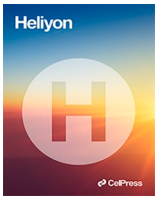
Heliyon 10 (2024) e39158

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Odontogenic myxoma: A clinicopathological study over 15 years and immunohistochemical analysis

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ARTICLE INFO

Keywords:
Odontogenic myxoma
Odontogenic tumor
Peripheral
Bcl-2
Mast cell

ABSTRACT

Objective: and rationale: Odontogenic myxoma is an uncommon odontogenic tumor with locally aggressive behavior. The clinicopathological studies of odontogenic myxoma in Asian countries are very limited and only few studies have investigated the immunohistochemical profiles of the tumor. This study aims to investigate the clinicopathological and immunohistochemical features of odontogenic myxoma at the Faculty of Dentistry, Mahidol University over a 15-year period.
Methods: Archives of our institute were reviewed. Cases diagnosed as odontogenic myxoma were retrieved. Demographic, clinical, radiographic, and histopathological features of these cases were analyzed. In addition, immunohistochemical markers including vimentin, Ki-67, Bcl-2, and CD117 were performed. The correlation between immunohistochemical profiles and clinicopathological characteristics was evaluated.
Results: Sixteen cases of odontogenic myxoma were discovered. Fourteen cases were central type while two cases were peripheral type. The mean age of patients was 34.6 years with male-to-female ratio of 1:2.2. Mandible (68.8 %) was more affected than the maxilla (31.2 %). Bony expansion or jaw swelling (43.8 %) was the most common clinical feature. Most cases (71.4 %) presented with multilocular radiolucency. Histopathologically, tumors show stellate and spindle-shaped cells in a myxoid stroma with varying amounts of collagen fiber. All cases were positive for vimentin and Bcl-2. Half of the cases showed positive for Ki-67. Mast cells were presented in most cases (75.0 %). A significant correlation was found between the immunoexpression level of Bcl-2 and border of lesion in radiograph ($p = 0.024$).
Conclusions: This study contributes to better understanding of the characteristics of odontogenic myxoma. Clinicians and pathologists should be aware of odontogenic myxoma, as its clinical and histopathological features may overlap with other tumors. The expression of Bcl-2 and presence of mast cell in this tumor may relate to its growth and aggressiveness. Despite its benign nature, odontogenic myxoma exhibits high recurrence, especially in lesion managed conservatively.

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https://doi.org/10.1016/j.heliyon.2024.e39158
Received 16 July 2024; Received in revised form 7 October 2024; Accepted 8 October 2024
Available online 9 October 2024

1. Introduction

Odontogenic myxoma (OM), also called "myxoma", is an uncommon benign odontogenic tumor of the oral and maxillofacial region. In the past, the origin of OM was debatable, whether it occurred from the mesenchyme of dental tissue or embryonic tissue [1]. Until 2022, the World Health Organization (WHO) officially classified OM in the group of benign mesenchymal odontogenic tumor [2]. The prevalence of OM varies between 0.5 % and 19 % among odontogenic tumors, with variations observed across different countries [3]. The clinical feature of OM is a locally aggressive tumor with slow permeative growth [2,3]. Majority of OM is central type presenting as intrabony lesion. This type of OM is asymptomatic when it is small, but bone perforation and infiltration of tumor into the surrounding structures are observed in large lesion [2]. Previous studies show that central OM has a high recurrence rate, ranging from 10 to 43 % [4–6]. In very rare situations, OM occurs as an extraosseous lesion known as peripheral OM. Unlike its central counterpart, it tends to be a slow-growing tumor with a lower rate of local recurrence [7].

Radiographic features of OM vary from unilocular to multilocular with well- or ill-defined radiolucency on plain film. However, its margins appear relatively diffuse on computed tomography (CT) or magnetic resonance imaging (MRI) [8]. The typical histopathological features of OM consist of stellate, spindle-shaped, and round cells. These three cell types are scattered in an abundant, loose myxoid stroma with a small number of collagen fibers. Cords or nests of odontogenic epithelial rests may be found in tumor stroma but they are presented in a small minority of OMs [2].

With respect to the locally aggressive behavior of OM, previous studies revealed that OM exhibits positivity for various immunohistochemistry markers associated with cellular proliferation and apoptosis [9–11]. Bcl-2 is a family of proteins involved in the regulation of apoptosis and plays a crucial role in controlling the balance between cell survival and cell death. Iezzi et al. [10] found that Bcl-2 overexpression in the epithelial components of OM and may relate to the growth of tumors. Ki-67 is a protein marker used to determine cell proliferation [12]. The expression of this marker was also observed in OM, but at a low level [10,13]. In addition to these markers, previous studies [14–16] demonstrated that the presence of mast cells in odontogenic lesions may relate to their locally aggressive behavior. Gomez-Herrera et al. [13] performed mast cell tryptase to highlight mast cells in OM and suggested that OM with a higher mast cell count showed more invasion potential than those with a lower mast cell count.

The clinicopathological studies of OM in Asian countries are very limited [17–22]. The most recent study was conducted in Japan in the year 2018 [21]. Moreover, only five studies [9–11,13,18] investigated immunohistochemical profiles in OMs. Therefore, our study aims to investigate the clinicopathological features of OM at the Faculty of Dentistry, Mahidol University, over a 15-year period. The radiographic features of all cases have been recorded and discussed. Demographic data, clinical and radiographic features of OM in English language literature were also reviewed and tabulated. Immunohistochemical markers, including vimentin, Ki-67, Bcl-2, and CD117, were performed, and the immunohistochemical profiles of OMs were summarized. Additionally, the correlation between the expression levels of these markers and the clinicopathological features of OMs was analyzed.

2. Materials and methods

During the 15-year study period (2005–2019), all cases with histopathological diagnoses of odontogenic myxoma or myxoma were retrieved from the archives of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Mahidol University. The diagnosis of these cases was confirmed by a board-certified oral pathologist (RJ) based on the latest WHO classification of head and neck tumors [2]. These diagnostic criteria included histopathological features of stellate or spindle-shaped cells in myxoid stroma and the location of tumor in gnathic bones or tooth-bearing areas. Cases that did not meet the diagnostic criteria from the WHO classification were excluded from our study. Clinical and radiographic data of all selected cases, including sex, age, location, clinical features, and radiographic features, were recorded.

The location of OM was categorized into anterior, posterior, or anteroposterior regions. The anterior region was designated as the area extending from the central incisors to the canines, while the posterior region was described as the area that extended from the first premolar to the tuberosity in the maxilla or the ramus in the mandible. The anteroposterior region indicated the area extending from the anterior to the posterior region.

The radiographic features of OM were classified in terms of the border and locularity of the lesions. The border of the lesion was classified as well-defined or ill-defined. A well-defined border was attributed to a lesion that its periphery could be clearly traced by an imaginary line. Conversely, an ill-defined border indicated a lesion that difficult to trace an exact outline. The locularity was categorized as unilocular or multilocular. A lesion was classified as unilocular if it displayed a single radiolucent area without any septa, while it was categorized as multilocular if it featured at least two compartments separated by internal septa.

Paraffin-embedded blocks of all OMs were retrieved. New 4 μm thickness of tissue sections were cut and stained with hematoxylin and eosin (H&E) to study the histopathology. Immunohistochemistry was processed by an automated immunostainer according to the manufacturer's protocols. A panel of antibodies, including vimentin, Ki-67, Bcl-2, and CD117 was performed. The rationale for each marker was as follows: vimentin was a mesenchymal marker that used to confirm the mesenchymal origin of OM; Ki-67 was a well-established proliferation marker that assessed the proliferation rate of tumor cells; Bcl-2 was a protein involved in apoptotic pathways and served as a prognostic marker in several tumors; and CD117 was a marker for mast cells that aided in detecting mast cells within lesions. Positive reactions were identified by the presence of brown labeling within the tumor cells for vimentin, Ki-67, and Bcl-2, and within the mast cells for CD117. The details of the antibodies used in this study are described as follows: Vimentin (clone IgG/k; diluted 1:450; Cell Marque™, CA, USA), Ki-67 (clone MIB-1; diluted 1:300; Dako™, CA, USA), Bcl-2 (clone IgG_1/k; diluted 1:1500; Cell Marque™, CA, USA), and CD-117 (diluted 1:700; DakoTM, CA, USA).

The percentages of positive tumor cells stained for vimentin, Ki-67, and Bcl-2 were determined using a 40x microscope objective to

assess the immunoexpression throughout the tumoral tissue on the glass slides. The immunoexpression was semiquantitatively scored on a four-level scale as follows: 0 indicating negative staining; 1 (low level) indicating 1–10 % positive cells; 2 (intermediate level) indicating 11–50 % positive cells; and 3 (high level) indicating more than 50 % positive cells. This scoring system was previously used to evaluate Ki-67 and Bcl-2 expression in OM [13]. CD117 was highlighted in mast cells in the tumoral tissue. The number of mast cells was counted in five high-power fields (H.P.F.) under a 40x microscope objective according to the method proposed by Bologna-Molina R et al. [13]. An average number of mast cells in five H.P.F. was calculated and recorded as a mast cell count. To evaluate immunoexpression for all markers, two experienced pathologists (RJ and TK) independently graded immunoexpression levels and quantified the mast cell count. Disagreement cases were discussed until a consensus was reached.

The Pearson Chi-square test was used to analyze the association between clinical and radiographic features and the immunoexpression levels of vimentin, Bcl-2, Ki-67 and mast cell count. The software used for all statistical analyses was IBM SPSS Statistics for Windows (Version 18.0, IBM Corp., Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

The Institutional Ethical Committee Review Board, Faculty of Dentistry/Faculty of Pharmacy, Mahidol University (MU-DT/PY-IRB 2019/025.0205) reviewed and approved this study.

3. Results

Between 2005 and 2019, a total of 11,175 specimens were collected from the archive of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Mahidol University. Of these, 658 cases were diagnosed as odontogenic tumors, and 16 cases (2.4 %) were confirmed as OM. Fourteen cases of OM were central type while two cases were peripheral type. It is important to mention that some of the data presented in this study have been taken from our previous work [23].

3.1. Demographic data

Out of the 16 patients, 11 cases were female (68.8 %) and 5 cases were male (31.2 %), with a male-to-female ratio of 1:2.2. The age of the patients ranged from 23 to 68 years, with a mean age of 34.6 years. Most of the cases (7 cases, 43.8 %) were found in the third decade of life. The distribution of age and sex in OMs is shown in Table 1.

Eleven patients (68.8 %) presented with lesions in the mandible, while five patients (31.2 %) had lesions in the maxilla. Among the 16 cases of OMs, the majority of lesions occurred in the posterior region (11 cases), followed by the anteroposterior region (4 cases), and the anterior region (1 case), as presented in Table 2.

3.2. Clinical features

The most common clinical presentation of OM was bony expansion or jaw swelling (7 cases, 43.8 %), followed by delayed tooth eruption (4 cases, 25.0 %), and exophytic mass (3 cases, 18.8 %). The remaining two cases of OMs were asymptomatic. One of them was accidently found as a cystic lesion in a radiograph, while the other case caused tooth discoloration and had no other symptoms. The distribution according to clinical presentation of OMs is summarized in Table 3.

3.3. Radiographic features

Out of 16 cases of OMs, 2 were categorized as peripheral type, which showed no changes on the radiographs. The remaining 14 cases were central type and exhibited radiolucent lesions on radiographs. Ten out of fourteen cases demonstrated multilocular radiolucency (71.4 %), while four cases showed unilocular radiolucency (28.6 %). All four cases with unilocular radiolucency demonstrated a well-defined margin. In 10 cases of OMs with multilocular, they showed a well-defined margin and an ill-defined margin equally (5 cases each). The radiographic features of 14 cases of OMs are summarized in Table 4.

Table 1
Distribution of 16 cases of odontogenic myxoma according to age and sex.

Age group (years)	Male	Female	Total
0–9	–	–	–
10–19	–	–	–
20–29	1	6	7
30–39	3	2	5
40–49	1	1	2
50–59	–	1	1
60–69	–	1	1
Age range	25–48	23–68	23–68
Mean age	33.2	35.3	34.6
Total	5	11	16

Table 2
Distribution of 16 cases of odontogenic myxoma according to locations.

Locations	Maxilla	Mandible	Total
Anterior	1	–	1
Posterior	3	8	11
Anteroposterior	1	3	4
Total	5	11	16

Table 3
Distribution of 16 cases of odontogenic myxoma according to clinical features.

Clinical features	Maxilla	Mandible	Total
Bone expansion/jaw swelling	3	4	7
Delayed tooth eruption	–	4	4
Soft tissue mass	1	2	3[a]
Intrabony cystic lesion	–	1	1
Tooth discoloration	1	–	1
Total	5	11	16

[a] Two cases are peripheral type. One case is central type, which perforates the cortical bone and presents as an exophytic mass on mandible.

Table 4
Distribution of 14 cases of central odontogenic myxoma according to radiographic features.

Radiographic features	Maxilla	Mandible	Total
Unilocular, well-defined	–	4	4
Unilocular, ill-defined	–	–	–
Multilocular, well-defined	1	4	5
Multilocular, ill-defined	3	2	5
Total	4	10	14

3.4. Histopathological features

All OMs consisted of stellate and spindle-shaped mesenchymal cells with long, fine cytoplasmic processes scattered within a loose myxoid connective tissue (Fig. 1A and B). Fourteen cases (87.5 %) presented varying amounts of collagen fibers in the myxoid tissue (Fig. 1C and D), while two cases (12.5 %) showed purely myxoid stroma. Islands of odontogenic epithelium were detected in only three cases (18.8 %) (Fig. 1F). Trabeculae of residual bone were found in seven cases (43.8 %). Ten cases (62.5 %) of OMs exhibited chronic inflammatory cell infiltration. The number of inflammatory cells varied among cases.

3.5. Immunohistochemistry findings

Table 5 summarizes the number and percentage of OMs according to the immunoexpression levels of vimentin, Ki-67, and Bcl-2. The immunoreactivity of vimentin was present in tumor cells of all OMs (16 cases, 100.0 %) and the immunoexpression level of all cases was high (Fig. 2A). This result confirmed the mesenchymal origin of OMs.

Ki-67 marker was presented in the nucleus of tumor cells. Half of the cases (8 cases, 50.0 %) showed positive for this marker and the majority of them (5 cases, 31.2 %) showed a moderate level of immunoexpression (Fig. 2B).

Bcl-2 showed positivity in the cytoplasm of the tumor cells in all OMs (16 cases, 100.0 %). The level of immunoexpression varied from low to high. Most cases of OMs (9 cases, 56.2 %) showed a high level of immunoexpression as depicted in Fig. 2C.

Mast cells were identified by CD117 marker as round or oval cells with strong membrane positivity. Generally, these cells are scattered within myxoid stroma. In cases with intra-tumoral residual bones, mast cells are often found adjacent to these bones. Mast cells were detected in 12 out of 16 OMs (75.0 %). The mast cell count varied from 1.7 to 18.2 cells per H.P.F. The average number of mast cells was 4.0 cells per case. Representative of CD117 expression in mast cells of OM is shown in Fig. 2D.

This study revealed a significant correlation ($p = 0.024$) between the immunoexpression level of Bcl-2 and the border of OMs in the radiograph. Nevertheless, no significant correlation was observed between the immunoexpression levels of Bcl-2, Ki-67, mast cell count, and the remaining features.

4. Discussion

OM is an uncommon, benign odontogenic tumor derived from the ectomesenchymal cells. Although this tumor generally shows slow growth, it tends to be locally invasive. Our study shows that OMs accounted for 2.4 % of all odontogenic tumors. This result confirms the rarity of OM and is in line with previous studies indicating that OMs account for approximately 1.9 % of all odontogenic

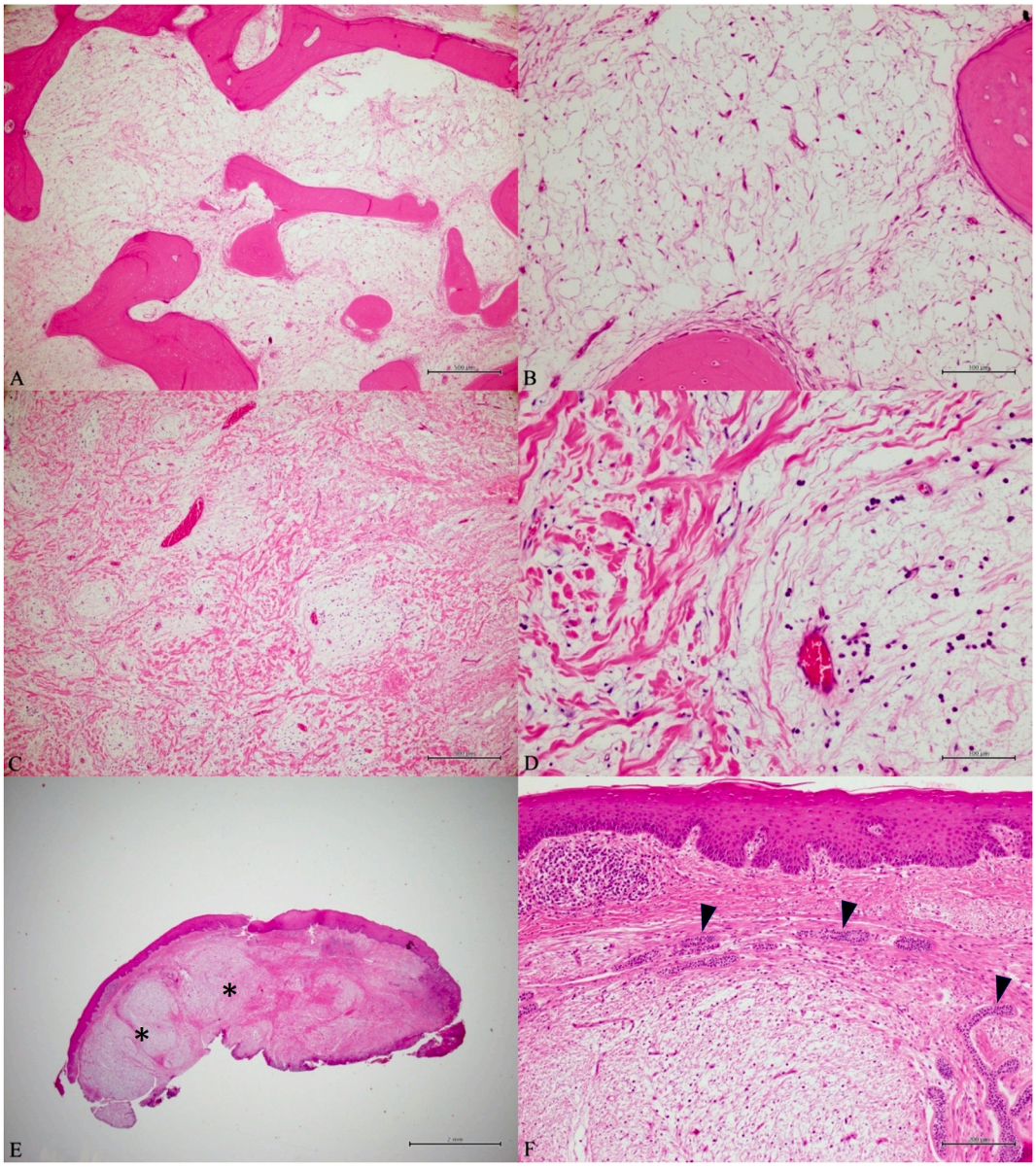

Fig. 1. The histopathological features of odontogenic myxoma.
A representative of typical odontogenic myxoma exhibiting loose myxoid stroma (A, B). (A) A loose myxoid tumor infiltrates in the marrow space between bony trabeculae (H&E, x100). (B) Stellate and spindle-shaped mesenchymal cells with long, fine cytoplasmic processes are scattered within the myxoid stroma (H&E, x200).
A representative of odontogenic myxoma presenting a large amount of collagen fiber (C, D). (C) The tumor exhibits predominantly dense collagenous stroma. Patchy areas of myxoid stroma are observed between collagen fibers (H&E, x100). (D) Dense collagenous background is observed on the left, whereas classic myxoid stroma is present on the right (H&E, x200).
A representative of peripheral odontogenic myxoma (E, F). (E) An unencapsulated tumor mass (asterisks) consisting of a large amount of myxoid stroma is presented in the underlying connective tissue of the oral mucosa (H&E, x2.5). (F) The tumor comprises loosely myxoid stroma in the bottom. Several strands of odontogenic epithelium are clearly observed adjacent to the myxoid areas (arrowheads) (H&E, x100).

tumors in Asian populations [21,24]. Nevertheless, Africa exhibited a significant prevalence of OM to 9.1 %. These findings highlight the diverse distribution of OMs across different countries, indicating variations in their occurrence.

A summary of the demographic, clinical, and radiographic data of OMs from the present study and previous studies is shown in Table 6. The present study found a slight female predominance in OM cases, with a male-to-female ratio of 1:2.2. This finding is in accordance with most previous studies that report the male-to-female ratio ranging from 1:1.1 to 1:3.7 [3,10,11,17,20,21,25–32]. However, there are two studies that demonstrate a slightly male preponderance in OMs [18,19].

Table 5
Distribution of immunoexpression level in 16 cases of odontogenic myxoma.

Antibody	Immunoexpression				
	Negative	Low	Moderate	High	Total
Vimentin	0 (0 %)	0 (0 %)	0 (0 %)	16 (100 %)	16 (100 %)
Ki-67	8 (50.0 %)	3 (18.8 %)	5 (31.2 %)	0 (0 %)	16 (100 %)
Bcl-2	0 (0 %)	4 (25.0 %)	3 (18.8 %)	9 (56.2 %)	16 (100 %)

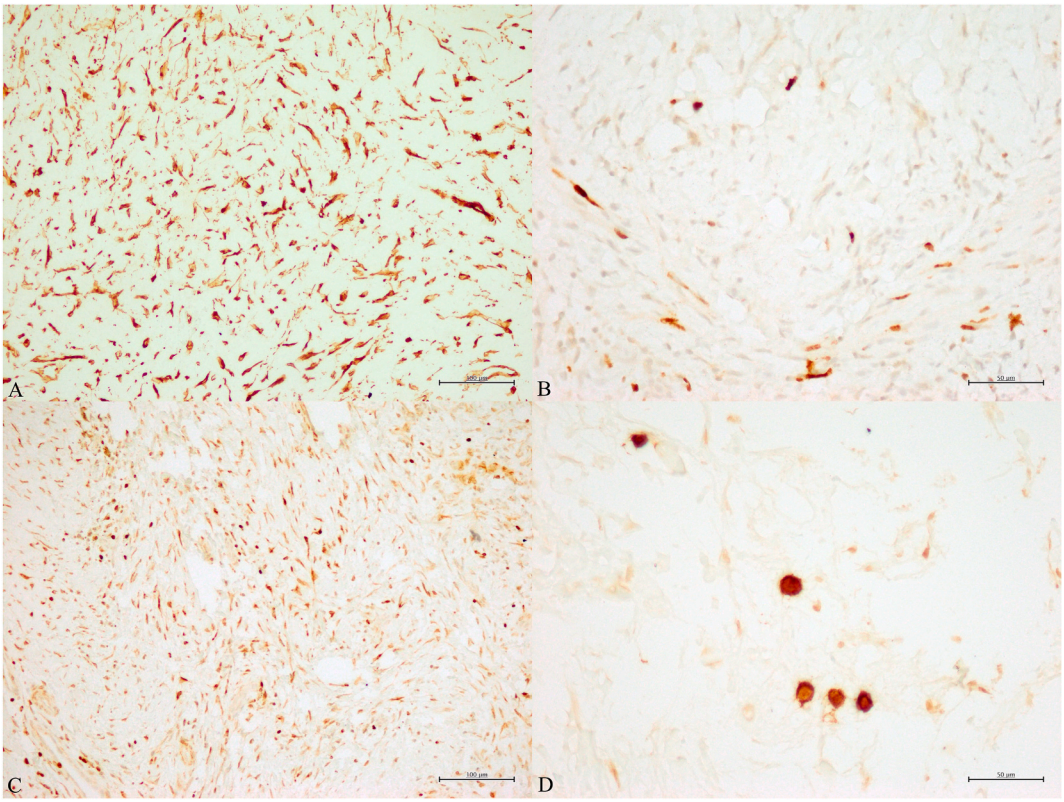

Fig. 2. Representative of the immunohistochemical findings of odontogenic myxoma. (A) Brown staining of vimentin is observed in the cytoplasm of nearly all tumor cells (Vimentin, x200). (B) Yellow brown staining of Ki-67 is observed in the nucleus of some tumor cells (Ki-67, x400). (C) Yellow brown staining of Bcl-2 is presented in the cytoplasm of nearly all tumor cells (Bcl-2, x200). (D) CD117 decorates the cell membrane of mast cells. Five mast cells are detected in this field (CD117, x400).

Although OM presented a wide age range from the third to the eighth decade of life, the peak age of diagnosis in our study was in the third decade. This finding is consistent with the majority of the previous studies [3,9,11,18,19,26–28,32]. However, two studies [30,31] found that the peak age diagnosis was the second decade, and the other two studies [20,22] show the peak age diagnosis was the fourth decade.

Regarding the location of OM, our study shows that OM was predominantly located in the mandible (68.8 %). This result is consistent with most studies indicating a higher prevalence of OM in the mandible compared to the maxilla [3,9–11,19,20,25–31]. However, three studies [17,18,30] reported a preponderance of OM in the maxilla, and another study [21] demonstrated equal distribution between maxillary and mandibular lesions. In consistent with nearly all of previous studies [3,10,11,20,22,25–29,32], this study found that the posterior region is the most common area of OM in both the maxilla and mandible. From the findings of this study and the previous studies, it can be concluded that the posterior mandible is the most common location of OM.

Clinical feature of OMs is variable showing expansion or swelling of the jaws, tooth mobility, or oral mass [11,18,31,32]. Previous studies [11,18,26,27,31] show that the most prevalent clinical feature of OM is bone expansion or jaw swelling which is consistent with our result. Interestingly, our study found two cases of peripheral OM, constituting 12.5 % of the total cases. According to previous studies [33–35], the peripheral OM is very rare. Only 14 cases has been reported in the literature [7]. In our two cases, patients presented with a gingival mass located at the posterior regions of the maxilla (1 case) and the mandible (1 case). This clinical presentation of peripheral OM is in accordance with the findings from previous studies [33,35]. However, Mascitti et al. [35] described the anterior region as the most common site of peripheral OM. Because the clinical presentation of peripheral OMs often manifests as

Table 6
Demographic, clinical, and radiographic characteristics of patients with odontogenic myxoma in the English-language literature.

Author	Year	Country	Period	No. of cases	Sex (M: F)	Age Range (years)	Mean age (years)	Age group (years)	Site (Max: Man)	Location (A: P: A + P)	Locularity (Uni: Multi)	Border (Well: Ill)	Most common clinical features
This study	2024	Thailand	2005–2019	16	1: 2.2	21–68	34.6	20-29 (43.8 %)	5: 11	1: 11: 4	4: 10	9: 5	Bony expansion/jaw swelling (43.8 %)
Banasser [27]	2020	USA	1994–2017	38	1: 1.9	6–84	37.5	20-29 (18.4 %)	15: 23	7: 31: 0	8: 11 19 N/A	N/A	Bony expansion/jaw swelling (60.5 %)
Takahashi [21]	2018	Japan	2001–2015	12	1: 2	27–65	41.5	N/A	6: 6	1: 4: 7	6: 6	10: 2	N/A
Vasconcelos [28]	2018	Brazil	1952–2016	85	1: 1.1	10–61	30.7	20-29 (30.6 %)	44: 39 2 N/A	26: 42: 0 17 N/A	17: 14 54 N/A	N/A	N/A
Rowland [31]	2017	Nigeria	1997–2015	16	1: 1.7	5–70	27.06	10-19 (31.3 %)	7: 9	0: 4: 3 9 N/A	N/A	N/A	Bony expansion/jaw swelling (100.0 %)
Wang [22]	2017	China	2009–2016	18	1: 2	6–75	35.5	31-40 (22.2 %)	6: 12	0: 11: 3 4 N/A	3: 15	14: 4	N/A
Francisco [30]	2017	Brazil	1980–2010	14	1: 3.7	7–51	21.6	10-19 (35.7 %)	3: 11	N/A	5: 9	12: 2	Bony expansion/jaw swelling (100.0 %)
Titinchi [3]	2016	South Africa	1971–2011	29	1: 2.6	7–44	21.3	20-29 (37.9 %)	11: 18	0: 21: 5 3 N/A	8: 18 3 N/A	25: 4	Bony expansion/jaw swelling (58.6 %)
Etemad-Moghadam [20]	2014	Iran	1967–2008	40	1: 1.4	6–55	27.9	30-39 (N/A)	14: 26	1: 29: 10	N/A	N/A	Bony expansion/jaw swelling (N/A)
Friedrich [29]	2012	Germany	30 years	14	1: 3.7	8–45	26.5	30-39 (35.7 %)	5: 9	4: 7: 3	9: 4 1 N/A	8: 6	N/A
Martinez-Mata [11]	2008	Mexico, Guatemala, Brazil	N/A	62	1: 2.3	9–71	28.0	20-29 (45.2 %)	25: 37	13: 38: 7 4 N/A	28: 39	N/A	Bony expansion/jaw swelling (100.0 %)
Iezzi [10]	2007	Italy	N/A	12	1: 1.4	18–47	34.4	N/A	1: 11	1: 11: 0	4: 8	N/A	Asymptomatic (100.0 %)
Zhang [19]	2007	China (West)	1964–2005	41	1.2: 1	4–63	29.0	20-29 (36.6 %)	17: 24	N/A	7: 12 22 N/A	9: 32	N/A
Noffke [26]	2007	South Africa	23 years	30	1: 2.3	11–70	31.3	21-30 (37.0 %)	11: 19	1: 24: 5	6: 24	N/A	N/A
Li [18]	2006	China	1985–2005	25	1.1: 1	6–66	28.8	20-29 (28.0 %)	13: 12	1: 11: 13	1: 22 2 N/A	12:10 3 N/A	Bony expansion/jaw swelling (100.0 %)
Simon [32]	2004	Tanzania	1982–2002	33	1: 1.8	0–64	26.1	20-29 (39.4 %)	8: 24 1 N/A	7: 20: 5 1 N/A	4: 16 13 N/A	N/A	Bone perforation (33.3 %)
Bast [9]	2003	USA	1974–1988	26	1: 1.2	14–68	35.0	N/A	11: 15	N/A	N/A	N/A	N/A
Macdonald-Jankowsk [17]	2002	Hong Kong	1989–2000	10	1: 1.5	17–79	36.9	N/A	6: 4	2: 1: 7	6: 4	6: 4	Bony expansion/jaw swelling (70.0 %)
Lo Muzio [25]	1996	Italy	N/A	10	1: 2.3	15–65	32.7	10-19, 20-29 (30.0 % each)	4: 6	1: 5: 0 4 N/A	4: 6	N/A	N/A

Abbreviations: USA, United States of America; M, male; F, female; Max, maxilla; Man, mandible; A, anterior; P, posterior; A + P, anteroposterior; Uni, unilocular; Multi, multilocular; Well, well-defined; Ill, ill-defined; N/A, not applicable.

gingival mass that resembles several reactive lesions such as irritation fibroma or pyogenic granuloma [35], it is not surprising that the two cases in our study were clinically diagnosed as pyogenic granuloma and fibroma. To avoid misdiagnosis and improper management, submission of excised tissue for histopathological examination are recommended. The histopathological features of one peripheral OM in our study are shown in Fig. 1E and F.

The radiographic features of 14 cases of central OM in our study revealed a predominant multilocular radiolucency (71.4 %). This finding is in accordance with most previous studies, which reported a predominance of multilocular radiolucent ranging from 60.0 % to 95.7 % of OMs [3,11,18,25,26,30]. However, two studies [28,29] presented a slightly predominant unilocular radiolucency in OM (54.8 % and 64.3 %). The high prevalence of unilocular radiolucency in the study of Vasconcelos [28] may be resulted from an absence of information regarding the locularity in 54 of 85 cases. Although OMs are typically unencapsulated and frequently infiltrate into the surrounding bone, most of OMs (64.3 %) in this study show a well-defined border. This finding is consistent with previous studies [3, 18] that also reported a higher prevalence of well-defined borders than ill-defined borders in OMs. In our study, 5 cases (35.7 %) of OMs showed ill-defined multilocular radiolucency. This radiographic feature may resemble malignant tumors and may lead clinicians to misdiagnose it as malignant tumor. Some malignant tumors, such as osteosarcoma and metastatic tumors, should be included in radiographically differential diagnosis of OM with such radiographic features [36].

Previous studies indicate that odontogenic epithelium is rarely observed in the histopathology of OM [2,10,27]. Only three OMs (18.8 %) in our study contained cords and nests of the odontogenic epithelium. This result is in accordance with several studies [10,11, 18,27] that consistently indicated a low prevalence of odontogenic epithelium in OM ranging from 7.6 % to 25.0 %. This finding suggests that the odontogenic epithelium likely does not play a substantial role in the pathogenesis of OM [9,11,13]. Besides, according to WHO 2022 [2], the presence of odontogenic epithelium is not an essential criterion in diagnosis this tumor. OM without odontogenic epithelium may histopathologically resemble myxoma of bone and soft tissue [7,35]. However, its specific anatomical location in the gnathic bones and tooth-bearing areas is sufficient for diagnosing OM [2].

Although typical histopathological features of OMs consist of stellate and spindle-shaped cells scattered in loose myxoid connective tissue [8], our study found that most OMs exhibited varying amounts of collagen fibers in tumor stroma. Out of 16 cases, 14 (87.5 %) show a high amount of collagen fibers. OM characterized by prominent collagen fibers is sometimes called as “myxofibroma” or “fibromyxoma” [2,8]. Because OMs typically demonstrate abundant myxoid stroma, central type of myxoid neurofibroma should be included in the histopathological differential diagnosis of OM. Immunohistochemistry for S-100 protein can confirm the neural origin of the tumor and help to distinguish myxoid neurofibroma from OM. The diagnosis of OM may become more challenging, particularly when dense collagen fibers are predominantly presented (Fig. 1C and D). These histopathological features of OM may resemble odontogenic fibroma, which is characterized by mature fibrous connective tissue containing variable amounts of odontogenic epithelium. A varying myxoid stroma in tumor suggests the diagnosis of OM. Moreover, odontogenic epithelium, dentinoid, or cementum-like materials are commonly found in odontogenic fibroma and the presence of these structures may support its diagnosis [2]. For peripheral OM, peripheral nerve sheath tumors with myxoid feature, such as myxoid neurofibroma and nerve sheath myxoma, should be included in the histopathological differential diagnosis [33,34]. However, these tumors are positive to neural marker such as S-100 protein while OM shows negative to this marker. Additionally, the presence of odontogenic epithelium, as observed in our case (Fig. 1E and F), firmly supports the diagnosis of peripheral OM.

In our study, we used Ki-67 as a marker to estimate the proliferation index of OM. Ki-67 expression is typically observed in the nuclei of proliferating cells and its expression tends to increase in both pre-neoplastic and neoplastic lesions of the oral mucosa [37]. Our study showed negative immunoexpression of Ki-67 in the odontogenic epithelial rests, indicating these cells are inactive. However, our study and previous studies [9,11,13] observed expression of Ki-67 in the mesenchymal cells of OM. These findings suggest that the growth and progression of OM may primarily associate with the mesenchymal component, not the epithelium component.

Bcl-2, an anti-apoptotic protein, appears to play a significant role in cancer development and progression [38]. To date, only three studies investigated the expression of Bcl-2 in OM. Our study showed that the mesenchymal tumor cells in all cases are positive for Bcl-2 and most cases (56.3 %) demonstrating a high level of immunoexpression. This result is in accordance with Bast’s study [9], which detected a high level of Bcl-2 expression in the tumor cells of OM. They proposed that the production of this antiapoptotic protein in OM can reduce cell death, leading to increased tumor growth. However, our results contradict to the results of Iezzi et al. and Martinez-Mata et al. [10,11]. They found that only the epithelial components in OM are positive for Bcl-2. Nevertheless, Iezzi et al. [10] found that Bcl-2 expression in their study was only weakly positive and Martinez-Mata et al. [11] reported a very low expression of Bcl-2 in epithelium of OM. Although the high Bcl-2 expression was proposed as a poor prognostic marker in several tumors such as activated B-cell-like diffuse large B-cell lymphoma [39], triple-negative breast cancer [40,41] and ameloblastoma [42]. The prognostic value of this marker in OM is still unproven.

CD117 is an important cell surface marker that can be used to identify mast cells. Until now, two studies have evaluated mast cells in OM, both of which used mast cell tryptase for detection. Our study showed that mast cells were detected in most OMs (75.0 %). This result is consistent with Gómez-Herrera et al. [13] which reported that mast cells were observed in 72.6–100.0 % of OM. The exact role of mast cells in OM remains unclear. Several studies [43–45] suggested that mast cells may play a role in promoting tumor growth through angiogenesis in odontogenic tumors. The key role of mast cells involves releasing of several pro-angiogenic mediators such as vascular endothelial growth factor (VEGF) that promote the formation and remodeling of blood vessels [43,44]. Additionally, our results showed that mast cells were often found adjacent to intra-tumoral residual bones in OMs. This finding is consistent with De Assis Caldas Pereira’s study [46] which found that mast cells in OMs are more frequently located adjacent to the bone trabeculae within the tumor stroma. They suggest that mast cells also play a role in remodeling the extracellular matrix in OM and may be associated with its invasiveness [46].

Although, our study showed a significant correlation between the expression of Bcl-2 and the border of OMs in the radiograph. The

radiographic data used in this study were recorded from plain films. The disadvantage of this type of radiograph is that it shows low detail of borders compared to CT images [8]. Previous studies show that most OMs have an ill-defined border on CT images, which contrasts to the findings on plain films [47,48]. Further studies using radiographic data from CT images are recommended to better understand the association of radiographic features and other parameters. The other limitation of our study is that most patients lost to follow-up after treatment. Thus, the correlation between the immunohistochemical profile and the recurrent rate of OM was not available.

The management of OM is of clinical significance because OM exhibits locally aggressive behavior and high recurrence rate, ranging from 10 to 43 % [2,4–6,49]. Some surgeons recommended conservative treatment to minimize patient morbidity, while others advocated for radical resection with 0.5–1.5 cm margin to prevent recurrence [4,49,50]. A systematic review on recurrent rate of OMs revealed that OM treated with conservative methods including curettage, enucleation or excision showed an approximately threefold higher recurrence rate (19 %) compared to OM treated with resection (6 %). Moreover, maxillary lesions exhibited higher recurrence rate after resection than mandibular lesions. The authors proposed that maxillary lesions had more space to spread before they became clinically evident, making them difficult to treat properly and contributing to recurrence [4].

5. Conclusion

OM is an uncommon odontogenic tumor. In this study, fourteen cases of central type and two cases of peripheral type were discovered. OMs mostly occurred in the third decade of life and were located on posterior mandibular area. Most cases presented with jaw swelling and radiographic features predominantly demonstrated multilocular radiolucency. Because OMs can present varying amounts of collagen and numbers of odontogenic epithelium in histopathology, these features may mimic other tumors and cause difficulties for pathologists in diagnosis. The expression of Bcl-2 and finding of mast cells in these tumors may be related to its growth and locally aggressive behavior. Clinicians should be aware that OM treated conservatively and OM in maxillary location possess high recurrence.

CRediT authorship contribution statement

Rachai Juengsomjit: Writing – review & editing, Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Raweewan Arayasantiparb:** Writing – review & editing, Investigation, Funding acquisition, Data curation. **Ahmad Badruddin Ghazali:** Writing – review & editing, Investigation, Data curation. **Theerachai Kosanwat:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Conceptualization.

Ethics and consent

The Institutional Ethical Committee Review Board, Faculty of Dentistry/Faculty of Pharmacy, Mahidol University (MU-DT/PY-IRB 2019/025.0205) reviewed and approved this study.

Written informed consent for the publication of images, clinical data, and other information in the manuscript was obtained from the patients or their relative/guardian.

Data availability statement

Data will be made available on request.

Funding

This study was financially supported by a grant from the Faculty of Dentistry, Mahidol University, Thailand.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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