10.5005/jp-journals-10037-1101

CASE REPORT

Primary Intraosseous Squamous Cell Carcinoma

[1]Pradeesh Sathyan, [2]S Jeslin, [3]Isaac Joseph, [4]KL Girish

ABSTRACT

Introduction: Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare malignant tumor of the jaw. It is common in adults, with mean age of 52 years and predominantly located in the posterior mandible. It may arise within the jaws either from a previous odontogenic cyst or *de novo*. Clinically, patients may present with pain, swelling, and paresthesia. It is locally aggressive and has a poor prognosis.

Case report: Here, we report a case of PIOSCC in the mandible of a 40-year-old male patient, with the clinical, radiological, and histological features described.

Management and prognosis: The patient was referred to Cancer Centre for further management. The patient underwent segmental mandibulectomy followed by radiotherapy. The patient is under observation.

Conclusion: The case presented as a dental problem wherein it was an aggressive malignant tumor. Hence an accurate knowledge of this rare entity is needed to prevent delay in diagnosis and effective management.

Keywords: Odontogenic carcinoma, Primary intraosseous carcinoma, Squamous cell carcinoma.

How to cite this article: Sathyan P, Jeslin S, Joseph I, Girish KL. Primary Intraosseous Squamous Cell Carcinoma. Oral Maxillofac Pathol J 2017;8(1):52-55.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare malignancy arising within the jawbone without any connection to the oral mucosa.[1] It was first described by Loos in 1913 and named as intraalveolar epidermoid carcinoma by Wills in 1948. The term primary intraosseous carcinoma (PIOC) was suggested by Pinborg et al in 1972.[2] According to the World Health Organization (WHO) classification, PIOC is defined as "a squamous cell carcinoma arising within the jaw, having no initial connection with the oral mucosa, and presumably developing from residues of the odontogenic epithelium."[3] In the literature several cases of malignant transformation of odontogenic cysts into PIOC have been reported, whereas PIOC occurring *de novo* is rare. Here we report a case of PIOSCC in the mandible arising *de novo* in a middle-aged male patient.

[1]Reader, [2]Postgraduate Student, [3,4]Professor

[1-4]Department of Oral and Maxillofacial Pathology, Sree Mookambika Institute of Dental Sciences, Kanyakumari, Tamil Nadu, India

Corresponding Author: S Jeslin, Postgraduate Student Department of Oral and Maxillofacial Pathology, Sree Mookambika Institute of Dental Sciences, Kanyakumari, Tamil Nadu, India, e-mail: aromadcc@gmail.com

CASE REPORT

A 40-year-old male patient was referred to the Department of Oral and Maxillofacial Pathology from a dental clinic with pain and swelling in his lower right back tooth region, for 3 weeks. Swelling was insidious in onset and gradually progressed to the present size of 2 × 3 cm. The associated pain was described as mild, dull, and intermittent in nature. Past dental history revealed extraction of right mandibular first and second molars 5 years back, which was reportedly, uneventful. Numbness of lower lip was present for 1 week, at the time of reporting. The patient had a history of cigarette smoking for the past 12 years and reportedly smoked 4 to 5 cigarettes per day and was continuing the habit at the time of examination.

On extraoral examination, a diffuse swelling of size 2 × 3 cm was seen on the right side of face extending anteriorly, 4 cm from the midline up to the ramus of the mandible, posteriorly. No visible pulsations, pus, or blood discharge were noted. Right submandibular lymph nodes were palpable and nontender. Intraorally, the swelling was bony hard, tender, and overlying mucosa was normal (Fig. 1). The lower right third molar within the lesion showed grade III mobility.

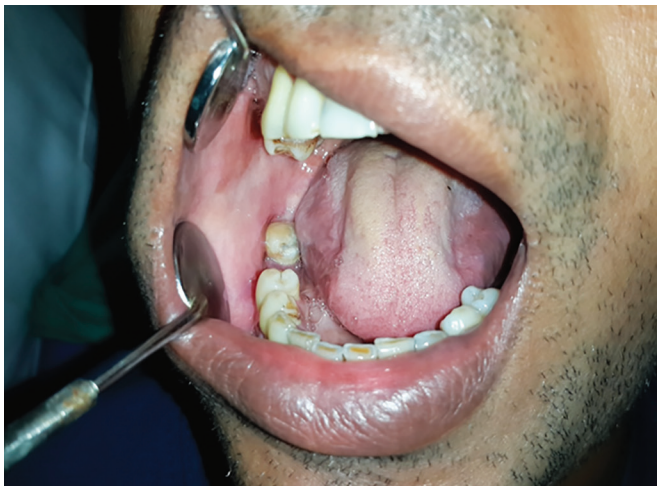

Fig. 1: Intraoral photograph no apparent swelling and normal overlying mucosa without ulceration

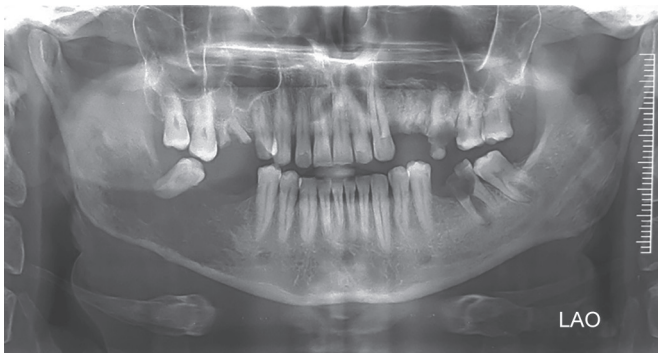

Fig. 2: Orthopantomogram poorly defined radiolucent lesion with ragged borders that shows permeate type of destruction and floating tooth appearance

Orthopantomogram demonstrated a diffuse radiolucency extending from distal aspect of 45 to ascending ramus involving the root of 48 and extending inferiorly, leaving only a thin border of the mandible (Fig. 2). With these findings, a provisional diagnosis of primary malignancy of bone was made. The lower right third molar was extracted and soft tissue within the socket was removed by curettage. The curetted tissue was sent for histopathologic examination. The extraction socket was sutured and hemostasis achieved.

Histopathological evaluation of hematoxylin and eosin (H&E) stained tissue section revealed moderately differentiated neoplastic cells in a highly cellular connective tissue stroma. The neoplastic cells are arranged in sheets and islands. Some areas showed attempted keratin pearl formation and individual cell keratinization (Figs 3 and 4). A histological diagnosis of moderately differentiated squamous cell carcinoma was made.

A chest radiograph and whole abdomen ultrasound was done to rule out any primary metastatic lesions. Routine laboratory investigations were within normal limits. In correlation with the clinical, radiological, and histopathologic findings, a diagnosis of solid-type PIOSCC was made. The patient was referred to the Regional Cancer Centre for further management and is currently being treated for PIOSCC for the past one year.

DISCUSSION

Primary intraosseous squamous cell carcinoma is a rare malignant odontogenic tumor arising in the jaws. In a review by To et al[4] in 1991, 21 well-documented cases of PIOC arising *de novo* were reported. According to Lugakingira et al,[5] there was a male predilection (male:female ratio, 3:1) and most *de novo* PIOSCC develop in the molar-ramus region of the mandible. The age groups of patients were between 24 and 76 years old, with more than 80% in the 5th to 7th decades. The most frequent clinical features were swelling, pain/tooth ache. As the lesion enlarges paresthesia and trismus occur due to the mandibular nerve and muscle infiltration. In the present case, the chief complaint, gender, and site of the lesion were in accordance with the findings of PIOSCC reported in the literature.

According to the 2005 WHO classification of tumors, PIOSCC is categorized into three types:

1. A solid tumor that invades bone marrow spaces and induces osseous resorption,
2. A squamous cell carcinoma arising from the lining epithelium of an odontogenic cyst, and
3. A squamous cell carcinoma in association with other benign epithelial odontogenic tumors.[1]

Waldron and Mustoe[6] proposed a modified classification system described in Table 1.

The present case may be classified under type-3a PIOC, based on the histological findings of the individual

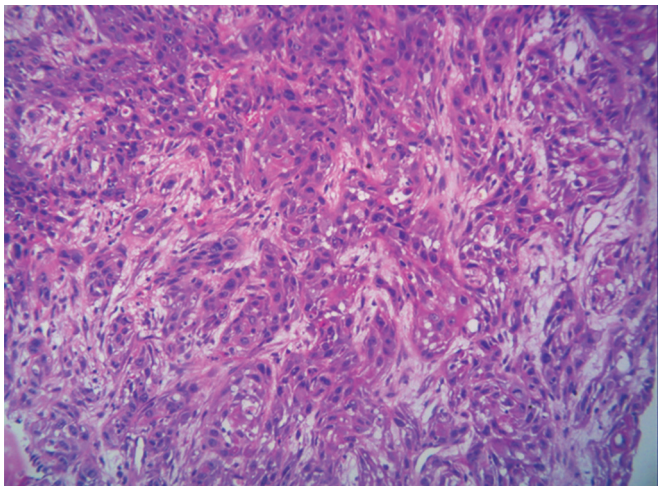

Fig. 3: Histopathology sheets and islands of moderately differentiated neoplastic cells in a highly cellular connective tissue stroma (H&E staining, 100×)

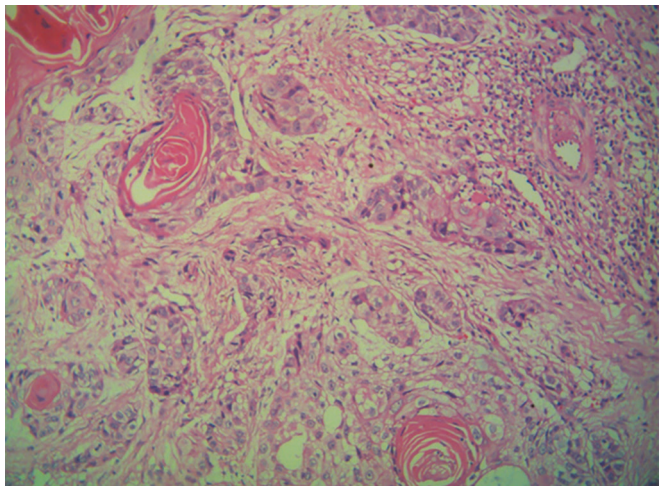

Fig. 4: Histopathology attempted keratin pearl formation and individual cell keratinization within islands of neoplastic cells (H&E staining, 400×)

Table 1: Classification of PIOC according to Waldron and Mustoe (1989)

Type 1	PIOC ex odontogenic cyst
Type 2a	Malignant ameloblastoma
Type 2b	Ameloblastic carcinoma arising *de novo*
	Ex ameloblastoma, ex odontogenic cyst
Type 3	PIOC arising *de novo*
	(a) Keratinizing type
	(b) Nonkeratinizing type
Type 4	Intraosseous mucoepidermoid carcinoma

cell keratosis. Type-3a and 3b PIOCs are distinguished based on the finding that the former type possesses keratin pearls and/or individual keratosis, whereas the latter does not show these features histologically.

According to Suei et al,[7] to define a lesion in the jaws as PIOC, three specific criteria must be present:

1. Histological evidence of squamous cell carcinoma,
2. Absence of ulcer formation on the overlying mucosa, and
3. Absence of a distant primary tumor at the time of diagnosis and at least 6 months during the follow-up period. Presently, the reported case satisfied all these criteria.

Primary intraosseous carcinoma shows radiolucency with varied presentations. According to a study by Thomas et al,[8] the radiolucency in PIOC was described as small radiolucent loculations, well-defined lesions, cup or dish-shaped patterns, and poorly defined moth-eaten appearance. Well-defined peripheries are often seen in slow-growing tumors, whereas poorly defined, ragged borders with permeate type of destruction are seen in rapidly expanding lesions. Degree of raggedness of the border may reflect the aggressiveness of the lesion. Another unique radiographic pattern is floating teeth which are rarely seen in other benign odontogenic tumors and cysts. Pathological fracture may occur due to thinning of the cortical plate with subsequent step deformity. The reported case showed poorly defined, ragged borders with permeate type of destruction, and floating tooth appearance.

Yamada et al[9] in his clinicopathologic study of five cases of PIOC found three cases of well-differentiated carcinoma, one moderately differentiated carcinoma, all those three arising *de novo* and the one arising from an odontogenic cyst. In the present case, the lesion was a moderately differentiated SCC with no evidence of the cystic component.

Considering various differential diagnosis, the PIOC must be distinguished first from a primary mucosal carcinoma. In the latter one, the tumor is clinically visible before any noticeable bone resorption occurs. Conversely, in PIOC bone breakdown is apparent before any clinical evidence of mucosal ulceration.[10]

Histologically, the PIOC can be confused with a squamous odontogenic tumor, an acanthomatous ameloblastoma, malignant ameloblastoma (ameloblastic carcinoma), or a central mucoepidermoid carcinoma.

The squamous odontogenic tumor is devoid of peripheral layer of palisaded cells, mitoses, and epithelial dysplasia. Furthermore, the calcification commonly associated with this neoplasm is not a feature of PIOC. Distinction between ameloblastic carcinoma and PIOC may be difficult but the latter lacks the typical ameloblastic differentiation. Ameloblastic carcinoma demonstrates malignant features along with prominent peripheral palisading and reverse nuclear polarization which are absent in PIOC. Primary intraosseous carcinoma can be distinguished from mucoepidermoid carcinoma based on the positive reaction for mucin in the latter tumor.[11] The possibility of a metastatic lesion must be excluded by a thorough clinical, systemic, and radiographic examination.

Immunohistochemical analysis for identifying odontogenic tumors is still to be improved. Cytokeratin (CK)-19 was found to be a useful marker for identifying cells of odontogenic origin of various odontogenic carcinomas, including PIOC, and might be useful in distinguishing PIOC from gingival SCC. Positive expression of cytokeratin cell adhesion molecule CK-CAM-5 and CAM-6 is found in the basal epithelial cells and in all the squamous cells, but is absent from almost all the ameloblastic cells.[12] MIB-1 (MindbombE3 ubiquitin protein ligase 1)/Ki-67 protein expression in the cytoplasm of basal epithelial cells and in the tumor cells is a measure of high proliferative index and can be helpful in differentiating malignant odontogenic tumors from ameloblastoma.[13]

In comparison to the oral SCC, the prognosis in cases of PIOC is poor and usually associated with high recurrence rate. Out of 12 cases of *de novo* PIOC reported by Elzay,[14] a 40% two-year survival rate was observed. Similarly in a study by Thomas et al[8] out of 28 cases of *de novo* carcinoma, 46% of the patients survived for a period varying from 6 months to 5 years.

The treatment of choice is aggressive surgical treatment comprising segmental mandibulectomy with reconstruction by vascularized fibula free flap either singly or in combination with radiotherapy or chemotherapy. Fibula is preferred among vascularized free flaps since it provides abundant periosteal blood supply, enough bone length, and has low donor-site morbidity.[15] Other reconstructive options include bridging plates and distraction osteogenesis. The tumor may metastasize to the cervical lymph nodes. Hence prophylactic neck dissection should be recommended even in No neck.[16]

CONCLUSION

The importance of this case was that it illustrates the central origin of the tumor, which presented as a dental problem, and it was a relatively rapidly growing tumor. Primary intraosseous squamous cell carcinoma is a rare malignant odontogenic tumor whose clinical presentation is similar to other comparatively common lesions, including periodontal infection and periapical lesions. Its diagnosis can be confirmed only by a thorough clinical, radiographic, and, most importantly, histopathologic examination. Primary intraosseous squamous cell carcinoma has a very poor prognosis and the treatment modalities are different and aggressive. Hence an accurate knowledge of this rare entity is needed to prevent delayed diagnosis.

REFERENCES

1. Barnes, L.; Eveson, JW.; Reichart, P.; Sidransky, D. World Health Organization classification of tumours: pathology and genetics of head and neck tumours. Lyon: IARC Press; 2005. p. 290-291.
2. Pinborg, JJ.; Kramer, IRH. Histologic typing of odontogenic tumours, jaw cysts and allied lesions in World Health Organization. Springer-verlag, Geneva; 1972.
3. Kramer, IRH.; Pinborg, JJ.; Shear, M. Histological typing of odontogenic tumors in World Health Organization. Springer-verlag, Geneva; 1992.
4. To EH, Brown JS, Avery BS, Ward-Booth RP. Primary intraosseous carcinoma of the jaws. Three new cases and a review of the literature. Br J Oral Maxillofac Surg 1991 Feb;29(1): 19-25.
5. Lugakingira M, Pytynia K, Kolokythas A, Miloro M. Primary intraosseous carcinoma of the mandible: case report and review of the literature. J Oral Maxillofac Surg 2010 Oct;68(10): 2623-2629.
6. Waldron CA, Mustoe TA. Primary intraosseous carcinoma of the mandible with probable origin in an odontogenic cyst. Oral Surg Oral Med Oral Pathol 1989 Jun;67(6):716-724.
7. Suei Y, Tanimoto K, Taguchi A, Wada T. Primary intraosseous carcinoma: review of the literature and diagnostic criteria. J Oral Maxillofac Surg 1994 Jun;52(6):580-583.
8. Thomas G, Pandey M, Mathew A, Abraham EK, Francis A, Somanathan T, Iype M, Sebastian P, Nair MK. Primary intraosseous carcinoma of the jaw: pooled analysis of world literature and report of two new cases. Int J Oral Maxillofac Surg 2001 Aug;30(4):349-355.
9. Yamada T, Ueno T, Moritani N, Mishima K, Hirata A, Matsumura T. Primary intraosseous squamous cell carcinomas: five new clinicopathologic case studies. J Craniomaxillofac Surg 2009 Dec;37(8):448-453.
10. González-García R, Sastre-Pérez J, Nam-Cha SH, Muñoz-Guerra MF, Rodríguez-Campo FJ, Naval-Gías L. Primary intraosseous carcinomas of the jaws arising within an odontogenic cyst, ameloblastoma, and de novo: report of new cases with reconstruction considerations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007 Feb;103(2):29-33.
11. Barnes, L.; Eveson, JW.; Reichart, P.; Sidransky, D. Textbook of surgical pathology of head and neck. 3rd ed. Vol. 3. Florida: CRC Press; 2008. p. 1610-1611.
12. Kawai S, Ito E, Yamaguchi A, Eishi Y, Okada N. Immunohistochemical characteristics of odontogenic carcinomas: their use in diagnosing and elucidating histogenesis. Oral Med Pathol 2009;13(2):55-63.
13. Angiero F, Borloni R, Macchi M, Stefani M. Ameloblastic carcinoma of the maxillary sinus. Anticancer Res 2008 Nov-Dec; 28(6B):3847-3854.
14. Elzay RP. Primary intraosseous carcinoma of the jaws. Review and update of odontogenic carcinomas. Oral Surg Oral Med Oral Pathol 1982 Sep;54(3):299-303.
15. Zwetyenga N, Pinsolle J, Rivel J, Majoufre-Lefebvre C, Faucher A, Pinsolle V. Primary intraosseous carcinoma of the jaws. Arch Otolaryngol Head Neck Surg 2001 Jul;127(7):794-797.
16. Gallego L, Junquera L, Villarreal P, Fresno MF. Primary de novo intraosseous carcinoma: report of a new case. Med Oral Patol Oral Cir Bucal 2010 Jan;15(1):e48-e51.