



## Primary intraosseous squamous cell carcinoma of the mandible: A case report

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### ABSTRACT

Carcinoma as a primary tumor within the jaw is a rare phenomenon which usually arises from the epithelial lining of oral cavity or salivary glands. Primary intraosseous squamous cell carcinoma is a malignant neoplasm with no initial connection to oral mucosa. In this article, we reported two rare cases of primary intra-mandibular squamous cell carcinoma with clinical, radiographic, and histopathologic features and reviewed the literature.

**Keywords:** Oral cancer; Squamous cell carcinoma; Malignancy.

### Introduction

Oral squamous cell carcinoma (OSCC) is the most prevalent type of oral cancer, constituting 95% of localized neoplasms in the oral cavity [1]. Malignant lesions of soft palate, floor of mouth, and lateral and ventral aspects of tongue, which are surfaced by unkeratinized mucosa are common manifestations. Carcinogens dissolved in the saliva are presumed to have prolonged contact with a thin mucosal barrier, thus providing better access to surface epithelial squamous cells [2]. Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare malignant tumor defined as a SCC developing within the jaw and arises from odontogenic epithelium remnants

with no initial connection to oral mucosa [3,4]. The etiology and diagnostic criteria for PIOSCC are obscure, which makes it difficult to diagnose. Although reactive inflammatory stimulus as an etiologic factor is probable [5].

According to the 2005 World Health Organization (WHO) Classification of Tumors, PIOSCC is categorized into three subtypes: solid tumors which invade bone marrow spaces and induce osseous resorption, SCCs arising from odontogenic keratocysts, and SCCs arising from other benign epithelial odontogenic tumors [6]. Precise clinical, imaging, and histopathological information are

required to determine the origin [7].

### Case 1

A 49-year-old Iranian housewife female was presented to the Department of Oral Medicine, School of Dentistry, Tehran University of Medical Sciences with a chief complaint of pain and swelling in the right mandibular molar region which was first noticed by the patient 3 months earlier. She reported that initially there had been a gradual increase in size, but during the last month, she began experiencing rapid growth. At the onset of pain, she went to a dental clinic and a general dentist performed root canal therapy on the right mandibular 2<sup>nd</sup> molar which showed signs and symptoms of periodontal disease. Afterwards, the pain and swelling didn't get better. After some days, posterior tooth became loose and was extracted.

Upon intraoral examination, swelling in lingual overlying mucosa of the right mandibular 2<sup>nd</sup> molar was noticed. An unhealed painful extraction socket containing lobular mass in lower right 3<sup>rd</sup> molar region was also detected (Fig 1). No other significant findings were found by general examination. Her past medical history revealed that she was taking calcium supplements and levothyroxine tablets for a period of time. Her social history showed that she did not have any hazardous habits such as smoking or alcohol consumption. Her family history was not significant for cancer, either.

In CBCT, cross-sectional and axial images, an ill-defined radiolucent lesion measuring 35.5×8.4×7.9 was observed in the right mandibular molars region. Unhealed extraction socket of third molar in this region also showed ill-defined borders. The upper border of mandibular canal was destructed by the lesion. No PDL widening or root resorption was seen in adjacent teeth (Fig 2). Radiographic features were highly suggestive of a malignant lesion in bone, thus with the patient's consent, an incisional biopsy was performed on the mass, under local anesthesia. This specimen was then submitted for histopathologic examination in formalin. Microscopic examinations showed a malignant epithelial tumor consisting of infiltrating nests of epithelial cells infiltrating between the bone trabeculae by forming individual cells and small nests. In the superficial part, the tumor revealed abundant keratin pearl formation, marked cellular polymorphism, increased mitotic figures and occasional atypical mitosis (Fig 3). Hence on the basis of microscopic examination, clinical findings, and radiographic features, this case

was diagnosed as primary intraosseous squamous cell carcinoma, solid type (moderately differentiated, keratinizing type). Then the patient referred to an expert oncologist. A whole body CT scan was performed and excluded any abnormality and evidence of metastatic migration in other parts of her body. Finally, she was treated with radical surgery, neck dissection, and post-operative radiotherapy.

### Case 2

A 46-year-old Iranian female was referred to the department of oral and maxillofacial pathology, School of Dentistry, Tehran University of Medical Sciences with an exophytic lesion on gingiva for two months after extraction of right 2<sup>nd</sup> mandibular molar tooth. Upon intraoral examination there were no other obvious mucosal changes. General examination of the patient revealed no significant findings, too. Overlying skin was normal in color and texture and had no palpable spots. No cervical lymphadenopathy was detected on her right submandibular area and all vital signs were in normal range. Her past medical history revealed that she was taking losartan for about 4 years. Her social and family history did not reveal any important information.

In CBCT, cross-sectional and axial views, a radiolucent lesion measuring 29×14×15mm with ill-defined borders was observed distal to 1<sup>st</sup> mandibular molar. Buccal and cortical plates were destructed by the lesion. No root resorption or displacement was detected in the adjacent tooth. Mandibular canal borders were remained intact (Fig 4). Radiographic features were suggestive of a malignant lesion, so an incisional biopsy was performed on the exophytic part of the lesion, under local anesthesia, and submitted in formalin. Microscopic sections showed proliferation of large epithelial cells with severe pleomorphism demonstrating numerous atypical mitotic features and some cells with hyperchromatic nuclei admixed with scattered large cells with foamy and clear cytoplasm. The tumoral cells were arranged in small nests and short strands and also single cells. Superficially parakeratotic stratified squamous epithelium was ulcerated in many areas (Fig 5). The features of this case were in favour of primary intraosseous squamous cell carcinoma, solid type, but to rule out metastatic carcinomas, patient's workup was performed and finally approved the diagnose. she was treated with neck dissection and local radical surgery, in combination with postoperative radiotherapy.



Fig 1.

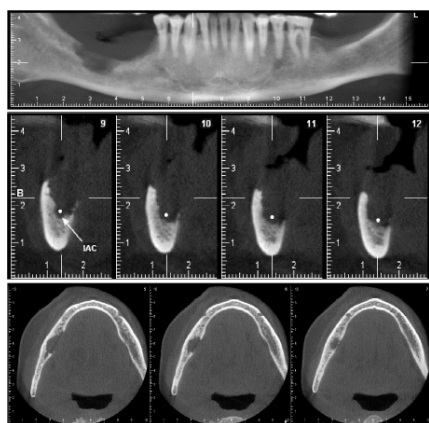


Fig 2.

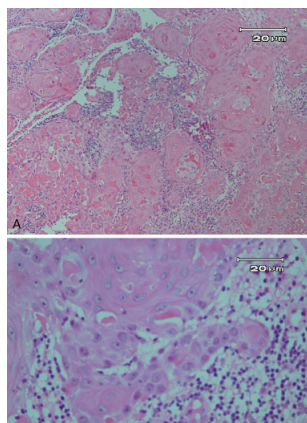


Fig 3.

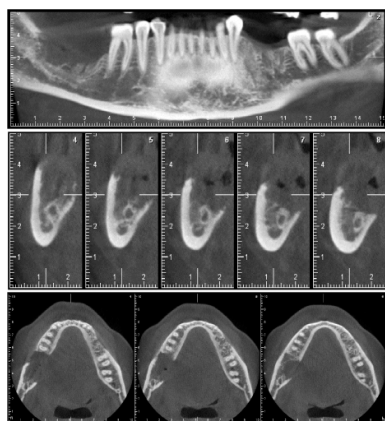


Fig 4.

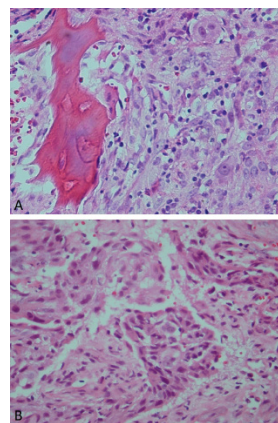


Fig 5.

## Discussion

PIOSCC must be differentiated from other carcinomas, including SCCs arising from the overlying soft tissue, tumors of the maxillary sinus, and tumors that have metastasized to the jaw from other sites [8]. Kaffe et al. [9] have proposed that an important feature of PIOSCC is the presence of indistinct margins without sclerotic outline; hence, this feature could be used as a diagnostic criterion; Although its radiologic features are varied in size, shape, and border, including radiolucent appearance, small or massive amounts of bone resorption, well-defined lesions with cortical preservation, and sometimes with irregular borders [10]. SCC bone invasion is mainly facilitated by osteoclasts. The bone is enhanced with TGF- $\beta$ , which allows for tumor proliferation and apoptosis inhibition. In addition, prostaglandins E2 and F2, IL-6, PTHrP, and receptor activator of nuclear factor kappa- $\beta$  ligand, were discovered to be produced by SCC to boost osteoclastogenesis. These mediators are supposed to help SCC bone invasion [11]. Based on clinical and radiologic findings, and since dental problems occur more frequently and only a few dentists consider other diseases, PIOSCC may be misdiagnosed as odontogenic infections, leading to incorrect dental operations and delay in diagnose. In this regard, Yamada et al. [12] described PIOSCCs which were considered to be infections after tooth extraction and preoperative dental operations were performed in 30 of 53 cases that Naruse et al. [13] reviewed. According to To et al. [14] delay in definitive diagnosis ranges from a few weeks to 18 months.

Some PIOSCC patients presented with a non-healing extraction socket at the time of diagnosis [15]. Infection and alveolar osteitis are the most common reasons for delayed healing or failure of dental socket to heal [16], but in some cases it could be the result of

tumor being present in the region. A neoplastic lesion, particularly an aggressive one, may cause ischemia, tissue necrosis, and may serve as a barrier to the in-growth of reparative cells and all these happening interfere with the healing process [17]. Among patients who were treated at Nanjing stomatological hospital between 2005 and 2015, 77 patients with PIOSCC were included in the study of Wenguang et al [15]. Surgery alone and then radiotherapy alone were the most common treatments for patients. When determining the prognostic factors of PIOSCC, 16 patients were excluded. In their study, positive nodal status, high histological grade, and advanced N classification were significantly poor prognostic factors, and the role of postoperative adjuvant radiotherapy or chemotherapy was unknown. In another study to review the literature, Bodner et al. [3] collected all well-documented cases of PIOSCC, published during the period 1938-2010, and selected just those PIOSCCs arising from the lining of an odontogenic cyst, including the keratocystic odontogenic tumor. Surgery alone or in combination with radiotherapy was the most common approach in their review. Also Huang et al. [18] retrieved pathologic files of Peking University School and Hospital of Stomatology between 1985 and 2006. They confirmed diagnosis of 39 cases of solid type PIOSCC. Among them, 37 patients had follow-up information. Radiotherapy in

combination with surgery, and surgery alone, were the most common approaches in this study. They concluded that histopathological grade and regional lymph node metastasis may be good indicators for prognosis and influence of postoperative adjuvant chemotherapy or radiotherapy remained uncertain. The other details in these studies are shown in Table 1.

Many patients with PIOSCC visit dentists as their first professional contact, so in their early detection and management, dentists play an important role; hence, dentist's suspicion should be increased to diagnose of PIOSCC, specially while masquerading many conditions in oral cavity, with a range of manifestation including: jaw swelling, mass, pain, unhealed dental socket, specifically when it happens in mandibular bone of old males. Other conditions should be considered too.

## Conclusion

PIOSCC is an uncommon carcinoma with a wide range of manifestation. Misdiagnosis and delay in diagnose can be resolved with accurate examinations (clinical, microscopic, radiologic) and a good knowledge in this topic.

Author	Number of cases	Age range	Mean age	Male: female	Most common location	Most common presenting symptoms	Overall survival rate at 2 years	Overall survival rate at 5 years
Wenguang et al. [15] (2016)	77	37-81	58.8	3.05:1	Mandible (posterior)	Jaw swelling (followed by lip or facial numbness)	68.9%	38.8%
Bodner et al. [3] (2011)	116	1.3-90	60.2	2.22:1	Mandible	Mass, pain	62%	38%
Huang et al. [18] (2009)	39	24-82	54	2:1	Mandible (posterior)	Jaw swelling, pain, sign of lip or facial numbness, non-healing extraction socket	69.8%	36.3%

Table 1.



## Conflict of Interest

There has been no conflict of interest in this study.

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