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Original Article

Retrospective analysis of primary intraosseous malignancies in mandible and maxilla in a population of Taiwanese patients

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KEYWORDS
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Background/Purpose: Due to the rarity and diversity of primary intraosseous malignancies in jawbones, we aimed to evaluate the clinicopathological features and discuss the findings of our collected cases with the literatures.
Methods: Twenty-nine patients (2000–2020) diagnosed with primary central malignancies of jawbones were selected from the database of Oral Pathology Department in our institution. Clinical features, radiographic appearance, and histopathological diagnosis of the 29 cases were analyzed.
Results: Twenty-nine patients aged between 19 and 84 years (average, 57.4 years) with a male to female ratio of 1.2:1 were included. The most frequent site was the mandibular body and ramus, followed by the posterior maxilla and mandibular symphysis. The most common diagnosis was osteogenic sarcoma ($n = 13$), followed by odontogenic carcinoma ($n = 7$), hematologic malignancies ($n = 5$), salivary gland malignancies ($n = 2$), and neurogenic sarcomas ($n = 2$). The most frequent symptoms were swelling, pain, paresthesia of lower lip, and mobile tooth. Radiographically, they usually presented as ill-defined osteolytic to osteoblastic lesions depending on the amount of ossification. Wide excision comprising partial maxillectomy and segmental mandibulectomy were the most common therapeutic methods.
Conclusion: Despite the rarity of primary central malignancies in jawbones, the clinical features may mimic infectious process or benign lesions. Detailed history-taking, clinical and imaging examination and awareness of the patient's signs and symptoms combining with the histopathological inspection are important for early diagnosis and improved prognosis. The

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current data contributes a useful basis for clinical investigation regarding intraosseous malignancies occurring in the jawbones.

Introduction

Malignant tumors affecting mandible and maxilla are predominantly invasion of oral squamous cell carcinoma arising from adjacent oral epithelium, such as floor of mouth and gingiva.[1] Other malignancies involving jawbones include carcinoma of minor salivary gland of oral cavity,[2] carcinoma from sinonasal area,[3] sarcoma from contiguous soft tissue,[4] metastatic lesions from other sites,[5] and primary cancer arising within jawbones.

The primary central malignancies develop in jawbones are extremely rare, and the jawbones differ from other skeletons mainly for the presence of odontogenic epithelium and ectopic tissues of salivary gland[6] contributing to the variety of diseases developing in jawbones including odontogenic lesions, salivary gland malignancies, mesenchymal cancers, osteogenic sarcomas, and hematopoietic malignant neoplasms.

Reviewing literatures, to the best of our knowledge, there has been no comprehensive case series study for primary intraosseous malignancies of jawbones in Taiwan. Thus, the current study is aimed to retrospectively investigate the clinicopathological features of 29 primary intraosseous malignancies of jawbones in a population of Taiwanese patients.

Materials and methods

Twenty-nine cases of primary intraosseous malignancies arising from mandible and maxilla were retrieved from the Department of Oral Pathology, Kaohsiung Medical University Hospital, Taiwan during a 21-year period from 2000 to 2020. The histopathological diagnoses were based on histological examination of hematoxylin and eosin-stained tissue sections and immunohistochemical stains by board-qualified oral & maxillofacial pathologists together with clinical and radiological correlations. The criteria for the diagnosis of primary central malignancy include: (1) occurrence with intact surface oral mucosa except the ulcer related to trauma or tooth extraction; (2) radiographic findings confirm an intraosseous lesion; (3) rule out a metastatic lesion from distant origin by pathological examination, further general surveys and throughout a follow-up period of more than six months. The clinical features, radiographic appearance, histopathological diagnosis, treatment modalities, and the follow-up data of the recruited 29 cases were subsequently analyzed. Informed consent was waived by the ethical committee because this was a retrospective analysis.

Results

The abbreviations of the clinical and pathological diagnoses for the 29 cases in the study were defined in Table 1; the summary of the clinicopathological details for the 29 patients is presented in Table 2. Cliniopathological features of representative cases (Case 4, 9, 10, and 28) are illustrated in Fig. 1.

As shown in Table 2, the most common cell origin of the 29 primary central malignancies of jawbones in the current study has been osteogenic origin (13 cases, 44.8%), followed by odontogenic origin (7 cases, 24.2%), hematological origin (5 cases, 17.2%), salivary gland origin (2 cases, 6.9%), and soft tissue origin (2 cases, 6.9%).

The 13 cases of osteogenic sarcoma consisted of nine cases of conventional osteosarcoma, three cases of low-grade central osteosarcoma, and one case of parosteal osteosarcoma. The seven cases of odontogenic carcinoma included five cases of primary intraosseous carcinoma, one case each for clear cell odontogenic carcinoma and ameloblastic carcinoma. In addition, the five cases of hematopoietic malignancy were two cases of solitary

Table 1 Full names of the abbreviations for the clinical and pathological diagnoses of the current study.

Abbreviations	Pathological diagnoses
AC	Ameloblastic carcinoma
AdCC	Adenoid cystic carcinoma
CCOC	Clear cell odontogenic carcinoma
COF	Cemento-ossifying fibroma
COS	Conventional osteosarcoma
DC	Dentigerous cyst
DLBCL	Diffuse large B-cell lymphoma
LGCOS	Low-grade central osteosarcoma
MEC	Mucoepidermoid carcinoma
MPNST	Malignant peripheral nerve sheath tumor
NK/T	Extranodal natural killer (NK)/T-cell lymphoma
OKC	Odontogenic keratocyst
OS	Osteogenic sarcoma
PG	Periapical granuloma
PIOC	Primary intraosseous carcinoma
PL	Plasmacytoma
POS	Parosteal osteosarcoma
RdC	Radicular cyst
RC	Residual cyst
SCC	Squamous cell carcinoma

Table 2 Summary of the 29 primary central malignancies of jawbones in the current study.

Origin	Case no.	Age (years)	Gender	Site	Symptoms and signs	Image findings	Clinical diagnosis[a]	Pathological diagnosis[a]	Treatment	Prognosis
Odontogenic origin	1	57	Male	Left mandibular body and ramus	Swelling	Well-defined multilocular radiolucency	Ameloblastoma	AC	Segmental resection	Multiple recurrences during 12 years post-operaive period; loss follow-up
	2	75	Male	Right mandibular body	Swelling; pain; numbness of lower lip	Ill-defined osteolytic lesion	Infected DC	PIOC	Segmental resection	Not available
	3	82	Female	Left mandibular body	Swelling; pain; numbness of lower lip; pus discharge	Ill-defined osteolytic lesion	Osteomyelitis	PIOC	Not available	Not available
	4	59	Fenale	Right posterior maxilla	Ulcerative swelling; pain and tenderness	Ill-defined osteolytic lesion	MEC	CCOC	Partial maxillectomy and radiotherapy	No recurrence for 4 years post-operative follow-up
	5	68	Male	Right mandibular body	Swelling; hypermobile tooth; numbness of lower lip	Ill-defined osteolytic lesion	OS	PIOC	Segmental resection	No recurrence for 3 years post-operative follow-up
	6	76	Male	Left mandibular body	Swelling; lower lip paresthesia; pus discharge	Ill-defined osteolytic lesion	Infected DC	PIOC	Segmental resection	No recurrence for 1 year post-operative follow-up
	7	65	Male	Right mandibular body	Swelling; pain; pus discharge	Ill-defined osteolytic lesion	Osteomyelitis	PIOC	Segmental resection	No recurrence for 1 year post-operative follow-up
Salivary gland origin	8	56	Male	Apical area of tooth 46	Pain	Well-defined radiolucency	PG	AdCC	Enucleation	No recurrence for 16 years post-operative follow-up

(*continued on next page*)

Table 2 (*continued*)

Origin	Case no.	Age (years)	Gender	Site	Symptoms and signs	Image findings	Clinical diagnosis[a]	Pathological diagnosis[a]	Treatment	Prognosis
	9	32	Male	Right mandibular ramus	Discomfort	Well-defined radiolucency	OKC	Adenocarcinoma, not otherwise specified (NOS)	Enucleation; segmental resection and CCRT	Recurrence of left neck 8 years later; No recurrence for 4 years post-2nd operative follow-up
Soft tissue origin	10	48	Female	Right mandibular body and ramus	Swelling; lower lip paresthesia	Ill-defined osteolytic lesion	Malignancy	MPNST	Segmental resection	N/A
	11	59	Male	Right mandibular body	Throbbing pain; swelling	Ill-defined osteolytic lesion	Osteomyelitis	MPNST	Segmental resection and chemotherapy	No recurrence for 12 years post-operative follow-up
Hematologic origin	12	78	Male	Left posterior maxilla	Pain; ulceration	Ill-defined osteolytic lesion	MEC	DLBCL	Not available	Not available
	13	43	Male	Left posterior maxilla	Swelling; tenderness; percussion pain of tooth 25	Ill-defined osteolytic lesion	Infected odontogenic tumor	DLBCL	chemotherapy	No recurrence for 12 years post-treatment follow-up
	14	41	Female	Right mandibular body	Swelling; pain	Saucerized bony defect	Malignancy	PL	Segmental resection and radiotherapy	No recurrence for 10 years post-treatment follow-up
	15	57	Male	Right mandibular body	Swelling; hypermobile tooth	Saucerized bony defect	SCC	PL	chemotherapy and radiotherapy	Expired 9 months later
	16	84	Male	Right mandibular body	Swelling; lip numbness; hypermobile tooth	Saucerized bony defect	OS	NK/T	Radiotherapy	Expired 4 months later
	17	21	Female	Right mandibular body	Swelling; painless	Well-defined radiolucent lesion	RC	LGCOS	Excision	No recurrence for 13 years post- operative follow-up
	18	43	Male	Left mandibular body	Asymptomatic	Ill-defined osteolytic lesion	Osteomyelitis	LGCOS	Excision	No recurrence for 5 years post- operative follow-up

	19	47	Female	Left mandibular body	Swelling	Well-defined radiolucent lesion	RdC	LGCOS	Enucleation	No recurrence for 11 years post-operative follow-up
	20	83	Male	Mandibular symphysis	Swelling	Exophytic radiopaque mass	Osteomyelitis	Parosteal OS	Not available	Not available
	21	55	Female	Left mandibular body	Swelling, hypermobile tooth	Ill-defined osteolytic lesion	Osteomyelitis	COS, fibroblastic	Not available	Not available
Osteogenic origin	22	62	Female	Right maxilla	Swelling; pain; ulceration	Ill-defined mixed lesion	SCC	COS, osteoblastic	Not available	Not available
	23	51	Female	Right mandibular body and ramus	Swelling; pain; paresthesia of lower lip	Ill-defined mixed lesion; external root resorption	COF	COS, osteoblastic	Segmental resection	No recurrence for 8.5 years post-operative follow-up
	24	19	Female	Left mandibular ramus	Swelling; pain	Ill-defined osteolytic lesion	Infected odontogenic tumor	COS, osteoblastic	Segmental resection and CCRT	Expired 7 months later
	25	68	Male	Mandibular symphysis	Swelling; pain	Ill-defined mixed lesion	Osteogenic tumor	COS, chondroblastic	Not available	Not available
	26	59	Female	Right maxilla	Swelling; tenderness	Ill-defined radiopaque lesion	Osteoma	COS, chondroblastic	Not available	Not available
	27	65	Female	Left maxilla	Swelling; pain	Ill-defined radiopaque lesion	OS	COS, mixed	Partial maxillectomy	Expired 1 year later
	28	39	Male	Right mandibular body	Swelling	Ill-defined mixed lesion; external root resorption	Odontogenic tumor	COS, osteoblastic	Segmental resection	No recurrence for 2 years post-operative follow-up
	29	72	Female	Right maxilla	Swelling	Ill-defined osteolytic lesion	COF	COS, fibroblastic	Partial maxillectomy and CCRT	No recurrence for 1 year post-operative follow-up

CCRT: concurrent postoperative chemotherapy and radiotherapy.
[a] Abbreviations of the clinical and pathological diagnoses were defined in Table 1.

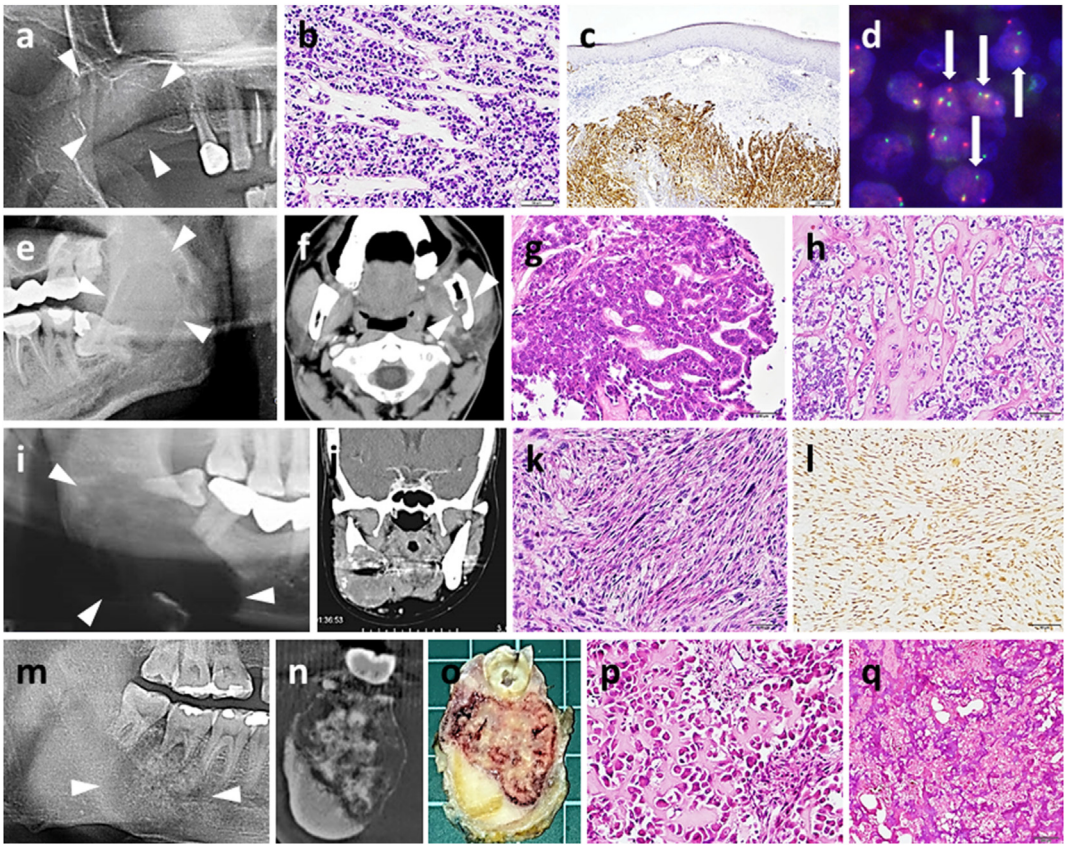

Figure 1 Radiographic, and microscopic photographs of selected cases of the current study (a—d) Case 4: clear cell odontogenic carcinoma, right posterior maxilla. (a) Panoramic radiography revealed an ill-defined osteolytic lesion of maxillary tuberosity. (b) The tumor cells with clear cytoplasm were arranged in strands and nests infiltrating in the fibrous stroma [hematoxylin and eosin (H&E) stain; magnification, 200 ×]. (c) Immunohistochemically, the tumor cells were positive for CK19 (magnification, 40 ×). (d) Split of the red signal from the green signal were identified, the break-apart fluorescence in situ hybridization (FISH) revealed that the tumor harbors EWSR1 rearrangement (e—h) Case 9: adenocarcinoma, not otherwise specified (NOS), left mandibular ramus. (e) Radiographic examination showed a well-defined unilocular radiolucency of the left ramus. (f) Computed tomography (CT) demonstrated a soft tissue lesion of left ramus with perforation of lingual border. (g) The tumor cells displayed glandular architecture (H&E stain; magnification, 200 ×). (h) A part of the tumor was composed of cords of monotonous cells with clear cytoplasm (H&E stain; magnification, 200 ×) (i—l) Case 10: malignant peripheral nerve sheath tumor, right mandibular body and ramus. (i) Panoramic radiography illustrated an ill-defined osteolytic lesion with perforation of lower cortical border (j) CT showed a soft tissue mass with prominent bony expansion and destruction of the borders over right mandible (k) The tumor composed of fascicles of spindle cells with nuclear atypia and pleomorphism (H&E stain; magnification, 200 ×) (l) The tumor cells were positive for the neurofilament protein (magnification, 200 ×) (m—q) Case 28: osteoblastic osteosarcoma, right mandibular body (m) Panoramic radiography revealed an ill-defined mixed radiolucent and radiopaque lesion over apical area of tooth 46 with spiking root resorption and thinning of lower cortical border (n) Cone beam CT revealed a central mixed lesion of mandibular body with buccolingual bony expansion. The border of the right mandibular canal was inconspicuous (○) Gross examination showed prominent calcified tissue formation of this lesion (p) The tumor constituted of atypical, plasmacytoid cells with adjacent lace-like osteoid materials (H&E stain; magnification, 200 ×) (q) The central area of the lesion composed entirely of osseous matrix (H&E stain; magnification, 40 ×).

plasmacytoma and diffuse large B cell lymphoma respectively, and one case of extranodal natural killer (NK)/T-cell lymphoma. The two cases of salivary gland malignancy were one case each of adenoid cystic carcinoma and adenocarcinoma, not otherwise specified (NOS) whereas the two cases of soft tissue malignancies were both malignant peripheral nerve sheath tumor.

There were 16 male (55.2%) and 13 female (44.8%) patients in the current study. The age of the 29 patients ranged from 19 to 84 years with a mean age of 57.4 years. The mean age of the male patients was 61.4 years while that of the female patients was 52.4 years. The mean age of patients with low-grade central osteosarcoma was 37.0 years, which was younger than the mean age of cases with conventional osteosarcoma (54.4 years). On the other hand, the mean age for patients involved by odontogenic carcinoma (68.9 years) was older than that for salivary gland cancer (44.0 years), malignant peripheral nerve sheath tumor (53.5 years), hematologic malignancy (60.6 years), and osteogenic sarcoma (52.6 years) respectively.

In the present study, mandible (22 cases, 75.9%) was the most common affected site in which mandibular body and/or ramus region (20 cases, 90.9%) was most frequently involved, and only two cases (9.1%) occurred in anterior segment of mandible. Only seven cases (24.1%) were present in maxilla with all cases located at premolar area to maxillary tuberosity.

The symptom most commonly presented in the study was swelling (25 cases, 86.2%), followed by pain (14 cases, 48.3%), paresthesia of lower lip (seven cases, 24.1%), hypermobile teeth (four cases, 13.8%), pus discharge (three cases, 10.3%), ulceration (two cases, 6.9%), and asymptomatic (one case, 3.4%).

Radiographically, an ill-defined osteolytic appearance was the most common feature (13 cases, 44.8%) in the present study. Ill-defined mixed or radiopaque features were present in six cases of conventional osteosarcoma. Five cases (17.2%) demonstrated well-defined radiolucent defects including one case of odontogenic carcinoma, two cases of salivary gland cancer, and two cases of low-grade central osteosarcoma. The saucerized bony defects were identified in two cases of solitary plasmacytoma, and one case of extranodal NK/T cell lymphoma. The case of parosteal osteosarcoma displayed an exophytic, radiopaque mass along the labial border of mandibular symphysis.

Most cases in the study were clinically diagnosed as malignancy or inflammatory diseases, such as osteomyelitis and infected odontogenic cyst/tumor according to their symptoms and radiological features. Noteworthy, there were serious discrepancies between clinical and pathological diagnoses for five cases (case 1, 8, 9, 17, and 19) revealing well-demarcated radiolucent appearance, which were clinically mistakenly diagnosed as ameloblastoma (case 1), periapical granuloma (case 8), odontogenic keratocyst (case 9), residual cyst (case 17), and radicular cyst (case 19).

The treatment modalities were well-documented in 22 cases in the present study. Moreover, 15 of the 22 patients (68.2%) with well-documented treatment modalities were surgically treated with segmental mandibulectomy or partial maxillectomy; and subsequent adjuvant radiotherapy and/or chemotherapy were performed in six of these 15 cases (40%). On the other hand, radiotherapy and/or chemotherapy were executed as primary therapy in only three of the 22 patients (13.6%) with available treatment modalities whereas the remaining four cases (18.1%) underwent enucleation or excision of the lesions.

Among the 29 cases in the current study, survival data was available in 19 cases. Additionally, 15 of the 19 cases (78.9%) with survival data were alive with disease free; the remaining four patients (case 15, 16, 24, and 27; 21.1%) succumbed to cachexia caused by cancer recurrence or disseminated disease during the first year follow-up period.

Discussion

Malignant tumors of the jaws are classified into three categories: (1) tumors invade to the mandible or maxilla from adjacent tumors, generally carcinomas of the oral cavity and sinonasal area; (2) metastatic jawbones lesions from other sites, and (3) primary cancers arising within the mandible and maxilla. The clinical and radiological manifestations of primary central malignancy of jaws are nonspecific; most cases, as noted in the present study, are present with a painful or painless swelling mass and as an osteolyitc lesion in radiographic examination. The presence of mucosal ulcer combining with saucer-shaped defect may suggest a periphery, mucosal origin. However, distinction between a metastatic tumor to jawbones and a primary intraosseous jawbone cancer is difficult because both lesions share similar clinical symptoms and radiological features. The mean age of patients with jawbone metastases was 52 years, and more than eighty percent of cases were found at mandible with predilection in the molar area.[7] The most common symptoms of metastatic cancers of jaws is pain, followed by paresthesia, swelling, and bleeding.[8] Radiographically, they usually appear as ill-defined osteolyitc lesion. Metastatic lesions from prostate, breast or kidney may show variable degree of ossification. A definitive histopathological examination with the aid of a panel of immunohistochemical stains, and thorough general medical survey can assist the diagnosis of a metastatic lesion.

Osteogenic sarcoma is the most common bone malignancies,[9] which is subclassified as osteosarcoma (including conventional, telangiectatic, small cell subtypes), low-grade central osteosarcoma, parosteal osteosarcoma, periosteal osteosarcoma, high-grade surface osteosarcoma, and secondary osteosarcoma in the recent released WHO classification of soft tissue and bone tumors.[10] Jawbone is the fourth common site of conventional osteosarcoma. Different to the conventional osteosarcoma of long bone having a bimodal age distribution (ages between 14 and 18 years, and age >40 years); the cases originating from jaws occur most in the third to fourth decades of life but over a broad age range.[10—12] However, the mean age of the cases in the current study was about 15 years older than the published literatures among different ethnicities.[10—12] This was probably due to the limited number of cases in the present study. Radiographically, osteosarcomas appear as ill-defined radiolucent to radiopaque lesions depending on the amount of osseous matrix formation. The classic "sun burst" periosteal reaction, spiking root resorption, as shown in Figure 1m of case 28, and widening of periodontal ligament space are also the radiographic features of gnathic osteosarcomas.[13] The prognosis of osteosarcomas is influenced by the anatomical location, the gnathic osteosarcomas reveals favorable prognosis and less frequency of distant metastasis. The 10 years survival rate is more than 80% as long as clear resection margins.[14]

In accordance with the location related to tooth and a well-demarcated, radiolucent feature in radiological examination, the intraosseous malignancies of jaws may mimic an odontogenic cyst or a periapical lesion.[15] In our cases, an intraosseous adenoid cystic carcinoma, and an adenocarcinoma, not otherwise specified (NOS) were clinically misdiagnosed as a periapical granuloma and odontogenic keratocyst respectively. Moreover, two cases of low-grade central osteosarcoma were previously considered as a radicular cyst and a residual cyst respectively. Although a clinically diagnosed benign gnathic lesion shifting to a pathologically confirmed malignant one is uncommon, it reminds clinical practitioners should be aware of the rare

possibility and emphasizes the importance of pathological examination.

Unlike conventional osteosarcomas, the low-grade central osteosarcomas usually show painless, long-term swelling and affect younger patients with the peak incidence in the third decade of life.[10] Radiographically, gnathic low-grade central osteosarcomas reveal as an ill-defined, osteolytic to sclerotic lesions.[16] Low-grade central osteosarcomas are composed of cellular fascicles of spindle cells with mild nuclear atypia and osseous production.[10] In view of the indolent clinical behavior and the histopathological features, low-grade central osteosarcomas may be misdiagnosed as benign fibro-osseous lesions such as fibrous dysplasia, cemento-ossifying fibroma or cemento-osseous dysplasia.[17] Previous research demonstrated that the immunoreactivity for MDM2 and CDK4 can assist the differential diagnosis of low-grade central osteosarcomas from benign mimics.[18]

The ectopic salivary gland tissue of jaws is one of the possible origins of the central salivary gland neoplasms. Not only in jawbones, the heterotopic salivary lesions had been reported in multiple locations, such as skin of the nose[19] and cervical lymph nodes.[20] The clinical and radiological features of central malignant salivary gland tumors are non-specific. The diagnosis relies on the histologic confirmation with the absence of any primary malignancies arising from adjacent major or minor salivary glands. In the current study, we presented two cases of mandibular malignant salivary gland tumors but no intraosseous maxillary case. The possible explanation may be due to the fact that upper jaw lesions originating from mucous gland of maxillary sinus or palatal minor salivary gland with invasion to maxilla might be difficult to discriminate from central lesions perforating the surrounding cortical borders.

Besides the ectopic salivary gland tissue, the metaplastic alteration of odontogenic epithelium is also considered as a possible origin of intraosseous salivary gland cancers.[21] The odontogenic lesions share some histological features with salivary gland tumors. For example, the metaplastic mucous cells or goblets cells are frequently identified in the lining epithelium of an odontogenic cyst. These features lead to the diagnostic dilemma between glandular odontogenic cyst and central mucoepidermoid carcinoma. Pires et al. found glandular odontogenic cyst and intraosseous mucoepidermoid carcinoma exhibiting different cytokeratin (CK) profiles, and CK18 and CK19 could be served as a tool in distinguishing both diseases.[22] The other instance for this diagnostic perplexity is the case 4 in our study, a case of clear cell odontogenic carcinoma, which displays similar histopathological characteristics to clear cell carcinoma of salivary gland. Clear cell carcinoma is a rare low-grade malignant salivary gland carcinoma composed of cells with clear cytoplasm lacking features of other clear cell rich salivary gland carcinomas with the most common sites of origin being the palate and tongue base; and usually arises in 60 years or older patients.[14] Clear cell odontogenic carcinoma is an extremely rare odontogenic carcinoma, with nearly 100 reported cases and 75% of them found in mandible.[14] Clear cell carcinoma and clear cell odontogenic carcinoma have extensive morphologic and immunohistochemical overlaps, and both of them harbor EWSR1 rearrangement.[23] Clear cell odontogenic carcinoma may represent a central example of clear cell carcinoma or, on the other hand, clear cell odontogenic carcinoma may be an odontogenic analogue to clear cell carcinoma. The positive reaction of CK19 was shown in various odontogenic epithelia[24] and could consider as a useful marker for recognizing odontogenic carcinoma.[25,26] For the location, radiographic features with extended bony destruction and diffuse expression for CK19 (Fig. 1c), a clear cell odontogenic carcinoma was rendered in cases 4.

Primary intraosseous carcinoma is defined as an odontogenic carcinoma with squamous differentiation, which is assumed to be derived from odontogenic epithelium such as epithelial lining of odontogenic cysts or other benign precursors.[14] Primary intraosseous carcinoma is a diagnosis of exclusion since its complexity makes it difficult to identify the origin. A metastatic squamous cell carcinoma, other odontogenic carcinoma, central salivary gland malignancy, and squamous cell carcinoma arising from adjacent epithelial tissue therefore must be excluded. The expression for CK19 in a central squamous differentiated carcinoma also indicates a possible odontogenic epithelial origin.[14] On the other hand, the patient of the only one case of ameloblastic carcinoma (Case 1) in the study was suffered from multiple recurrences during post-operative follow-up.

Many types of hematologic malignancy and primary soft tissue sarcoma arising in jawbones had been reported in the literatures, such as diffuse large B-cell lymphoma, plasmablastic lymphoma,[27] solitary plasmactyoma,[28] malignant peripheral nerve sheath tumor,[29] angiosarcoma,[30] Ewing sarcoma,[31] and synovial sarcoma.[32] Like other intraosseous malignancies, the clinical symptoms and radiological appearances of these diseases in jawbones are non-specific. The accurate diagnosis leading proper treatment relies on the histopathological features, analysis of immunological profiles,[33–35] and detection of molecular alterations.[36,37]

In conclusion, the current study indicates that primary intraosseous malignancy rarely affects gnathic area, and it shows predilection for mandible. It is important to realize that the diseases may manifest as pain or painless swelling mimicking infectious process, benign cysts or neoplasms. The clinical practitioners should be aware that localized advanced bony destruction combined with aggressive clinical course and lower lip paresthesia may be signs of malignant lesions. The early diagnosis and treatment are essential to patients' overall survival.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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