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CASE REPORT

Uncommon presentation of an intraosseous squamous cell carcinoma

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Abstract:

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare type of cancer, which commonly arises in the jaw without attachment to the oral mucosa epithelium and presumably develops from remnants of odontogenic epithelium or from odontogenic cysts and odontogenic benign tumors. We report here a case of a 49-year-old male patient who presented pain in the teeth 44 and 45 region. Radiographic examination revealed a small radiolucent and well circumscribed lesion, however, histopathological examination revealed a PISCC. The clinical and radiographic presentation of this tumor can be variable and nonspecific, and even small osteolytic lesions in the gnathic bones can be considered as differential diagnosis of malignant neoplasms of odontogenic origin. Incisional biopsy is fundamental to lead to early diagnosis and indicate appropriate treatment to optimize the prognosis of these cases.

Keywords: immunohistochemistry; Mouth Neoplasms; Carcinoma, Squamous Cell

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INTRODUCTION

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare type of odontogenic carcinoma that appears to develop from remnants of the odontogenic epithelium or dental lamina remnants. It accounts for approximately 1-2% of all oral cancers. This neoplasia was first described by Loos in 1913 and was called intra-alveolar squamous cell carcinoma in 1948 by Willis. The term primary intraosseous carcinoma was first used in 1972 by the World Health Organization (WHO)[1,2].

WHO (2005) ranked PISCC into three subcategories: PIOSCC solid type, PIOSCC arising from an odontogenic cyst and PIOSCC arising from a benign epithelial odontogenic tumor[3]. However, in the last WHO classification (2017) this neoplasia was once again classified as primary intraosseous carcinoma (PIC)[4].

The definitive diagnosis of PIOSCC is difficult, since the hypothesis of metastasis of distant tumors to gnathic bones, tumors of the lining mucosa that invading bone, tumors of the maxillary sinus and other odontogenic tumors should be ruled out[2-5].

Clinical features such as pain, swelling, perforation of the cortical bone, adhesion to the overlying bone are findings that can be found. In most cases, mandible is the most frequent anatomical site (79-90%) and the male gender is more frequently affected. Radiographically, this tumor presents as an uni or multilocular radiolucent image, and the lesion borders are poorly defined in most cases, however, well-defined borders can be seen in early tumors[2,5,6].

The clinical and radiographic presentation of this tumor are variable and few cases have been described in the literature in recent years, so our objective is to report an uncommon presentation of a solid type PIOSCC and to compare this case with others published in the literature in the last 5 years.

CASE REPORT

A 49-year-old male patient attended at public maxillofacial-surgery service presenting a painful swelling in the region of right lower premolars with one month duration. The intraoral clinical examination revealed a discreet irregular bulging in the region between teeth 44 and 45, however, the oral mucosa of the region was intact and normochromic (Figure 1).

Extraoral examination showed normal lymph nodes and none abnormality was observed. To evaluate a possible intraosseous lesion, a panoramic radiograph was requested. The image revealed a small, well delimited, unilocular (≈1cm) radiolucent lesion that was suggestive of Stafne bone defect, thickening of mental foramen, residual radicular cyst or benign intraosseous neural neoplasia (Figure 2).

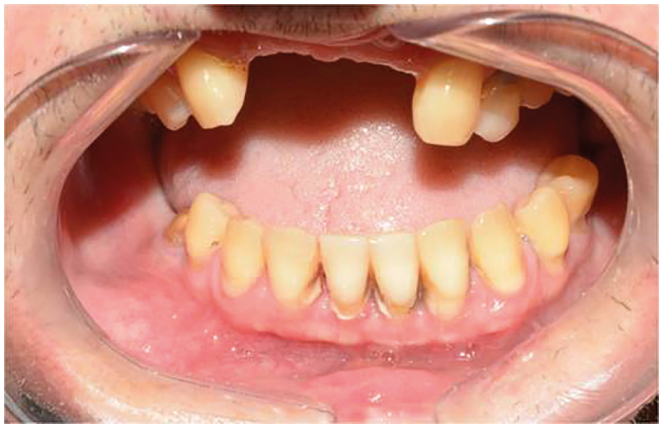

Figure 1. Clinical presentation of primary intraosseous squamous cell carcinoma. Normochromic and non-ulcerated oral mucosa.

Considering diagnostic hypotheses, an exploratory surgery was performed. After incision of the entire mucosa, was observed an irregular tissue mass that appeared came from the bone defect (Figure 3). An incisional biopsy was performed to establish the final diagnosis. Histopathological evaluation showed a malignant epithelial origin neoplasm, characterized by proliferation of squamous cells with varying degrees of pleomorphism and keratin pearls production, concluding the diagnosis of PIOSCC (Figure 4).

Immunohistochemical reactions were performed in order to investigate the biological behavior of the tumor. There was strong positivity for AE1/AE3 and cytokeratin-14 (Figure 5, A-B). Cytokeratins-7 and 19 were negative (Figure 5, C-D). We also observed strong and diffuse immunostaining for Ki-67 and p53 (Figure 5, E-F). The patient was referred to the cancer treatment at a head and neck surgery service renowned in the region, for total lesion resection.

DISCUSSION

PIOSCC is a rare lesion that develops within the maxillary bones without any connection to the oral mucosa[2]. This tumor may arise *de novo* or from pre-existing benign odontogenic lesions, including dentigerous cyst, periapical cyst and odontogenic keratocyst[2,7].

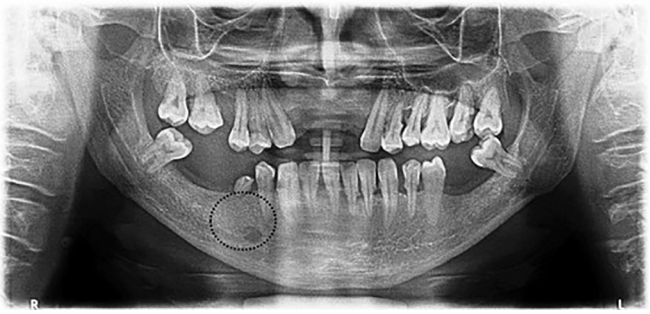

Figure 2. Image of the panoramic radiograph showing a radiolucent area with the upper and lower cortical bone preserved.

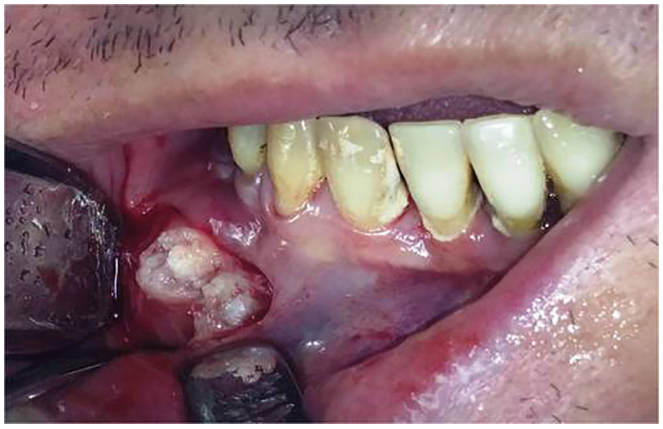

Figure 3. Intraoperative aspect of the incisional biopsy showing irregular bone.

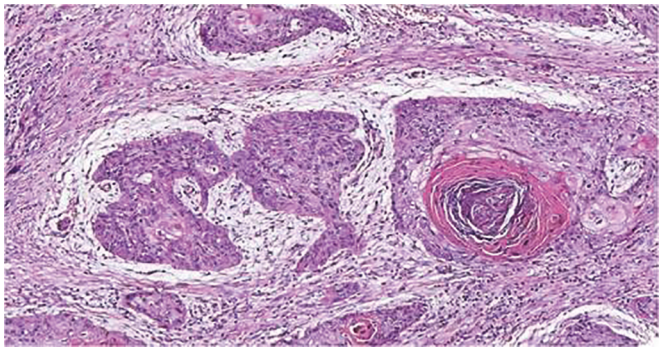

Figure 4. Photomicrography of the histopathological aspect, nests of malignant cells with presence of keratin are observed.

According to the reviewed literature (Table 1), adult male are more frequently affected with PIOSCC and mandible is the most frequent site. The age of the patients is between 36 and 66 years, being more common after the fifth decade of life. Additionally, in the study by Wenguang et al.[1], in a total of 55 mandibular PIOSCC, 41 involved the posterior mandible region. These characteristics are in agreement with the present case report.

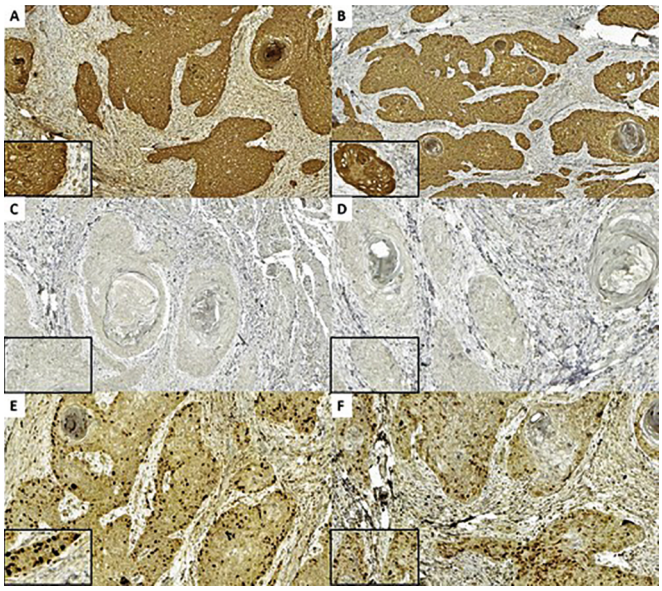

Figure 5. Images of immunohistochemical staining. (A) AE1/AE3 positive strong. (B) Citokeratin-14 positive strong. (C) Citokeratin-7 negative. (D) Citokeratin-19 negative. (E) Ki-67 positive diffuse. (F) p53 positive diffuse.

Localized swelling and pain are the most commonly associated symptoms (Table 1), also observed in our case; however, pain and paresthesia may also be associated, especially when the tumor reaches large dimensions[2,8].

Generally, radiographic image reveals a unilateral or multilocular radiolucent lesion with poorly defined borders (Table 1). However, well-delimited lesions may be observed in early-stage tumors, similar to the present report. In some cases, these indolent radiographic features may hinder and delay the diagnosis because it is confused with benign cysts and neoplasms[2,6].

Histopathologically, a pre-existing odontogenic cystic lesion should be investigated. The histopathological criteria used are the malignant transformation of the cystic lining with the transition from normal epithelium to the dysplastic and transformed epithelium[9]. The immunohistochemical labeling for CK-19 may also aid in the exclusion of a previous cystic lesion. This CK is considered a good marker for benign odontogenic lesions, presenting variable positivity in dentigerous cyst and odontogenic keratocyst[10]. In this case, the absence of histopathological findings of cystic components added to the immunohistochemical negativity for CK-19 confirmed a lesion which originates *de novo*.

Histopathological differential diagnosis of PIOSCC includes other malignant tumors including

Table 1. Features of intraosseous squamous cell carcinoma reported in the database PubMed / Medline (2012-2017).

Author	Age	Gender	Symptoms	Radiographic features	Localization	Diagnostic hypothesis clinical
Alotaibi et al. (2016)[13]	37	M	Pain	Undefined irregular radiolucency	Left mandibular ramus	Osteomyelitis, osteosarcoma, intraosseous carcinoma, ameloblastic carcinoma.
Iino et al. (2013)[14]	36	M	Pain	NI	Anterior maxillary region	NI
Choi et al. (2012)[15]	52	M	Pain	Undefined periapical rarefaction	Left mandible	Pericoronitis, osteomyelitis, primary intraosseous malignant tumor. Primary malignant tumor.
Matsuzaki et al. (2012)[16]	60	F	Discomfort deep in right ear	Radiolucent area with undefined margins	Right mandible	
Present Case (2017)	49	F	Pain	Radiolucent unilocular	Right mandible	Stafne bone defect, residual radicular cyst, benign intraosseous neural neoplasia Primary malignant tumor.
Present Case (2017)	49	F	Pain	Radiolucent unilocular	Right mandible	Stafne bone defect, residual radicular cyst, benign intraosseous neural neoplasia

Not informed = NI

ameloblastic carcinoma, clear cell odontogenic carcinoma and primary mucoepidermoid carcinoma. In addition, acanthomatous ameloblastoma, calcifying epithelial odontogenic tumor and squamous odontogenic tumor should be ruled out[11].

In the present report, histopathological features were typical of squamous cell carcinoma (SCC) and strong immunostaining for AE1/AE3, p53 and Ki-67 confirmed the malignant epithelial nature of the lesion reported[12]. We also emphasize that there was no immunohistochemical expression for CK-7, which excluded the possibility of an intraosseous mucoepidermoid carcinoma.

Before definitive diagnosis of PIOSCC, the existence of a primary tumor at another site should be excluded[8]. In this case, primary tumors in other locations were discarded. Carcinomas that invade bone from the underlying soft tissue should also be discarded[2]. In present case, the clinical image of normal oral mucosa (Figure 1) was important to rule out this possibility. Therefore, clinical, histopathological and immunohistochemical findings led to the diagnosis of PIOSCC.

The choice treatment is surgical resection with maxillectomy, or total or partial mandibulectomy. If necessary, radical neck dissection should be performed, as well as adjuvant therapies such as radiotherapy and chemotherapy when the tumors are extensive or non-operable[1]. In general, the prognosis is poor and overall patient survival after 5 years of treatment is less than 40% for tumors with advanced clinical staging[1,2].

CONCLUSION

In conclusion, we present an unusual case of PIOSCC in mandible with a focus on clinical and histopathological characteristics, which contributes to expand the information about this rare entity of variable presentation. Establishing the early diagnosis of this lesion is important to obtain a better prognosis, but it is still a challenge due to the lack of clinical criteria and its rare incidence.

Conflicts of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors. The authors declare there is no conflict of interest.

Ethical approval

The authors wish to declare that all experiments on human subjects were conducted in accordance with the Declaration of Helsinki. Ethical approval for this study was obtained from the relevant local ethics committees and patient consent was obtained.

Authorship

All authors have made substantial contributions to all of the following: (1 and 2) the conception and design of the study, acquisition of data, and analysis and interpretation of data; (3 and 4) drafting the article or revising it critically for important intellectual content; and (5) final approval of the version to be submitted.

REFERENCES

1. Wenguang X, Hao S, Xiaofeng Q, Zhiyong W, Yufeng W, Qingang H, et al. Prognostic Factors of Primary Intraosseous Squamous Cell Carcinoma (PIOSCC): A Retrospective Review. PLoS One. 2016;11:e0153646.
2. Bodner L, Manor E, Shear M, van der Waal I. Primary intraosseous squamous cell carcinoma arising in an odontogenic cyst: a clinicopathologic analysis of 116 reported cases. J Oral Pathol Med. 2011;40:733-8.
3. Boni P, Sozzi D, Novelli G, Pagni F, Valente G, Bozzetti A. Primary Intraosseous Squamous Cell Carcinoma of the Jaws: 6 New Cases, Experience, and Literature Comparison. J Oral Maxillofac Surg. 2016;74:541-6.
4. Wright JM, Vered M. Update from the 4th Edition of the World Health Organization Classification of Head and Neck Tumours: Odontogenic and Maxillofacial Bone Tumors. Head Neck Pathol. 2017;11:68-77.
5. Suei Y, Tanimoto K, Taguchi A, Wada T. Primary intraosseous carcinoma: review of the literature and diagnostic criteria. J Oral Maxillofac Surg. 1994;52:580-3.
6. Naruse T, Yanamoto S, Sakamoto Y, Ikeda T, Yamada SI, Umeda M. Clinicopathological Study of Primary Intraosseous Squamous Cell Carcinoma of the Jaw and a Review of the Literature. J Oral Maxillofac Surg 2016;74:2420-7.
7. Jain M, Mittal S, Gupta DK. Primary intraosseous squamous cell carcinoma arising in odontogenic cysts: an insight in pathogenesis. J Oral Maxillofac Surg. 2013;71:e7 14.
8. Grisar K, Schol M, Hauben E, Schoenaers J, Politis C. Primary intraosseous squamous cell carcinoma of the mandible arising from an infected odontogenic cyst: A case report and review of the literature. Oncol Lett. 2016;12:5327-31.
9. Tamgadge S, Tamgadge A, Modak N, Bhalerao S. Primary intraosseous squamous cell carcinoma arising from an odontogenic keratocyst: a case report and literature review. Ecancermedicalscience. 2013;7:316.
10. Kamath KP, Vidya M. Cytokeratin 19 expression patterns of dentigerous cysts and odontogenic keratocysts. Ann Med Health Sci Res. 2015;5:119-23.
11. Chaisuparat R, Coletti D, Kolokythas A, Ord RA, Nikitakis NG. Primary intraosseous odontogenic carcinoma arising in an odontogenic cyst or de novo: a clinicopathologic study of six new cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:194-200.
12. Martínez-Martínez M, Mosqueda-Taylor A, Delgado-Azañero W, Rumayor-Piña A, de Almeida OP. Primary intraosseous squamous cell carcinoma arising in an odontogenic keratocyst previously treated with marsupialization: case report and immunohistochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;121:e87-95.
13. Alotaibi O, Al-Zaher N, Alotaibi F, Khoja H, Qannam A. Solid--type primary intraosseous squamous-cell carcinoma in the mandible: Report of a rare case. Hematol Oncol Stem Cell Ther. 2016;9:118-22.
14. Iino M, Ishikawa S, Ozaki H, Kobayashi T, Tachibana H, Sakurai H, et al. Solid type primary intraosseous squamous cell carcinoma in the maxilla: report of a new case. BMC Ear Nose Throat Disord. 2013;13:13.
15. Choi YJ, Oh SH, Kang JH, Choi HY, Kim GT, Yu JJ, et al. Primary intraosseous squamous cell carcinoma mimicking periapical disease: a case report. Imaging Sci Dent. 2012;42:265-70.
16. Matsuzaki H, Katase N, Matsumura T, Hara M, Yanagi Y, Nagatsuka H, et al. Solid-type primary intraosseous squamous cell carcinoma of the mandible: a case report with histopathological and imaging features. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;114:e71-7.