Case Report

Primary Intraosseous Carcinoma of the Mandible

Revati Deshmukh, Priya Nimish Deo, Surekha Chavan, Rajshekhar Halli[1]

Departments of Oral Pathology and Microbiology and [1]Oral and Maxillofacial Surgery, Bharati Vidyapeeth Deemed University, Dental College and Hospital, Pune, Maharashtra, India

Abstract

Primary intraosseous carcinoma (PIOC) is a rare neoplasm occurring in the jaw bones, especially in younger patients which is locally aggressive and has a poor prognosis. It is believed to arise from the odontogenic epithelium. It is called as PIOC because it arises *de novo* which makes it primary and it develops centrally within the bone hence called as intraosseous. The early lesions are asymptomatic or a painful swelling is seen. To diagnose PIOC, basic criteria have been proposed. (1) Absence of ulcer in the oral mucosa overlying the tumor, (2) Absence of another primary tumor at the time of diagnosis and for at least 6 months during the follow-up, and (3) Histological evidence of squamous cell carcinoma. Till date, around 60 cases of PIOC are reported. Being rare, we would like to discuss the review of literature and a case report on PIOC.

Keywords: *De novo, mandible, primary intraosseous carcinoma*

Introduction

Primary intraosseous carcinoma (PIOC) is a rare lesion arising within the jaw bones, and it was first described by Loos in 1913 as central epidermoid carcinoma of the jaws. Since then, it has been known by a variety of names such as primary carcinoma of the mandible, primary epithelial tumor of the jaw, intraalveolar carcinoma of the jaw, primary intraalveolar epidermoid carcinoma, and primary intraalveolar squamous cell carcinoma (SCC) of the mandible. As stated by Sengupta, the term PIOC was coined by Pindborg *et al*. in 1971.[1] Although the etiology of this carcinoma is not clear, it is presumed to be derived from the remnants of the odontogenic epithelium, epithelial rests of Malassez or remnants of dental lamina. It may arise from the previous odontogenic cyst or tumor or *de novo*.[2]

According to the World Health Organization (WHO), 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." The WHO classified the lesion as odontogenic carcinoma. There are several classifications, but Waldron and Mustoe's classification is widely accepted and frequently cited according to which PIOC may have different origins.[3]

According to 2005 WHO classification of tumors, primary intraosseous squamous cell carcinoma (PIOSCC) is subcategorized into three different types: (i) PIOSCC solid type (*de novo*); (ii) PIOSCC originating from keratocystic odontogenic tumors, and (iii) PIOSCC originating from odontogenic cysts.[4]

This tumor is locally aggressive and rarely shows metastasis to lymph nodes. It has a poor prognosis. The prognosis becomes worse if there is a delay in the diagnosis and treatment planning.

Clinical and imaging features are nonspecific, and the first impression of both clinicians and radiologists usually favors the diagnosis of alveolar or gingival SCC with bone invasion or metastatic SCC.[5]

The diagnostic criteria proposed for PIOC are as follows– (1) Absence of ulcer in the oral mucosa overlying the tumor, (2) Absence of another primary tumor at the time of diagnosis and for at least 6 months during the follow-up, and (3) Histological evidence of SCC.[6]

Understanding of the clinical, radiographic, and histopathological features of this tumor allows accurate diagnosis and appropriate treatment of this rare malignancy.[7]

Till date, very few cases of PIOC are reported. The case discussed here does not show ulceration, no evidence of any primary tumor elsewhere was observed, and hence, PIOC was confirmed. This

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Address for correspondence:
Dr. Revati Deshmukh, Department of Oral Pathology and Microbiology, Bharati Vidyapeeth Deemed University, Dental College and Hospital, Pune - 411 043, Maharashtra, India.
E-mail: deshmukhsarojini45@gmail.com

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clinical and histopathologic evidence will improve our knowledge of the cell of origin and biological behavior of the neoplasm.

Case Report

A 30-year-old male patient reported to Bharati Vidyapeeth Deemed University, Dental College and Hospital, Pune, with a complaint of swelling in the lower anterior region since 6 months. Clinical examination revealed a diffuse swelling in lower left 31, 32, and 33 region, measuring about 2 cm × 2 cm in dimensions, soft to firm in consistency with no sinus formation or discharge. The overlying mucosa was intact, pinkish in color, soft to firm on palpation with no ulceration. There was no lymph node involvement and no similar lesion elsewhere. 31, 32 showed Grade III mobility and were displaced. The patient did not have fever, paresthesia, or loss of sensation in the lower lip and chin. There was no relevant past medical and dental history and no relevant habit history. An orthopantomograph showed a radiolucency in 31, 32, and 33 region. Erosion of the bone in the mandibular anterior region was also seen [Figure 1].

At the time of surgery, it was noted that the buccal cortex was destroyed, a large bony cavity 3.5 cm × 2.5 cm was noted, and no evidence of bleeding during enucleation was observed [Figure 2].

Histopathological findings revealed multiple sections. Section one showed epithelium and connective tissue. Epithelium showed dysplastic features such as nuclear and cellular pleomorphism, altered nuclear-cytoplasmic ratio, mitotic figures, individual cell keratinization, and nuclear hyperchromatism [Figure 1]. Here, the basement membrane appeared to be intact. The underlying connective tissue for this section revealed diffuse inflammatory infiltrate such as lymphocytes, plasma cells, and macrophages. Abundant hemorrhagic areas were also seen in the connective tissue.

Section two showed epithelium which appeared in the form of a plexus with proliferative dysplastic changes like epithelial pearl formation [Figure 3].

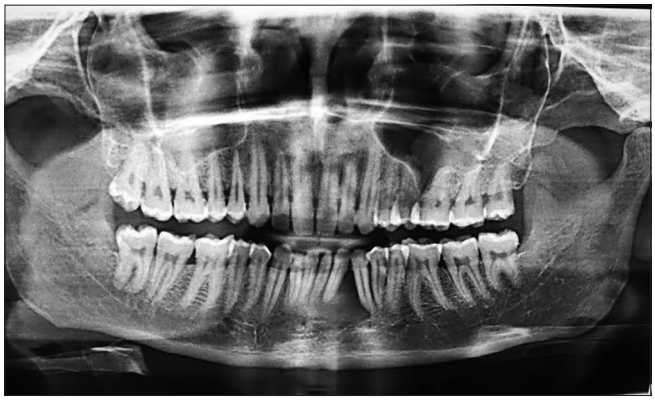

Figure 1: Radiolucency in 31, 32 and 33 region, erosion of the bone in the mandibular anterior region

In the third section, epithelium showed squamous differentiation with abundant dysplastic proliferation and intact basement membrane. The underlying connective tissue was scanty. Hemorrhagic areas were also seen. Serial sections did not show the presence of any odontogenic lining epithelium. Calretenin which is used for odontogenic epithelium, when used as a marker did not show positivity [Figure 4]. This ruled out ameloblastic Carcinoma. The patient was treated with a wide local excision. Keeping the clinicopathological observations in mind, Primary intraalveolar carcinoma was a favorable diagnosis. The overall picture was suggestive of PIOC – a clinicopathological correlation.

Discussion

PIOC is a rare malignant neoplasm which occurs exclusively in the jaw bones.[8] PIOC describes the SCC that develops likely from the residues of the odontogenic epithelium entrapped within the jaw with no connection to the surface oral mucosa. The origin of this tumor may be from the lining of the odontogenic cysts, from other odontogenic tumors, or *de novo* from odontogenic cell rests which are the remnants of the odontogenic apparatus.[8,9]

According to the most recent edition of the WHO classification for histological typing of odontogenic tumors, it is defined as a SCC arising within the jaw bone without connection to the oral mucosa, probably from odontogenic epithelial residues.[6]

This tumor was first labeled by Loos in 1913 as central epidermoid carcinoma of the jaw. Willis in 1948 renamed it as an intraalveolar epidermoid carcinoma. It was Pindborg, who coined the term PIOC in 1971.[6] The WHO in 1972 classified this entity as an odontogenic carcinoma. Elazy subsequently recommended a modification of this WHO classification after reviewing a sample of subjects with PIOC. Slootweg and Muller further modified Elazy's classification taking into account the various possible origins of PIOC.[6]

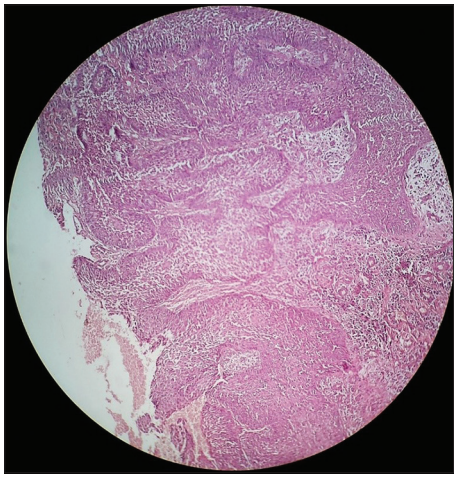

Figure 2: Epithelium showing dysplastic features

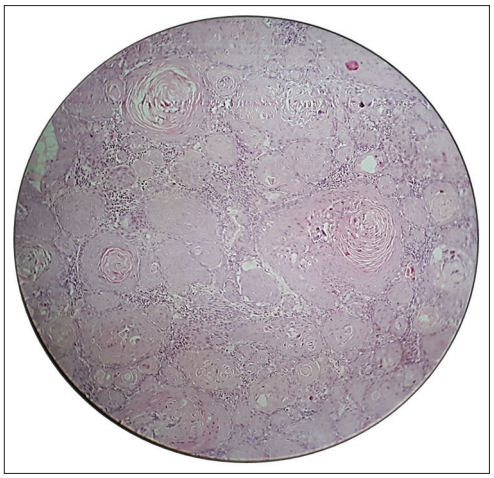

Figure 3: Epithelial pearl formation

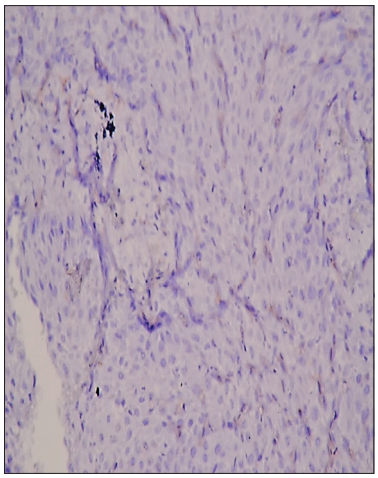

Figure 4: Calretenin negative

Most widely accepted and frequently cited classification of odontogenic carcinoma proposed by Waldron and Mustoe.

Waldron and Mustoe's classification:-

- Type 1: PIOC ex-odontogenic cyst
- Type 2A: Malignant ameloblastoma
- Type 2B: Ameloblastic carcinoma arising *de novo*, ex-ameloblastoma, or ex-odontogenic cyst
- Type 3: PIOC arising *de novo* (a) Keratinizing type (b) Nonkeratinizing type
- Type 4: Intraosseous mucoepidermoid carcinoma.[8]

According to this classification system, our case may be categorized as Type 3.

PIOC is more common in adults, in sixth to seventh decade of life with a male to female ratio of 3:1. It is usually situated in the posterior mandible. In a systematic collective analysis of world literature, the mean age of the patients at the time of diagnosis was 52.3 years with male-to-female ratio 2.5:1.[9] Our case was reported in young patient with the age of 30 years, and a diffuse swelling was seen in lower anterior region. Very few cases with the anterior maxillary involvement have also been stated. The most commonly associated symptoms are pain and swelling. Sensory disturbances such as paresthesia and numbness can also occur. Most malignant odontogenic tumors develop as intraosseous lesions and hence are initially asymptomatic. Later on, as they invade and destroy medullary bone, they produce cortical bone expansion with tooth loosening or displacement. In our case also, Grade III mobility with 31, 32 was seen. They also cause invasion or compression of the alveolar nerve, which explains the presence of pain and/or paresthesia. PIOC is occasionally but not always associated with metastasis to regional lymph nodes.[8] Careful history should be taken, and systemic evaluation should be done to exclude any metastatic disease or malignancy.

The absence of mucosal ulcers is one of the main characteristics for a diagnosis, which differentiates cases of PIOC from superficial squamous carcinoma arising in other parts of the oral cavity.[10] The overlying mucosa in the present case had a normal pinkish color and there was absence of surface ulceration. There was no abnormal growth seen anywhere else.

Prognosis is quite poor, with 5 years survival rate ranging from 30% to 40%. The diagnosis of PIOSCC can be difficult because it must be differentiated from other odontogenic carcinomas, such as malignant ameloblastoma, SCC arising from the overlying oral mucosa, from the primary tumors of the maxillary sinus or nasal mucosa, and from the tumors that have metastasized to the jaws from other primary sites.[11]

Suei *et al*. proposed a few diagnostic criteria for PIOC; they were as follows: (1) to differentiate PIOCs from SCCs of surface mucosal origin, no ulcer formation must be present on the overlying oral mucosa except when due to such causes as trauma or tooth extractions; (2) to rule out the possibility of other odontogenic carcinomas, serial sections of the histological specimens must demonstrate SCC without cystic components or other odontogenic tumor cells; and (3) to rule out a distant primary tumor, chest radiographs must be clear at the time of diagnosis and throughout a follow-up period of more than 6 months.[12]

Radiographical examination is an effective method for the diagnosis of PIOC. PIOC usually exhibits marked variation in the appearance of its border, and thus, it is worth considering as a differential diagnosis of jaw radiolucency while panoramic radiography is useful for obtaining an overall view of the disease, it may be limited by not providing an evaluation of bone destructive lesions with a ragged border, the margin, or the degree of extension and invasion of the surrounding tissue of the tumor mass.[13]

Nolan reported well-defined, smoothly contoured borders for slowly growing PIOC's and poorly defined, ragged borders for rapidly growing tumors. Due to such variations in radiological presentation of PIOC's margins, it is difficult

to differentiate them from other benign or malignant tumors.[14]

Diagnostic aids such as computed tomography scan, chest radiograph, and bone scan are helpful for general evaluation.

The histopathologic features of *de novo* PIOC are consistent with a diagnosis of SCC with or without keratinization. The microscopic differential diagnosis should, therefore, include any lesion that produces squamous epithelium, such as acanthomatous ameloblastoma, squamous odontogenic tumor, metastatic carcinomas, and central mucoepidermoid carcinoma. Microscopic examination of serial specimen sections is usually required to rule out the presence of odontogenic cyst lining epithelium or any other odontogenic tumor.[15]

The prognosis of *de novo* PIOC is generally poor. In the 12 cases of *de novo* PIOC reported by Elzay, a 40% 2 years survival was noted.[16] Similarly, in the review of 28 cases of *de novo* carcinoma reported by Thomas *et al*., 46% of the patients survived for a period varying from 6 months to 5 years.[17]

Treatment of PIOC is principally wide local resection and radiotherapy. Chemotherapy may be performed as adjunctive treatments. Careful evaluation for an early diagnosis is necessary which will help in a better treatment plan and further improve the prognosis of this rare and aggressive neoplasm. Documentation of more cases is essential which will give detailed information and improve the understanding of the biologic behavior of this rare and aggressive neoplasm.

Conclusion

PIOC is a rare and aggressive tumor occurring essentially in the jaw bones. The purpose of reporting this case was to add to the current literature, which will further help increase the information about the origin and the biologic behavior of this uncommon lesion. This will help us in improving the management of these patients. With early diagnosis, better management will be possible. One needs to have pretreatment evidence and posttreatment follow-up; as a nonulcerative lesion may surprise the operator with PIOC. Careful evaluation and close observation of these apparently innocuous appearing lesions will improve the prognosis of these aggressive neoplasms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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