RESEARCH

A clinicoradiological study of odontogenic carcinomas and their impact on clinical diagnosis

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Objectives: To investigate the clinical and radiological characteristics of odontogenic carcinomas (OCs) and evaluate their impact on early clinical diagnosis.

Methods: The clinical and radiological features of all patients with OCs in our pathology record from January 1988 to December 2009 were retrospectively reviewed. The impact on a tentative diagnosis before final histological examination of clinical, panoramic and CT features was investigated.

Results: Of 474 cases with malignant jaw tumours, 417 (88%) were gingival squamous cell carcinomas (SCCs) and 27 (6%) were OCs. The average age of the patients with OCs was significantly lower than that of those with gingival SCCs. 20 OCs were in the mandible and 7 were in the maxilla. 22 OC patients (81%) had pain and/or swelling as an initial symptom of the disease. Although the majority of OCs showed irregularly contoured radiolucency, one-third of the cases showed cyst-like radiolucency totally or partially surrounded by a sclerotic rim on panoramic radiography. Permeative or gross cortical bone destruction and mass extension outside the jaw bone were found on CT and a diagnosis of malignant tumour was more common. Mass extension outside the cortex had a significant influence on malignant diagnosis. However, 22% of the patients were still clinically diagnosed as having osteomyelitis after CT.

Conclusions: Although CT was useful to obtain a diagnosis of malignant tumour in OC patients, 22% of patients were clinically diagnosed as having osteomyelitis even after CT. When an osteomyelitis case is resistant to conventional therapy and gross bone destruction and/or mass extension is found on CT, a histopathological examination should be done.

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Introduction

Malignant odontogenic tumours are classified as odontogenic carcinomas and odontogenic sarcomas. According to the World Health Organization Classification of Tumours published in 2005, odontogenic carcinomas (OCs) include malignant ameloblastomas, ameloblastic carcinomas, primary intraosseous squamous cell carcinomas, clear cell odontogenic carcinomas and ghost cell odontogenic carcinomas.¹ Early diagnosis of the malignant disease has a significant influence on prognosis. However, recognition of OCs is sometimes delayed. One reason for this is that the clinical characteristics of the

disease are not well realized.^{2–7} Here, we report clinical and radiological features of 27 patients with OCs found on our pathological list from the past 20 years.

The aim of this paper was to investigate the clinical and radiological characteristics of odontogenic carcinomas and evaluate their impact on early clinical diagnosis.

Materials and methods

Patient selection

The clinical records and pathological reports of all patients who were pathologically diagnosed as having malignant tumours in the maxilla or the mandible at the department of Diagnostic Oral Pathology of the Dental

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Table 1 Histopathological classification and clinical data of 474 patients with malignant tumours in the jaws in our histological record (1998–2009)

Histopathology	Number of patients	Average age (years)	Male–female	Maxilla–Mandible
Squamous cell carcinomas	417 (88.1%)	67 ± 11	229:188	125:292
Odontogenic carcinomas	27 (5.7%)	60 ± 12	22:5	7:20
Other carcinomas ^a	21 (4.2%)	63 ± 12	11:10	8:13
Sarcomas ^b	9 (1.9%)	46 ± 14	7:2	4:5
Total patients	474	66 ± 12	269:205	144:330
Significant difference ^c		$p < 0.001$	NS	NS

NS, not significant.

^a2 undifferentiated carcinomas, 3 adenocarcinomas, 3 adenoid cystic carcinomas, and 13 mucoepidermoid carcinomas.^bThree malignant lymphomas; three malignant fibrous histiocytomas, three undefined sarcomas.^cAmong histopathological groups by χ^2 test. Significance level: $p = 0.05$.

Hospital, Tokyo Medical and Dental University, Tokyo, Japan, from January 1988 to December 2009 were retrospectively reviewed. Patients who were diagnosed as having malignant tumours at a distant site or who had previously undergone surgery or radiotherapy for a malignant tumour in the head and neck were excluded.

Diagnosis of OC

The diagnosis of OC was made on the basis of (1) the histopathological criteria defined by the WHO classification, or (2) when the pathological findings of the surgical specimen strongly suggested the possibility and the clinical record showed that there was no mucosal involvement before incisional biopsy. The patients who were diagnosed as having the primary site in the maxillary sinus or soft tissues adjacent to the jaws were excluded.

Imaging

All OC patients underwent orthopantomography at the first visit to the hospital. CT was done with a spiral CT scanner (Somatom[®] plus S; Siemens Medical Systems, Erlangen, Germany) before starting tumour treatment. Axial 4-mm-thick soft-tissue-contrasted images, 2-mm-thick bone-contrasted images and dental CT images reconstructed using a built-in program were analysed. All the images were evaluated by two experienced oral and maxillofacial radiologists (MI and AK) with consensus.

Statistical analysis

Statistical analysis was performed by the χ^2 test at a significance level of $p < 0.05$ using SPSS[®] v. 11.0 (SPSS, Chicago, IL).

This retrospective study was approved by the institutional review board, and the requirement to obtain informed consent was waived.

Results

Histopathological distribution of malignant tumours in the jaws

474 patients with malignant tumours in their jaws were found from the pathological file during the period. Table 1 shows the histopathological distribution and clinical features of the patients. The average ages of the

patients were significantly different among pathological groups. The average age of the patients in the sarcoma group was the youngest and that in the squamous cell carcinoma (SCC) group was the oldest. There were no significant differences in the gender ratio (male–female) among the pathological groups. Malignant tumours occurred more frequently in the mandible than in the maxilla in all pathological groups.

OC in the maxilla and the mandible

Of 474 patients with malignant tumours in the jaws, 27 (5.6%) were diagnosed to have OC. Clinical findings of patients with OC are shown in Table 2. 7 (26%) patients with OC had lesions in the maxilla and 20 (74%) had lesions in the mandible. The average age of the patients was 60 ± 12 (range 21–82) years. The average age of the patients with maxillary lesions was significantly lower than that of the patients with mandibular lesions. Most maxillary lesions occurred in the anterior jaw and all mandibular lesions occurred in the posterior jaw. 11 (55%) of the mandibular cases had lesions in the mandibular angle.

Clinical symptoms of OC

22 (81%) patients with OC had pain and/or swelling of the alveolar bone as an initial symptom of the disease. 5 (19%) patients with OC complained of paraesthesia or anaesthesia of the lip and gingiva. All of these patients had lesions in the mandible. The main complaint of three patients was a mobile tooth. Six patients had clinical symptoms related to impacted third molars (Figure 1–3). Two other patients were diagnosed as

Table 2 Clinical findings of 27 patients with odontogenic carcinomas (OCs): difference between the patients with OCs in the maxilla and those with OCs in the mandible

Characteristics	Maxilla	Mandible	Total	Significance ^a
Number of patients	7	20	27	
Average age ± SD (years)	49 ± 17	64 ± 11	60 ± 12	$p = 0.018$
Male–female	5:2	17:3	22:5	NS
Anterior jaw–posterior jaw	6:1	0:20	6:21	$p < 0.001$

NS, not significant; SD, standard deviation.

^aDifference between the maxilla and mandible by χ^2 test. Significance level: $p = 0.05$.

Figure 1 A 60-year-old female noticed pain and swelling in the right mandible over 1 month. Her dentist treated her for periodontitis in the right molar area, but as paraesthesia appeared in the right mental region, she was referred to our hospital. At the first visit, she had swelling in the right mandible without abnormal findings in the mucosa. (a) On orthopantomography, diffuse radiolucency without a corticated rim was found in the right mandible (arrows). The embedded right third molar was distally displaced and a gap appeared between 47 and 48 (arrowhead). (b) A bone-contrasted CT image. There was gross (arrows) and permeative bone destruction (arrowheads) in the right mandible

having tooth-related cysts (Figure 4). 10 (37%) patients underwent tooth extraction because of complaints before receiving a clinical diagnosis of malignancy.

The average period from the first visit to the local clinic and final histopathological diagnosis was 8 ± 6 weeks (range 3 days–5 months).

Figure 2 A 76-year-old female suffered from pain and swelling in the left mandible for two months. Antibiotics and non-steroidal anti-inflammatory drugs had no effect. (a) Orthopantomography showed an ill-defined radiolucency including the embedded third molar (arrows). The embedded tooth was extracted under a diagnosis of pericoronitis. (b) Orthopantomography 2 months after tooth extraction. The film showed large, ill-defined bone destruction in the right mandibular angle (arrows). (c) A contrast-enhanced CT image showed ragged bordered bone absorption and soft tissue mass in the left mandible (arrowheads)

Figure 3 A 66-year-old male noticed paraesthesia in the left mental region and pain in the left mandible. Medication had no effect. (a) An orthopantomography at his first visit showed a ragged bordered radiolucency under the embedded left third molar (arrows). (b) A soft tissue contrasted CT image showed tumour extension outside the bone (arrowheads). (c) A bone-contrasted CT showed an embedded tooth and gross buccal cortical bone destruction (arrow)

Orthopantomographic findings of OCs

Table 3 shows orthopantomographic findings of OCs. 70% of the patients had diffuse (Figure 1a) or irregular-shaped (Figures 2a and 3a) radiolucency without a sclerotic rim, 26% showed cystic radiolucency totally or partially demarcated by a sclerotic rim (Figure 4a), and one patient showed no recognizable radiolucency on panoramic radiography (Figure 5a).

The main location of the lesion on orthopantomography was in the alveolar bone in 9 (33%) patients and in the central area of the bone in 9 (33%) patients, and 8 (30%) patients had a large lesion including both the centre and periphery of the bone.

Clinical diagnosis after orthopantomography

After orthopantomography and before pathological examination, 13 (48%) patients were diagnosed with malignant tumours, while 9 (33%) were diagnosed with inflammation and 5 (19%) with benign tumours or cysts. The correlation between radiological features and the tentative diagnosis is shown in Table 4. The location, corticated rim, contour characteristics and

the relationship with teeth significantly influenced the tentative diagnosis. The lesions located peripheral to the central area were diagnosed as malignant, but other locations did not specially indicate a malignancy. All lesions diagnosed as benign tumours were centrally located and had smooth contours with a corticated rim.

Impact of CT examination on clinical diagnosis

After the CT examination, the diagnosis for 8 (30%) patients was correctly changed to malignant tumour. Four of eight cases had been diagnosed as inflammation, one as a benign tumour and three as cysts. Table 5 shows how CT findings influenced the change in imaging diagnosis. The periosteal reaction and permeative cortical destruction did not indicate the diagnosis of malignancy in preference to inflammation. Mass extension outside the cortex had a significant influence on determining a malignant diagnosis. Eventually, 21 (78%) patients were diagnosed with malignant tumours before histological examination. 6 (22%) patients were not suspected as malignant. Five of them were treated as inflammatory cases (one as failure of extracted

Figure 4 A 48-year-old male noticed paraesthesia in the right palate 3 months earlier. Because of swelling in the palate and tooth dislocation, the patient was referred to our hospital. (a) Orthopantomography showed a radiolucent lesion demarcated by a corticated rim in the anterior maxilla that included an embedded left canine (arrows). (b) A soft tissue contrasted CT showed gross cortical bone destruction and soft tissue extension to the buccal side (arrowheads)

Table 3 Orthopantomographic findings of the 27 cases with odontogenic carcinoma

Radiological findings	Maxilla	Mandible	Total (%)
Diffuse or ill-defined radiolucency	2	17	19 (70)
Partially corticated radiolucency	5	2	7 (26)
No discernible radiolucency	0	1	1 (4)

The distribution of the panoramic findings was significantly different between the maxilla and the mandible by chi-square test at $p=0.005$.

wound healing and four cases as osteomyelitis), and the remaining one case was treated as a patient with a cyst. The patient diagnosed with a cyst did not show any cortical bone abnormalities on the first CT examination. A significantly frequent CT abnormality found in the "malignant tumours" group against the "osteomyelitis" group was mass extension ($p=0.001$) outside the cortical bone. The average time period between the first visit to a clinic and final diagnosis for OCs by biopsy specimens was 7 ± 5 weeks for the malignant group and 12 ± 8 weeks for the osteomyelitic group. The difference was not significant using the χ^2 test ($p=0.074$).

Discussion

In previous studies, the frequency of primary intraosseous carcinomas in odontogenic tumours was diverse.⁸⁻¹⁰ Our study showed that 27 (6%) of 474 patients with malignant tumours in the jaws had OCs. When the tumour developed in the central part of the bone, it grew to destroy the cortex bone, and the tumour mass may have merged with the surface mucosa. In such cases, the OC cannot be distinguished from a gingiva-originated SCC and is diagnosed as a gingival SCC. Therefore, the frequency of OCs in oral malignant tumours may have been higher than the present estimate.

The majority of OCs showed irregularly shaped ill-defined radiolucency on orthopantomography. However, 30% of the present patients with OC did not show such a typical malignant pattern. 26% of the patients had smooth-contoured radiolucency partially demarcated with a cortical rim, especially those with OCs in the maxilla. This discrepancy in the radiographic pattern and histological diagnosis may be the main reason why less than half of the patients were diagnosed with malignant tumours before CT. As shown in Table 4, all five cases diagnosed as benign tumours or cysts had centrally located smooth-contoured radiolucency with a corticated rim. Comparing the clinical diagnoses for inflammation and malignant tumours, radiolucency including both the periphery and the central part of the jaw helped the observer to confirm malignancy (χ^2 test, $p=0.013$). It means that the large amount of bone destruction had a strong impact on the clinical diagnosis. Contour irregularity or absence of the corticated rims on orthopantomography had no significant impact on differentiating malignant tumour from inflammation.

CT is known to be useful for diagnosing OCs because of its three-dimensional imaging function.¹¹ After undergoing CT, 21 (78%) of the patients had suspected malignancies. The CT finding that gave the observer a significant suspicion for malignancy was mass extension outside the cortical bone.

However, 6 (22%) of the patients had no malignant diagnosis after CT. One lesion was totally surrounded by a sclerotic rim and was diagnosed as a benign tumour. The patient was found to have a malignant tumour after an open biopsy for the lesion. The remaining five were diagnosed as osteomyelitis. The majority of these cases showed gross or permeative cortical bone destruction with or without a periosteal reaction. One patient showed a mass extension outside the cortical bone, but the extent of the mass was slight. The period before final diagnosis by histological examination tended to be longer for cases that were initially diagnosed as

a **b**

Figure 5 A 57-year-old male referred to our hospital because of delayed healing of the extracted socket of the lower right second molar. There was no swelling or ulcer in the region. (a) Orthopantomography showed no discernible abnormality in the right mandible. (b) A CT image showed a slight alveolar absorption in the right mandible (arrow)

Table 4 Correlation between the radiographic pattern on panoramic tomography and the tentative diagnosis for the patients with odontogenic carcinoma

Orthopantomographic findings		Tentative diagnosis			Significance ^a
		Malignant tumour (%) (13 patients)	Inflammation (%) (9 patients)	Benign tumour (%) (5 patients)	
Location					
	Central	2 (15)	3 (33)	5 (100)	$p < 0.001$
	Peripheral	3 (23)	6 (67)	0	
	Peripheral to central	8 (62)	0	0	
Corticated rim (+)		1 (8)	1 (11)	5 (100)	$p < 0.001$
Contour		10 (77)	7 (78)	0	$p = 0.006$
	Smooth	3 (23)	1 (11)	5 (100)	
	Not discernible	0	1 (11)	0	
Relation with teeth					$p = 0.021$
	Including	4 (31%)	0	1 (20%)	
	Periapically located	1 (8%)	0	3 (60%)	
	Recently extracted site	3 (23%)	4 (44%)	0	
	Missing	5 (38%)	5 (56%)	1 (20%)	

^aSignificance of difference in frequency among tentative diagnosis groups by χ^2 test.

Table 5 CT findings affected effect on diagnoses

CT findings	Patients ^a	Clinical diagnoses after CT			Significance ^b
		malignant tumour (21 patients)	osteomyelitis (5 patients)	benign tumour (1 patient)	
Periosteal reaction	7	4	3	0	NS
Permeative cortical destruction	10	7	3	0	NS
Mass extension outside the cortex	20	19	1	0	$p = 0.001$
Gross cortical destruction	24	20	4	0	NS

NS, not significant.

^aNumber of the patients with CT findings.

^bDifference in number between patients diagnosed as malignant before and after CT, by χ^2 test.

inflammation, but the difference was not statistically significant. This is because our standard treatment for cases clinically diagnosed as chronic osteomyelitis that is resistant to treatment includes histopathological examination. Therefore, the delay before final diagnosis of malignancy was minimum in most of such cases.

All the patients underwent surgery with or without combined therapy. More cases will be needed before correlating the treatment outcome with radiological and clinical variations.

Conclusion

Of 474 cases with malignant tumours of the jaws, 417 (88%) were gingival SCCs and 27 (6%) were OCs. The average age of the patients with OCs was significantly younger than those with gingival SCCs. 20 OCs were in

the mandible and 7 were in the maxilla. 22 (81%) OC patients had pain and/or swelling as an initial symptom of the disease. Although the majority of OCs showed irregularly contoured radiolucency, one-third of the cases showed cyst-like radiolucency totally or partially surrounded by a sclerotic rim on panoramic radiography. CT was useful to diagnose malignant tumours. However, 22% of the patients were not diagnosed as having malignancy even after CT. Histopathological examination is mandatory when an osteomyelitis case is resistant to conventional therapy to differentiate from a malignant tumour.

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