Primary intraosseous carcinoma associated with impacted third molar of the mandible: review of the literature and report of a new case

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Abstract: This study investigated the clinicopathologic features of primary intraosseous carcinoma (PIOC) related to the third molar of the mandible. Six cases (5 from the literature and 1 new case; mean patient age 73 years) of PIOC associated with completely impacted lower third molar were analyzed. For comparison, 8 cases of PIOC presenting after extraction of the lower third molar were also evaluated, with a significantly lower mean patient age of 56 years. Most lesions were deceptively similar to those related to the lateral type of dentigerous cyst, and half of the impacted cases revealed an asymptomatic fracture of the mandible. In all patients except for the present case, metastasis had not been recorded. Surprisingly, no patients are known to have died of PIOC. In our experience the prognosis of PIOC associated with a completely impacted third molar is much better than commonly believed, although the number of cases involved is too small to make a general conclusion. However, delay in establishing the correct diagnosis followed by extraction without awareness of the carcinoma is known to adversely affect the prognosis. (J. Oral Sci. 43, 287-292, 2001)

Key words: primary intraosseous carcinoma; squamous cell carcinoma; impacted lower third molar; tooth extraction.

Introduction

Primary intraosseous carcinoma (PIOC) is a squamous cell carcinoma arising *de novo* within the jawbones from epithelial residues of the odontogenic apparatus (1). In adults, the reduced enamel epithelium surrounding the crown of an impacted tooth, the epithelial rests of Malassez within the periodontal ligaments, and the remnants of dental lamina in the bone may serve as identifiable sources of PIOC (2). True PIOC is completely enclosed in bone and exhibits a dentigerous relationship to the affected tooth. Although the third molar region of the mandible is the most commonly affected site, the relationship between PIOC and the third molar has not been fully discussed in the literature.

There are many potential pitfalls in the diagnosis of PIOC. Problems arise when ceratin cases appear after tooth extraction and when there are no pre-extraction radiographs available. Moreover, previous studies have not differentiated strictly between true PIOC and gingival squamous cell carcinoma, in which most of the tumor is situated in the bone and the mucosal lesion is minimal or absent (3,4).

The purpose of this study was twofold: (i) to analyze critically the clinicopathologic features of six cases of PIOC associated with a completely impacted third molar of the mandible (5-9), and (ii) to compare these results with those of eight cases of PIOC detected after removal of the lower third molar (10-16). In addition, the difficulties in distinguishing PIOC from the intraosseous growth of a gingival carcinoma are discussed by reviewing the literature.

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Fig. 1 Photograph showing that the covering mucosa was intact (mirror image of the oral cavity).

Fig. 2 Panoramic radiograph of the right mandible showing an irregular radiolucent area below the horizontally impacted third molar.

Fig. 3 Moderately differentiated squamous cell carcinoma invading bone tissue. HE, original magnification $\times 40$.

Case Report

A 74-year-old man was referred with a painful swelling in the right posterior mandible. The lesion had been noticed by the patient two weeks previously. His medical history was noncontributory. On examination, there was a firm, nonfluctuant, diffuse swelling at the retromolar pad. Except for a narrow fistula, the overlying mucosa was completely intact (Fig. 1). Radiographic examination revealed a horizontally impacted third molar with an associated poorly defined 3.2×2.5 cm radiolucency (Fig. 2). The right submandibular lymph nodes were palpable. Following the diagnosis of an infected odontogenic tumor, an incisional biopsy was performed. At biopsy the tumor was solid and contained no fluid. The histology was reported as squamous cell carcinoma. A full medical

Fig. 4 An abrupt transition from normal-appearing fistulous epithelium to carcinoma. HE, original magnification $\times 40$.

Fig. 5 Squamous cell carcinoma metastatic to submandibular lymph node. HE, original magnification $\times 100$.

examination did not reveal any evidence of a separate primary site. Partial mandibulectomy including from the right canine region to the right mandibular ramus except for the condylar process and a right radical neck dissection was performed, followed by chemotherapy and irradiation. The patient recovered well and has shown no recurrence after 12 months of follow-up.

Histologically, the surgical specimen consisted of a moderately differentiated squamous cell carcinoma with no evidence of a cystic component. The mandibular bone had been replaced by an extensive mass of carcinoma (Fig. 3). The tumor nests were superficially in contact with the normal-appearing fistulous mucosa, but they did not appear to be developing from it (Fig. 4). The carcinoma showed an intimate relationship with the impacted tooth but multiple histological samples did not show it to be continuous with the reduced enamel epithelium surrounding the crown. Sections from the regional lymph nodes revealed a metastatic carcinoma in 1 of 8 nodes (Fig. 5).

Materials and Methods

The English- and Japanese-language literature was critically reviewed for well-documented cases of PIOC associated with a completely impacted lower third molar. A total of six cases were found to be suitable for analysis: five from the literature (5-9) plus the present new case. The excluded cases included: (i) a case reported by Saito et al. (17) for which the only evidence of the lesion was a biopsy; (ii) a case reported by Lindqvist and Teppo (18),

in which no dentigerous relationship of the tumor to the third molar was available; (iii) three cases which probably represented malignant changes in dentigerous cysts (15,19,20); and several other cases which were not properly documented (8,21).

For comparison, eight cases in which PIOC presented after removal of the lower third molar were analyzed clinicopathologically (10-16).

Results

The clinicopathologic features of PIOC associated with a completely impacted lower third molar are summarized in Table 1. The mean age of the 6 patients was 73 years (range 69–76 years), and 3 were male. In nearly all of the lesions, the true duration was obscure. The impacted third molars were inverted (3 cases), horizontal (2 cases), or mesioangular (1 case). In most lesions the radiolucency appeared below the impacted tooth. Half of the patients exhibited a pathological fracture of the affected mandible. Except for the present patient, no lymph node metastasis was documented. In all cases carcinoma had not been suspected. Only 1 patient had died during the follow-up, which averaged 20 months, and thus the prognosis was excellent.

In the 8 cases in which PIOC was detected after removal of the third molar (Table 2), the mean age of the patients was 56 years (range 31–73 years), and 6 of the patients were male. The referring doctors erroneously diagnosed most lesions as pericoronitis. The mean time-interval between third-molar removal prior to referral and establishment of the correct diagnosis was 5.7 months, with a range of 1–11 months. Half of the patients had lymph node metastasis and are known to have died of PIOC; therefore the prognosis was worse than for the patients with an impacted molar.

Discussion

The results of the present study are in general agreement with a previous report (7). It is interesting that the mean age of patients without third-molar removal prior to referral was significantly higher than that of those with extraction (73 years versus 56 years). This suggests that PIOC itself may be a slow-growing lesion which can remain static for a long time. The prognosis overall was much better than is generally believed if the lower third molar involved in PIOC had not been needlessly extracted by the referring doctor.

The origin of a mandibular central carcinoma around the impacted third molar can be primary, secondary metastatic, or bony extension of a gingival tumor (1,2,22). Only lesions developing from the lung were squamous cell

Table 1 PIOC associated with completely impacted lower third molar

Author	Age/gender	Angular position of ITM	Location of radiolucency	Pathological fracture	Prognosis
Takeda et al. (5)	70/F	Horizontal	Below ITM	Yes	Alive at 24 months
Sluotweg (6)	73/M	Mesioangular	Mesial to ITM	Yes	Died 7 days*
To et al. (7)	76/M	Inverted	Below ITM	Yes	Alive at 12 months
Venta et al. (8)	69/F	Inverted	Below ITM	No	Alive at 18 months
Ide et al. (9)	74/F	Inverted	Pericoronal	No	Alive at 36 months
Shimoyama et al. (current case)	74/M	Horizontal	Below ITM	No	Alive at 12 months

ITM, impacted third molar.

*Pulmonary embolism.

Table 2 PIOC presenting after lower third molar extraction

Author	Patient age/gender	Range of delay in diagnosis	Lymph node metastasis	Prognosis
De Lathouwer and Verhest (10)	67/M	5 months	Yes	Died at 14 months
Nolan and Wood (11)	35/M	1.4 months	Yes	Died at 12 months
McGowan (12)	48/M	9 months	No	Alive at 18 months
Saito et al. (13)	31/M	1 month	Yes	Alive at 6 months
Usui et al. (14)	67/M	2 months	Not stated	Died at 8 months
	66/F	10 months	Yes	Died at 48 months
Papageorge and Lincoln (15)	73/F	11 months	No	Alive at 8 months
Watanabe et al. (16)	62/M	6 months	No	Alive at 19 months

carcinomas that metastasized to the mandible (1,7). The possibility of a metastatic tumor can be excluded by radiographic examination of the chest over a follow-up period of more than 6 months (7). The lack of surface mucosal changes such as an ulcer or tumor is one of the diagnostic clues that differentiates a PIOC from a gingival carcinoma (23). However, at discovery most PIOC have been present for a prolonged period, as indicated by their large size and the fact that the carcinoma has already destroyed the surrounding tissue. Moreover, the patients are usually referred for further evaluation of nonhealing extraction sites (10-16). Therefore it may not always be possible to demonstrate the intact oral mucosa.

Although PIOC is of putative odontogenic epithelial origin, histological similarities to the enamel organ are lacking in most – but not all – cases. Except for cases that convincingly arise from a reduced enamel epithelium (5-9), evidence for the odontogenic origin is only circumstantial (6,9). To our knowledge there are no published cases that showed evidence – at the microscopic level – of the transition from the rests of Malassez or dental lamina to the carcinoma. When a squamous cell carcinoma developing from the inner gingival sulcus of an impacted third molar presents intraosseous invasion, it is often indistinguishable from PIOC (3,4). Several well-documented cases of gingival carcinoma of sulcular epithelial origin have been reported (24-29). These carcinomas did not exhibit any visible evidence of malignancy. Subsequently, they may cause early bone involvement due to the immediate vicinity of the crown of the impacted tooth to mandibular bone. In advanced lesions, whatever their antecedent origin, the original point of malignant change may no longer be visible. Therefore, the definitive diagnosis of PIOC often necessitates the exclusion of gingival carcinoma (3,4,30,31), which makes initial radiographs before surgical intervention mandatory.

Regardless of origin, carcinoma associated with the lower third molar may present initial signs that are suggestive of a benign pericoronal infection (8,32). Since squamous cell carcinoma of the dentate gingiva itself has a particular propensity to mimic inflammatory conditions of dental origin (33,34), extraction of the teeth involved in the carcinoma is a common initial treatment (21). Venta et al. (8) reported such cases, among which one definitive example of PIOC was included. Surgical removal of the unerupted or impacted third molar is the single most common operation in dentistry (35). Early literature on the indication for prophylactic removal of asymptomatic third molars discussed the possibility of the development of cysts and tumors (36). However, there now is general agreement that such future risks are overemphasized (37,38). Recently

Guven et al. (39) discovered a single example of intraosseous carcinoma in their retrospective study of 9994 impacted third molars. Despite its rarity, great care should be taken to avoid missing an underlying PIOC masquerading as a pericoronitis.

Conclusion

We have presented a new case of PIOC associated with a completely impacted third molar of the mandible. The factor considered more likely to affect the prognosis is delayed diagnosis following erroneous extraction. To secure the diagnosis of PIOC, it is crucial to use clinical and histological techniques to rule out other types of lesion exhibiting squamous cell carcinoma histology.

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