

# Primary intraosseous squamous cell carcinoma - A rare odontogenic malignancy

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## Abstract

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare epithelial odontogenic malignancy affecting the jaws, especially in elderly population. It is a rare lesion, because very few cases of PIOSCC have been reported in the literature with not much of research done on this particular entity. In the present article, we report a case of PIOSCC with detailed discussion of clinical, radiographic and histopathologic features along with review of literature.

**Keywords:** Mandible, odontogenic tumor, primary intraosseous squamous cell carcinoma

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## INTRODUCTION

Primary intraosseous squamous cell carcinoma is a rare epithelial odontogenic malignancy affecting the jaws and having no initial connection with oral mucosa and presumably developing from remnants of the odontogenic epithelium or from an odontogenic cyst or tumor.<sup>[1]</sup> According to Morrison and Deeley, this tumor was first described by Loos in 1913. Wills, in 1948, renamed it as intra-alveolar epidermoid carcinoma. Shear later modified the name to primary intra-alveolar epidermoid carcinoma.<sup>[2,3]</sup> Both previous editions of the World Health Organization (WHO) classification of odontogenic tumors recommended the term primary intraosseous carcinoma (PIOC). In the new WHO classification, published in 2005, PIOSCC is designated to replace the older terms.<sup>[1]</sup>

Its subtypes include solid types, PIOSCC derived from keratocystic odontogenic tumors and those derived

from odontogenic cysts.<sup>[1]</sup> Thomas *et al.* in 2001, published a review of 35 cases, and they found that the mean age of the patients at the time of diagnosis was 52.3 years with a range of 4–81 years. Male to female ratio was 2.5:1. Posterior mandible was the predominant site.<sup>[4]</sup>

The purpose of this article is to represent the clinical, radiological and microscopic characteristics of PIOSCC. This case adds to the very few cases of PIOSCC in the literature.

## CASE REPORT

A 46-year-old female patient reported to the Department of Oral Pathology and Microbiology in our institute with the chief complaint of pain and numbness in the right lower jaw for 4 months. Medical history, family history and habit history were noncontributory. The patient gave a history of pain and swelling in 48 regions for which

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she underwent extraction 1½ year back. Later on, she developed pus discharge in the same region and underwent treatment for the same.

Extraoral examination revealed diffuse bony hard swelling in the right mandibular ramus region causing facial asymmetry. Right submandibular lymph node was palpable, fixed and tender.

On intraoral examination, no obvious swelling was seen; but on palpation, expansion in the right ramus region was felt. Diffuse erythema was seen extending from distal of 46 up to pterygomandibular raphe region. Area was tender on palpation. Sinus opening was noted in the alveolar ridge in retromolar area. 18 and 48 were clinically missing [Figure 1].

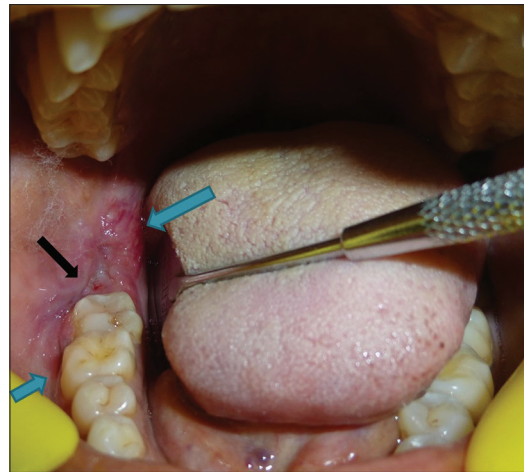
Clinically, a provisional diagnosis of infective swelling was considered, with the following differentials in mind osteomyelitis, benign odontogenic cyst and tumor.

The patient was subjected to radiologic examination, and orthopantomogram was made which revealed a radiolucent osteolytic lesion in the right mandibular ramus region extending superoinferiorly approximately 8 mm from sigmoid notch to 10 mm above the lower border, anteroposteriorly from anterior border of ramus to 10 mm anterior to the posterior border with irregular and ragged margins. Outline of inferior alveolar nerve canal was traceable, but was not seen distinctly in the lesional area [Figure 2].

The patient was then subjected to cone beam computed tomography examination, which revealed that the osteolytic lesion was extending from 48 till 10 mm away from the posterior border of ramus. Superoinferiorly, it extended 8 mm away from lower border of mandible till the level of sigmoid notch, and coronoid process involvement was also seen.

The lesion showed irregular and indistinct borders giving it a typical moth-eaten appearance. Few flecks of radiopacity representing the remnants of destroyed bone were noted within the lesion.

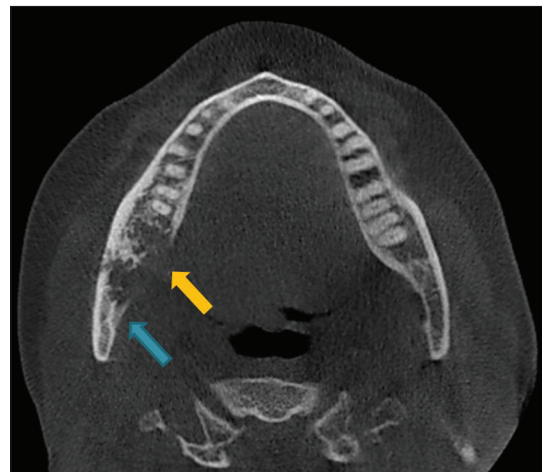
The lesion had destroyed buccal and lingual cortices of ramus and third molar region (more profound with lingual cortex) with thinning of the anterior border of ramus. Inferior alveolar nerve canal was not traceable within the lesion. Periosteal reaction was appreciated buccally and lingually. Sclerosis in surrounding bone was also noted along the margins of osteolytic lesion [Figure 3].



**Figure 1:** Clinical image shows diffuse erythema in retromolar area. Note the sinus opening distal to 46 shown with black arrow



**Figure 2:** Orthopantomogram shows osteolytic lesion with irregular borders



**Figure 3:** Axial section of cone beam computed tomography showing osteolytic radiolucent lesion with moth-eaten appearance. Note few flecks of radiopacity

Based on history, clinical and radiological findings, a provisional diagnosis of chronic suppurative osteomyelitis was made.

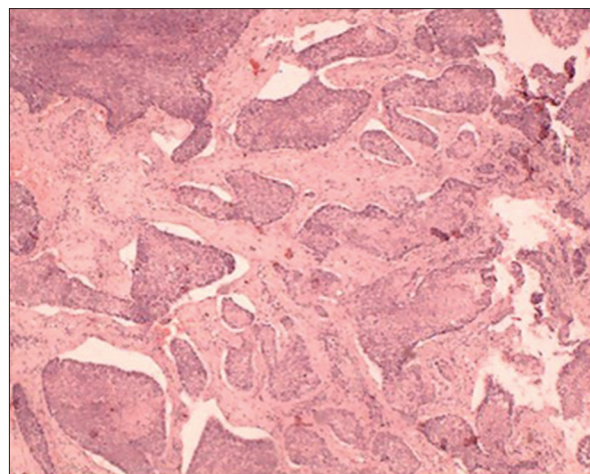
The following differential diagnoses were also considered:

1. Odontogenic carcinoma: This is a broader term which includes metastasizing (malignant) ameloblastoma,

ameloblastic carcinoma, primary intraosseous squamous cell carcinoma – solid type and primary intraosseous squamous cell carcinoma derived from keratocystic odontogenic tumor or from odontogenic cysts and other lesion. This was considered as first differential diagnosis because radiographic lesion was destructive with ill-defined and ragged borders but provisional diagnosis of osteomyelitis was considered as patient gave history of extraction, pus discharge and radiographic features such as periosteal reaction, sclerosis of surrounding bone were seen which are commonly seen in case of osteomyelitis

2. Metastatic carcinoma: It was considered in differential diagnosis not as provisional diagnosis because patient did not give history of primary tumor elsewhere in the body
3. Sarcomas: Osteosarcoma and chondrosarcoma were considered. Chondrosarcomas are rarely found in jaws and generally occur in the anterior alveolar process of the maxilla, alveolar ridge of premolar-molar region and angle of the mandible. However, it is slow growing and painless in early stages. Osteosarcomas are more frequently seen in long bones and rarely in jaw bones accounting for only 7% among all osteosarcomas. It grows rapidly giving a moth-eaten appearance in the initial osteolytic stage. The mean age of occurrence is 33 years. Radiographic findings did not show sunray appearance and Codman's triangle which is seen in 25% of cases, that is why it was not considered as provisional diagnosis and considered in differential diagnosis
4. Odontogenic cyst and odontogenic tumor: Despite being most common lesion occurring in jaws especially in posterior mandible, these were considered last in differential diagnosis, because lesion on radiograph showed ill-defined radiolucency with ragged margins.

The patient was subjected to blood investigations for incisional biopsy which were within normal range, and incisional biopsy was performed intraorally in ramus region. Histopathological examination revealed fibro-cellular connective tissue stroma interspersed with hyperchromatic epithelial tumor cells in the form of islands and cords. These tumor islands comprised of malignant epithelial cells exhibiting cellular and nuclear pleomorphism with prominent nucleoli. Some of the tumor islands were showing palisaded appearance of basal columnar cells with reverse polarity of nuclei. Some central cells of epithelial island appeared as squamous type, and some resembled stellate reticulum like - cells. Periodic acid–Schiff was done to rule out possibility of central mucoepidermoid carcinoma which was negative. On the basis of incisional biopsy, diagnosis of ameloblastic carcinoma was made [Figure 4].



**Figure 4:** Histopathological image shows hyperchromatic epithelial tumor cells in the form of islands (H&E, x40)

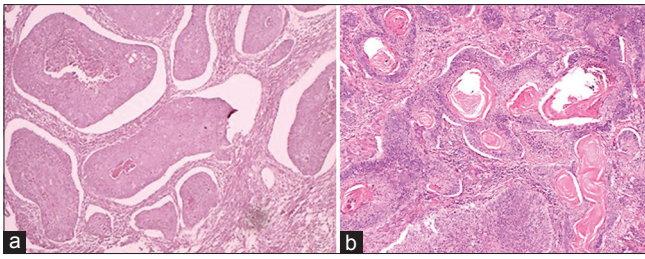
The patient was referred to higher center for further treatment, where segmental mandibulectomy was done. Histopathological examination of H&E stained slides revealed numerous irregular-shaped solid epithelial islands of varying sizes in the connective tissue. Some islands were arranged in alveolar pattern. Keratin pearl formation was seen within some epithelial islands. Areas of degeneration and necrosis were also noted [Figure 5a and b].

Peripheral hyperchromatic cells showing palisading appearance, reverse polarity and subnuclear vacuolization. High power view showed epithelial islands, marked cellular and nuclear pleomorphism, altered nuclear-cytoplasmic ratio, loss of cohesion, increased mitosis and abnormal mitotic figures (feature of carcinoma). Areas of necrotic bone with neoplastic epithelial islands infiltrating the marrow spaces were also noted [Figure 6a and b].

Based on the microscopic findings a final diagnosis of PIOSCC -solid type was given.

## DISCUSSION

PIOSCC is a rare odontogenic carcinoma.<sup>[2]</sup> According to the most recent edition of the WHO classification of odontogenic tumors, primary intraosseous squamous cell carcinoma (PIOSCC) is a central jaw carcinoma derived from odontogenic epithelial remnants. Subcategories of PIOSCC include (1) a solid tumor that invades marrow spaces and induces osseous resorption, (2) squamous cancer arising from the lining of an odontogenic cyst and (3) a squamous cell carcinoma (SCC) in association with other benign epithelial odontogenic tumors.<sup>[5]</sup> In the past, the term PIOC has been used for carcinoma arising within the jaw. Furthermore, considerable confusion has existed in past about definition and classification of odontogenic



**Figure 5:** (a) Histopathological image shows epithelial islands showing arrangement in alveolar pattern with central area of degeneration and necrosis (H&E,  $\times 40$ ). (b) Histopathological image shows keratin pearl formation within some epithelial islands (H&E,  $\times 40$ )

carcinomas.<sup>[2]</sup> In 1982, Elzay' proposed a modification of the first WHO classification (1971). This included primary (de novo) PISC and PISC arising ex ameloblastoma in addition to distinguishing between a well-differentiated variant (malignant ameloblastoma, type A) and a poorly differentiated variant (ameloblastic carcinoma, type B). Slootweg and Muller presented a slight modification of Elzay's classification that has considerable merit. This classification accounts for the various possible origins of a PIOC. PIOC (odontogenic carcinoma) of the jaws (after Slootweg and Miller):<sup>[2,6]</sup>

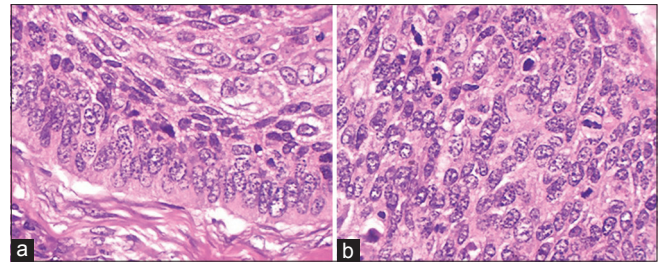
- Type 1: PIOC ex odontogenic cyst
- Type 2a: Malignant ameloblastoma
- Type 2b: Ameloblastic carcinoma arising *de novo*, ex ameloblastoma or ex odontogenic cyst
- Type 3: PIOC arising *de novo*:
  - a. Keratinizing type
  - b. Nonkeratinizing type.

The classification of WHO (1971), Elzay or Slootweg and Muller did not include intraosseous mucoepidermoid carcinoma, however Waldron and Mulstoe later included it as a fourth type of PIOC because of origin from the epithelial lining of odontogenic cyst.

- Type 4: Intraosseous mucoepidermoid carcinoma.<sup>[4-7]</sup>

In WHO classification 2005, PIOC arising *de novo* (keratinizing type) is classified as PIOSCC (Primary intraosseous squamous cell carcinoma) which is the final diagnosis given in this case.

Diagnosis of PIOSCC is very difficult as it must be distinguished from carcinoma of the alveolar mucosa that has invaded the bone, from carcinoma of the maxillary sinus and from carcinoma metastatic to the jaw. Due to rarity of PIOSCC, its incidence, prevalence and etiology are still not known. In a pooled analysis of world literature by Thomas *et al.*, the mean age of the patients at the time of diagnosis was 52.3 years with an age range of 4–81 years. Male to female ratio was 2.5:1, and posterior mandible was



**Figure 6:** (a) Histopathological image shows peripheral hyperchromatic cells with palisading, reverse polarity and subnuclear vacuolization (H&E,  $\times 400$ ). (b) Histopathological image shows epithelial islands, marked cellular and nuclear pleomorphism, altered nuclear-cytoplasmic ratio, loss of cohesion, increased mitosis and abnormal mitotic figures (H&E,  $\times 400$ )

the predominant site.<sup>[4]</sup> In our case, female patient aged 46 years was affected, and site was molar-ramus region.

These findings are in concordance with the Huang *et al.* published data. They studied a total of 39 PIOSCCs (solid type) cases retrieved from the pathologic files of Peking University School and Hospital of Stomatology (Beijing, China) during the period 1985–2006.<sup>[1]</sup> Their findings were similar to findings of Thomas *et al.* The etiology of PIOC is not clear, however the most common factor may be a reactive inflammatory stimulus with or without a predisposing genetic cofactor.<sup>[4]</sup>

Common clinical features of PIOSCC include pain and swelling. In a pooled analysis of 33 cases recorded in world literature, performed by Thomas *et al.*, pain was the most common presenting feature in 17 (54.8%) patients followed by swelling of the jaw in 16 (51.6%) and sensory disturbances in five (16.1%).<sup>[4]</sup> In our case, pain, swelling and paresthesia were seen.

Radiographically, in most cases, osteolytic bone changes are characteristic with poorly defined, diffuse and irregular margins.<sup>[2]</sup> Kaffe *et al.* studied radiographic features of 24 cases of PIOSCC. In their review, they found that 87% lesions were radiolucent and 13% were mixed radiolucent-radiopaque, the latter were all located in the mandible. None of the cases had corticated borders. Defined borders but noncorticated were found in 56.5% cases and diffuse borders in 43.5%.<sup>[8]</sup> In our case, the lesion was radiolucent with remnants of destroyed bone giving it a mixed appearance. The borders were ill defined and noncorticated.

### Histopathological features

Histologically, picture may vary from well-differentiated tumors exhibiting significant keratinization to nonkeratinizing poorly differentiated carcinomas. Primary

intraosseous squamous cell carcinomas may reveal a distinct odontogenic pattern with basal-type cells forming alveoli or arranged in a plexiform pattern with palisading of the peripheral cells. The nuclei of these cells are often oriented away from the basement membrane.<sup>[2]</sup> Therefore, PIOSCC must be considered in the differential diagnosis of malignant tumors of odontogenic epithelium, including ameloblastic carcinoma, clear cell odontogenic carcinoma, central mucoepidermoid carcinoma, odontogenic ghost cell carcinoma and a malignant variant of calcifying epithelial odontogenic tumor. Foci of central necrosis or degeneration within the epithelial islands have also been observed.<sup>[1]</sup>

Suei *et al.* proposed the following three criteria for the diagnosis of PIOC:

1. No ulceration of surface mucosa except due to trauma or tooth extraction.
2. To rule out the possibility of another odontogenic carcinoma, the serial sections of the histologic specimen must demonstrate SCC without cystic components or other odontogenic tumor cells
3. To rule out a distant primary tumor, chest radiographs must be clear at the time of diagnosis and throughout the follow-up period of more than 6 months.<sup>[9]</sup>

In our case, above criteria were considered, and diagnosis of PIOSCC (older term PIOC *de novo* keratinizing type) was given.

### Treatment

Primary intraosseous squamous cell carcinoma is considered a highly malignant tumor that should be treated aggressively. Radical surgery is accepted as the primary mode of therapy for PIOSCCs. Involvement of the lymph nodes requires block resection combined with the excision of the primary tumor.

The prognosis for patients with PIOSCCs is difficult to determine because of the small number of reported cases, the different treatment modalities and the variable follow-up time. In case of conventional OSCC, the 5-year survival rate was 66.2% under 40 years of age, and in the older patient group (>40 years), 5-year survival rate was 57.6%,<sup>[10]</sup> whereas in case of PIOSCC, it is reported between 30%–46% suggesting its poor prognosis compared

to conventional OSCC. Early diagnosis and management eventually yields a better prognosis of these rare tumors.<sup>[1,2]</sup>

### CONCLUSION

PIOSCC is a rare tumor with poor prognosis and histopathologically, it may be confused with other intraosseous carcinomas, especially ameloblastic carcinoma. Whenever a case with persistent pain and swelling along with intraosseous osteolytic lesion with irregular borders is noted, one should also consider the possibility of intraosseous carcinomas and rule out other intraosseous carcinomas to reach the final diagnosis of PIOSCC.

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### Conflicts of interest

There are no conflicts of interest.

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