 40.69% of the lesions were found in the maxilla. There were only 19 cases (0.26%) with lesions in both the maxilla and the mandible.

Table 1 shows the distributions and associations between the lesion groups and independent variables including age ($P < 0.001$), age group ($P < 0.001$), gender ($P < 0.001$) and location ($P < 0.001$).

Overall, the most prevalent intraosseous jaw lesion was radicular cyst followed in the descending order of frequency by dentigerous cyst and ameloblastoma [Table 2]. For the pediatric participants, the most common intra-osseous jaw lesion was dentigerous cyst followed by ameloblastoma and odontogenic keratocyst, while the most frequent one in the geriatric participants was radicular cyst followed by osteomyelitis and dentigerous cyst.

The DRI and the TTL groups elicited a female predominance ($P < 0.001$ and $P < 0.001$, respectively), while the cystic group revealed a male predilection ($P < 0.001$). The mean age of the participants in the DRI group was statistically higher than those in the cystic and the TTL groups, respectively ($P < 0.001$). The DRI group showed the most frequent proportion in the 6th decade of life than others ($P < 0.001$), whereas the TTL groups demonstrated the highest proportion in the 3rd decade of life than others ($P = 0.001$). The cystic group also showed the highest proportion in the 3rd decade of life, but there was no statistically significant difference from others ($P = 0.751$). The DRI and the TTL groups elicited a female predominance, while the cystic group revealed a slight male predilection.

The DRI group demonstrated that the posterior part of the mandible was the site of predilection (40.76%). The cystic and the TTL groups also showed that the posterior part of the mandible as the site of predilection (41.37% and 51.30%, respectively). Both the pediatric and the geriatric participants had the predilection site in the posterior part of the mandible (40.98% and 42.19%, respectively) followed by the anterior part of the maxilla (24.61% and 17.77%, respectively). All the lesion groups showed statistically higher proportion in the posterior part of the mandible than in other sites ($P = 0.046$, $P < 0.001$ and $P < 0.001$, respectively).

Table 1: The distribution and association between the lesion groups and independent variables

Variables	Group I: Developmental/reactive/inflammatory group	Group II: Cystic group	Group III: TTL group	*P*
Age, mean±SD[a]	44.59±18.14	35.75±17.61[c]	33.48±17.12[c, d]	<0.001
Age group, *n* (%)[b]				
0–9	10 (1.27)	131 (2.9)	53 (2.54)	<0.001
10–19	59 (7.52)	783 (17.35)	439 (21.07)	
20–29	111 (14.14)	991 (21.96)	510 (24.47)	
30–39	144 (18.34)	866 (19.19)	388 (18.62)	
40–49	129 (16.43)	702 (15.56)	291 (13.96)	
50–59	151 (19.24)	527 (11.68)	221 (10.60)	
60–69	118 (15.03)	324 (7.18)	117 (5.61)	
70–79	42 (5.35)	151 (3.35)	49 (2.35)	
80–89	19 (2.42)	31 (0.69)	16 (0.77)	
90–99	2 (0.25)	7 (0.16)	0 (0)	
Gender, *n* (%)[b]				
Male	288 (36.69)	2310 (51.19)	888 (42.61)	<0.001
Female	497 (63.31)	2203 (48.81)	1196 (57.39)	
Location, *n* (%)[b]				
Anterior maxilla	246 (31.34)	1250 (27.70)	169 (8.11)	<0.001
Posterior maxilla	116 (14.78)	523 (11.59)	203 (9.74)	
Anterior-posterior maxilla	13 (1.66)	305 (6.76)	103 (4.94)	
Maxilla, NOS	9 (1.15)	42 (0.93)	25 (1.20)	
Anterior mandible	55 (7.01)	274 (6.07)	195 (9.36)	
Posterior mandible	320 (40.76)	1867 (41.37)	1069 (51.30)	
Anterior-posterior mandible	19 (2.42)	223 (4.94)	284 (13.63)	
Mandible, NOS	7 (2.42)	14 (0.31)	32 (1.54)	
Maxilla and mandible	0(0)	15 (0.33)	4 (0.19)	

[a]Differences among lesion groups were analyzed using Welch one-way ANOVA followed by Games Howell *post hoc* analysis, [b]Differences among lesion groups were analyzed using the Chi-square test, [c]A significant difference from Groups I: Developmental/reactive/inflammatory group at $P<0.001$, [d]A significant difference from Group II: Cystic group at $P<0.001$. NOS: Not otherwise specified; SD: Standard deviation; TTL: Tumors and tumor-like

Table 2: Top 10 most common lesions according to age, gender, and site of predilection

Pathological diagnosis	*n* (%)	Mean age±SD	Male: female ratio	Site of predilection
Radicular cyst	1419 (19.22)	40.37±16.22	0.96:1	Anterior maxilla
Dentigerous cyst	1351 (18.30)	31.66±17.83	1.18:1	Posterior mandible
Ameloblastona	1003 (13.59)	36.61±16.55	1.04:1	Posterior mandible
Odontogenic keratocyst	755 (10.23)	34.37±17.65	1.09:1	Posterior mandible
Cyst not otherwise specified	534 (7.23)	35.42±17.06	1.09:1	Posterior mandible
Periapical granuloma	361 (4.98)	41.43±14.60	0.58:1	Anterior maxilla
Osteomyelitis	315 (4.27)	48.45±20.88	0.53:1	Posterior mandible
Odontoma	256 (3.47)	23.20±13.19	0.65:1	Posterior mandible
Residual cyst	144 (1.95)	44.97±16.45	1.18:1	Anterior maxilla
Unicystic ameloblastoma	133 (1.80)	24.86±12.12	0.82:1	Posterior mandible

SD: Standard deviation

The DRI group accounted for 10.62% of the intra-osseous jaw lesions and periapical granuloma was the most prevalent lesion followed in the descending order of frequency by osteomyelitis and periapical abscess. The cystic group comprised 61.15% of the intra-osseous jaw lesions. Odontogenic cyst constituted 96.73% of all the cysts after excluding cysts not otherwise specified and radicular cyst was the most frequent odontogenic cyst followed in the descending order of frequency by dentigerous cyst and odontogenic keratocyst, while the most common nonodontogenic cyst in the present study was nasopalatine duct cyst. The relative frequencies of odontogenic cysts and tumors are shown in Supplementary Table 1. The TTL group constituted 28.23% of the intra-osseous jaw lesions. Odontogenic tumors accounted for 83.40% of the TTL group and ameloblastoma was the most prevalent lesion in the odontogenic tumor group followed in the descending order of frequency by odontoma and unicystic ameloblastoma. Nonodontogenic tumors comprised 6.86% of the TTL group and osteoid osteoma was the most frequent lesion followed in the descending order of frequency by osteosarcoma and lymphoma. The most common tumor-like condition in the present study was fibrous dysplasia followed in the descending order of frequency by cemento-osseous dysplasia and central giant cell granuloma.

There were 113 malignant tumors which constituted 0.48% of all accessioned cases and 1.53% of the intra-osseous jaw lesions. Of these, 76 cases (67.26%) were nonodontogenic in origin. The most common malignant tumor was osteosarcoma followed by ameloblastic carcinoma and lymphoma, respectively. The most prevalent malignant odontogenic tumor was ameloblastic carcinoma.

DISCUSSION

The present study represents the largest series of intra-osseous jaw lesions from Thailand ever reported in the English language literature. However, it is somewhat difficult to compare the findings of the present study with the previous ones due to different classifications and inclusion criteria used. Most of the previous studies focused on the specific groups of lesions such as odontogenic or nonodontogenic cysts,[1,4-10] odontogenic or nonodontogenic tumors[11-14] or individual cyst[15] and tumor,[16] while others on the specific groups such as pediatric participants[17-19] or participants in the specific geographical areas.[5-7,20-24]

The mean age of the participants in the present study was 36.05 years which is comparable to those of previous studies,[8,21,24-27] but higher than 24.59 years by Silva *et al*.[23] and lower than 68.0 years by Silva *et al*.[28] The study by Silva *et al*.[23] was conducted on participants aged 20–30 years, whereas the study by Silva *et al*.[28] was conducted on the elderly subjects. Most studies on intra-osseous jaw cysts and tumors[7,8,13,14,21,24,26,27,29,30] reported from almost an equal gender distribution to male predominance, while the present study showed a slight female predominance as in some previous studies.[17,25,28]

The most prevalent intra-osseous jaw lesion was radicular cyst followed in the descending order of frequency by dentigerous cyst and ameloblastoma. This finding is in accordance with previous studies[21-23,25-27,31-33] in that radicular cyst was ranked as the most prevalent jaw lesion; however, the second and the third ranks varied among dentigerous cyst, odontogenic keratocyst, periapical granuloma, chronic apical periodontitis, odontoma, odontogenic cysts not otherwise specified and simple bone cyst.

Intra-osseous jaw cysts constituted 19.34% of all accessioned cases which is comparable to several previous studies,[10,20,21,29] even though certain studies did report lower relative frequencies for jaw cysts.[1,5,6,9,19] In all intraosseous jaw lesions, jaw cysts comprised 61.15% which is lower than in previous studies.[20,24,29] Odontogenic cysts constituted 96.73% of the cystic lesions after excluding cysts not otherwise specified, which is comparable to previous studies.[5,7-9,19-21,23,28,32] The most prevalent odontogenic cyst was radicular cyst followed by dentigerous cyst and odontogenic keratocyst. This finding is in accordance with several previous studies.[4,5,10,20,21,24,26,27,29,31,33] Studies on pediatric intra-osseous jaw lesions including the

present study revealed that dentigerous cyst was the most common lesion.[18,19] However, study by Del Corso *et al*.[7] revealed that radicular cyst slightly outnumbered dentigerous cyst, but they used 18 years and younger as a cut off point for paediatric subjects which is different from 16 years and younger in the present study. The most common intraosseous jaw lesion in the geriatric subjects was radicular cyst which is in accordance with the study by Silva *et al*.[28] On the other hand, almost all previous studies listed nasopalatine duct cyst as the most frequent nonodontogenic cyst.[4,6,7,10,21,26,27,33] Likewise, all previous studies[10,15,21,22,26,27] reported the anterior part of the maxilla as the predilection site for nasopalatine duct cyst.

One significant change in the latest WHO Classification of Head and Neck Tumours was the reinstatement of odontogenic keratocyst and calcifying odontogenic cyst back to the cyst category.[3] Odontogenic keratocyst was classified as keratocystic odontogenic tumour in the 2005 WHO Classification of tumours due to its aggressive behaviour and the association with a mutation or inactivation of *PTCH1* gene. However, alteration of *PTCH1* gene is not specific for odontogenic keratocyst and can be found in other developmental cysts.[2,34] In addition, there were reports that marsupialization was an effective treatment for odontogenic keratocyst due to the reversion of the epithelium to normal.[35,36] These features do not support the neoplasm concept of odontogenic keratocyst. From the aforementioned reasons, the WHO consensus group concluded that there was insufficient evidence to support the neoplastic origin of odontogenic keratocyst.[2] Some studies showed that the majority of the ghost cell lesions were simple cysts. Only a small number of the lesions were solid lesions and can be regarded as a tumour called dentinogenic ghost cell tumour. In addition, the cystic lesions rarely recur.[37,38] The WHO consensus group hence classified the cystic ghost cell lesions as the original name "calcifying odontogenic cyst" and the solid neoplasm as the "dentinogenic ghost cell tumour."[3] This leads to a decrease in the number of odontogenic tumours and a proportional increase in the number of odontogenic cysts compared to studies using the 2005 Classification of Head and Neck Tumours.

In the TTL group, ameloblastoma was the most prevalent odontogenic tumour followed by odontoma which is in accordance with several previous studies.[6,11-13,28,30] However, a number of studies reported odontoma to be the most common odontogenic tumour.[5,20,25,26,29,34] The plausible explanation for this disparity, especially from Asia and Africa may be attributed to the underestimation of odontomas. People in developing countries do not usually have routine dental check-up. Since odontomas do not usually cause pain or gross disfigurement as in ameloblastoma, patients having odontomas may not seek medical attention and remained undetected, despite having odontomas. In addition, some of the odontomas were diagnosed by radiographic appearance only and were not submitted for histopathological examination when removed from the patients due to the innocuous appearance.[6,12,30,39] Fregnani *et al*.[39] presented an interesting observation that the relative frequency of odontogenic tumours depended on the place where the studies were conducted. Studies carried out in the medical schools had a tendency to have a higher relative frequency of ameloblastoma over odontoma.

Malignant tumours accounted for a small percentage (1.77%) of the intra-osseous jaw lesions which is comparable to previous studies.[17,21,22,25,32,33] The most frequent malignant tumour was osteosarcoma, which is in accordance with the previous studies.[17,25,33]

Regarding the newly recognized entities, we found 18 cases of orthokeratinized odontogenic cyst and 1 case of primordial odontogenic tumour. Odontogenic keratocyst previously encompassed both the orthokeratinized and parakeratinized variants.[1] Even though the clinical features of orthokeratinized odontogenic cyst are similar to those of odontogenic keratocyst, the main difference from odontogenic keratocyst is the orthokeratinized stratified squamous epithelial lining with prominent granular cell layer. In addition, there has been no evidence of association with the nevoid basal cell carcinoma syndrome and the lesions rarely recur even after simple enucleation.[2] Consequently, orthokeratinized odontogenic cyst was segregated as a separate entity rather than being regarded as a variant of odontogenic keratocyst. According to the systematic review of primordial odontogenic tumour by Bologna-Molina *et al*.[40] published in 2020, there have been only 16 cases in the literature.

The latest WHO Classification of Head and Neck Tumours also removed ameloblastic fibrodentinoma and ameloblastic fibro-odontoma from its classification because there was evidence that once dental hard tissues were formed, these lesions were programmed to develop into odontomas.[3,6] We thus reclassified our previously diagnosed cases of ameloblastic fibro-odontoma as odontomas.

It is noteworthy to point out differences between paediatric and geriatric subjects. In the paediatric subjects, developmental cysts outnumber inflammatory cysts and

dentigerous cyst is the most frequent intra-osseous jaw cyst, while inflammatory cysts occur more often than developmental cysts and radicular cyst is the most common intra-osseous jaw cyst in the geriatric subjects.

A number of odontogenic cysts and tumours possess similar to indistinguishable clinical and radiographic features from one another; therefore, information on the relative frequency, age distribution and site of predilection may guide clinicians toward the most likely clinical diagnosis.[1,5] However, the final diagnosis is ultimately based on the histopathological examination of the biopsied specimen, so it is imperative that all tissue removed from the patient be submitted for histopathological examination. Correct diagnosis is essential since some of these lesions have a locally aggressive behaviour as well as a propensity to recur, so they should be detected as soon as possible to minimize any necessary surgery and be closely followed in subsequent visits to monitor possible recurrence after treatment.[1]

CONCLUSIONS

This study is the largest study on intraosseous jaw lesions encompassing several pathological entities ever conducted from Thailand. It thus provides an invaluable database for clinicians to formulate a differential diagnosis as well as for the pathologists to render the final diagnosis. Moreover, the reported results herein are in accordance with previous studies in general. This study also highlights the paediatric as well as the geriatric patients which possess different characteristics from the adult patients.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Relative frequencies of odontogenic cysts and tumors

Diagnosis	Number of cases	Relative frequency (%)
Odontogenic cyst	3850	52.15
Radicular cyst	1419	19.22
Dentigerous cyst	1351	18.30
Odontogenic keratocyst	755	10.23
Residual cyst	144	1.95
Calcifying odontogenic cyst	125	1.69
Inflammatory collateral cyst	23	0.31
Orthokeratinized odontogenic cyst	18	0.24
Lateral periodontal cyst	11	0.15
Glandular odontogenic cyst	4	0.05
Benign odontogenic tumor	1700	23.03
Ameloblastoma	1003	13.59
Odontoma	256	3.47
Unicystic ameloblastoma	133	1.80
Cemento-ossifying fibroma	112	1.52
Adenomatoid odontogenic tumor	74	1.00
Odontogenic myxoma/myxofibroma	42	0.57
Cementoblastoma	36	0.49
Calcifying epithelial odontogenic tumor	22	0.30
Ameloblastic fibroma	15	0.20
Squamous odontogenic tumor	3	0.04
Odontogenic fibroma	3	0.04
Primordial odontogenic tumor	1	0.01
Malignant odontogenic tumor	37	0.50
Ameloblastic carcinoma	17	0.23
Clear cell odontogenic carcinoma	10	0.14
Primary intraosseous carcinoma	8	0.11
Ghost cell odontogenic carcinoma	1	0.01
Odontogenic sarcoma	1	0.01