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CASE REPORT

PRIMARY INTRAOSSOUS SQUAMOUS CELL CARCINOMA OF MANDIBLE- A DE NOVO DISPARITY

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ABSTRACT:
Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare jaw bone tumor. PIOSCC arises either from epithelial lining of odontogenic cyst or de novo from odontogenic rests. In literature PIOSCC was first described by Loos in 1913 as central epidermoid carcinoma which showed classical features of squamous cell carcinoma but do not arise from surface epithelium primarily. A PIOSCC is difficult to diagnose due to its rare nature and when it do not show classical features of squamous cell carcinoma. Here we present a case where immunohistochemistry plays an important role in the diagnosis of a de novo PIOSCC.

Key words: Primary intraosseous squamous cell carcinoma, Jaw tumor, immunohistochemistry.

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INTRODUCTION:

Primary Intraosseous Squamous Cell Carcinoma (PIOSCC) is a rare malignancy of jaws. In 1913 Loos described this entity as central epidermoid carcinoma. In 1972 Pindborg classified it as primary intraossous carcinoma in WHO tumor classification.[1,2] Eversole used the term PIOSCC in WHO tumor reclassification in 2005 and WHO defined it as a squamous cell carcinoma arising within the jaw bones without any initial connection with the oral mucosa or sinus mucosa and thought to develop from remnants of odontogenic epithelium.[3,4] In the Latest classification by WHO 2005, PIOSCC has three categories.[3]

- Solid tumor that invade marrow spaces and induce osseous resorption
- PIOSCC arising from the lining of an odontogenic cyst
  - Specifically OKC/KCOT
  - Any other odontogenic cyst
- PIOSCC in association with other odontogenic benign tumor

Although in the literature there are more than 100 cases of PIOSCC has been discussed, the diagnosis is delayed as the information about differential diagnosis remains limited. WHO have been clearly defined diagnostic criteria for PIOSCC which are as follows [1]

- Histologic evidence of squamous cell carcinoma.
- Absence of ulcer on overlying mucosa.
- Absence of distant primary tumor.

PIOSCC may arise from epithelial lining of odontogenic cyst or de novo from residual odontogenic epithelium. Literature review shows 60 % occurrence in radicular or residual cyst, 16 % in dentigerous cyst, 14 % in OKC and 1% in lateral periodontal cyst. [4,5] The cystic epithelium may show changes like cystic expansion, keratinization, mucous prosoplasia and dysplastic transformation. Adenomatoid odontogenic tumor, ameloblastoma and pleomorphic adenoma are common benign neoplasm arising from cystic epithelium.[6,7] Although odontogenic cyst lining may show malignant

transformation into squamous cell carcinoma and mucoepidermoid carcinoma also.
Here we discuss a case of PIOSCC arising de novo in a 52 yr old male and also emphasize the differential diagnosis with the role of immunohistochemistry in PIOSCC diagnosis.

CASE REPORT:

A male patient aged 52 yrs reported to a Prosthodontist at private dental setup with a complaint of missing teeth in lower right posterior jaw and wanted them to be replaced by implants. Clinician diagnosed an asymptomatic swelling in lower right posterior region of mouth and asked for history. Patient gave a history of multiple extractions of root stumps in the same region an year back at the local dental hospital. The patient had continuous mild pain for 2-3 months which was relieved by medication. There was non availability of any previous radiograph associated with root stumps. Patient had no history of obvious systemic diseases and he gave a supportive evidence of extraction of root stumps due to trauma in the lesional area. Intraorally an asymptomatic swelling was visible with diffuse margins, having normal appearing overlying mucosa. The Swelling extended from premolar to third molar region. No obvious cortical expansion was found. On palpation a firm bony hard and tender swelling was encountered. No sign of pus discharge was evident. The Swelling extended anteroposteriorly in the mandible. Radiographically there was an ill defined radiolucency extended from premolar to third molar area.(Figure 1) Differential diagnosis included keratocystic odontogenic tumor, ameloblastoma, squamous cell carcinoma and mucoepidermoid carcinoma. Histopathological evaluation showed epithelial islands, nests and cords in mature stroma.(Figure 2) No abnormal keratinization was seen in any part, few islands showed clear cell changes.(Figure 3) Abnormal mitosis and anaplasia was present. (Figure 4) Immunohistochemistry analysis revealed positivity with CK 14 and 19, CK 5 and 6, p63 and negative staining with mucicarmine and carletnin.(Figure 5) On the basis of clinical and histopathological analysis a diagnosis of primary intraosseous squamous cell carcinoma of mandible was given.

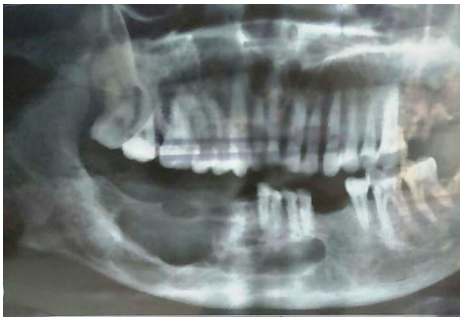

Figure 1- OPG showing ill defined radiolucency without sclerotic margins.

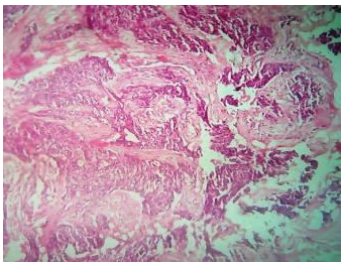

Figure 2- Islands and cords of epithelial cells in mature connective tissue

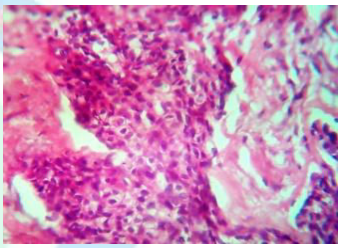

Figure 3- Epithelial islands showing some clear cells

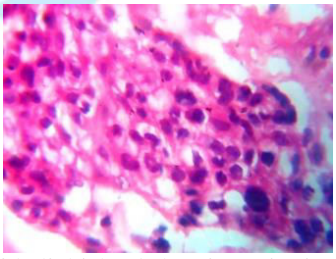

Figure 4- Epithelial island showing mitotic Figureures and anaplasia

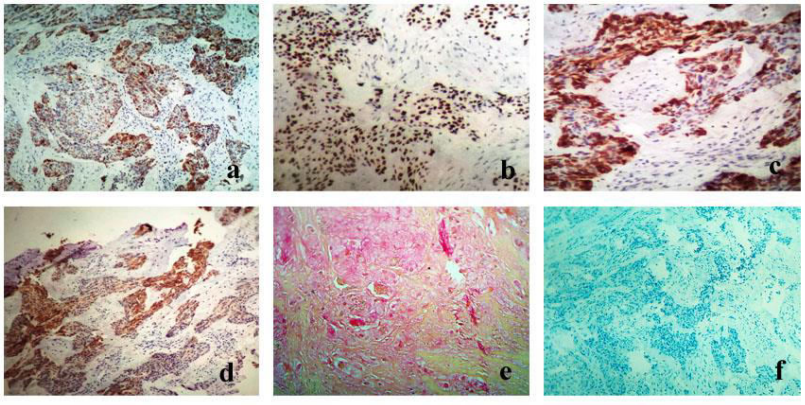

Figure 5- IHC profile showing. a) CK 14 positivity of epithelial islands, b) p53 positivity of epithelial cells, c) CK 19 positivity of epithelial cells, D) CK 5&6 positivity of epithelial cells, e) Mucicarmine negativity for clear cells and f) Carletinine negativity of cells.

DISCUSSION:

The odontogenic carcinomas are a rare entity. They were first described by Loos in 1913 as central epidermoid carcinoma later named as primary intraosseous carcinoma (PIOC) in first edition of WHO classification by Pindborg.[1] Waldron and Mustoe added central mucoepidermoid carcinoma to this classification which became most accepted classification in the literature. Eversole et al reframed the name of PIOC to PIOSCC (Primary Intraosseous Squamous Cell Carcinoma).[1,8]

Classification of PIOC according to Waldron and Mustoe as :-

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 and

Type 4 – Intraosseous mucoepidemoid carcinoma.

PIOSCC may arise as de novo or in preexisting odontogenic cysts or tumors. Pathogenesis of PIOSCC from an odontogenic cyst has been described in the literature by many authors like Schwimmer, Gardner, Keszler and Tan et al but is still unclear.[9,10] Bodner reviewed 116 cases of odontogenic cysts and summarized the pathogenesis in the following three mechanisms-[4]

1- Chronic inflammation is often accompanied by the formation of reactive oxygen and nitrogen species by phagocytes. These have the potential to damage DNA, proteins, and cell membranes, modulate enzyme activities and gene expression, promoting carcinogenesis. Moreover, chronic inflammation appears to promote apoptosis of normal cells that leads to a compensatory proliferative response by the remaining cells. This process increases the number of cells that are dividing and therefore are subject to DNA damage and promotes the growth of malignant cells.
2- Infectious agents may directly transform cells by inserting active oncogenes into the host genome, inhibiting tumour suppressor or stimulating mitoses.
3- Infectious agents may induce immunosuppression with consequent reduced immunosurveillance

Genetic factors may also play a role in the pathogenesis of carcinoma development in the cystic lining.

PIOSCC affect wide range of age group usually 4-90 years with a mean age of 57 years.[11] Males show predominance against female with a ratio of 2.5:1.[8,12] PIOSCC predominantly affects the posterior mandible in comparison to maxilla where anterior region is involved.[1,12] Clinically patient complains of pain and swelling but early phases of PIOSCC are symptomless. Present case showed no symptoms till the time it was reported. The late phase show cortical expansions, paraesthesia due to nerve compression and the mobility of teeth. Regional lymph nodes are involved but not always. Radiographically PIOSCC usually represent unicystic or multicystic radiolucency having ill defined border without sclerotic margins. The tumor extends around the teeth and do not show any root resorption as the tumor progress to the way of least resistance. Some time it produces a classical feature of "floating teeth".[12] Microscopic examination of the tumor shows normal surface mucosa, stratified squamous epithelium without any ulceration or breach in the continuity of basement membrane. The underlying connective tissue has cords, islands and nests of epithelial cells. Epithelial cells show malignant features and abnormal keratinization. The present case showed epithelial islands and nests having no palisading peripheral cells and no keratinization. There was no evidence of odontogenic cyst component also. Few islands rich in clear cells were seen. To clarify the squamous nature of cells we used CK 5/6 and CK 14/19 markers.

PIOSCC should be differentiated histopathologically from malignant odontogenic tumors & central mucoepidermoid carcinoma and must be ruled out from mucosal squamous cell carcinoma and other benign odontogenic tumors.

The malignant odontogenic tumors, ameloblastic carcinoma show characteristic peripheral columnar cells with palisidation and reverse polarization of nucleus along with prominent malignant features. These features are absent in PIOSCC as seen in our case.[7] Although PIOSCC may demonstate few prominent clear cell islands and sheets, along with keratin pearls, clear cell odontogenic carcinomas do not show keratin pearl formation at all. The histpathological features noted in the Shear study of PIOSCC was the absence of keratinization. Evaluation of histologic features of this case supports the concept that PIOSCCs may also be nonkeratinizing.[12,13] The keratin cannot be the sole discriminative feature between both entities; a tumor marker plays a vital role. The clear cells in PIOSCC should also demonstrate negative mucocarcarmine staining (Figure 5) in an otherwise central mucoepidermoid carcinoma should be considered in the diagnosis. Calcifying odontogenic carcinoma displays its peculiar features like ghost cells and calcified material, which are completely absent in PIOSCC.[12,14]

Mucosal squamous cell carcinoma histopathologically shows malignant surface epithelium and infiltrating epithelial islands and sheets originated from surface epithelium. PIOSCC shows epithelial islands and sheets without any connection with surface epithelium. So, atypia is seen only in islands and sheet but not in surface epithelium. Benign odontogenic tumors like ameloblastoma and CEOT show local invasion but are not as aggressive as in case of PIOSCC.[14]

Primary intraosseous squamous cell carcinoma is considered a highly malignant tumor that should be treated aggressively.[12] In phase one eneucleation or incisional biopsy should be done and if carcinoma is diagnosed, phase two comprises of radical resection, neck dissection or radiation or chemotherapy. Radiotherapy and chemotherapy should be considered only in lesions that cannot be controlled surgically. Some

cases may need removal of the lymph nodes when tumor infiltrates the surrounding bone.[7] 66% cases showed recurrence of tumor. Two years Survival period is in 53% patients.[7,11] PIOSCCs originating from odontogenic cysts have a better prognosis than the *de novo* lesions.

CONCLUSION:

To conclude de novo PIOSCC originating from odontogenic cell rests usually histopathologically may show keratinizing or nonkeratinizing pattern. Non keratinizing PIOSCC demanded immunohistochemical as well as special stains to rule out other odontogenic carcinomas and other carcinomas of jaw as it is difficult to diagnose it in the routine protocol and has poorer prognosis.

REFERENCES:

1. M Arivuselvi Anadakumar, S. Ramasamy, J Venkatesh, K Ramya, Ravi David Austin, Primary Intraosseous Squamous Cell Carcinoma Arising from Parakeratinized Kerato – Cystic Odontogenic Tumor Associated with Impacted Mandibular Canine: A Rare Entity. IJSS Case Reports & Reviews, November 2015, Vol 2, Issue 6 page 4-9.
2. 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.
3. Eversole LR, Siar CH, van der Waal I. Primaryintraosseoussquamouscell carcinomas. In: Barnes L, Evson JW, Reichart P, idransky D, eds. WorldHealthOrganizationclassification of tumors. Pathology andgenetics head and necktumors. worldHealthOrganization international Agency forResearchonCancer. Lyon: IACR Press, 2005; 290–1.
4. Bodner L, Manor E, Shear M, van der Waal I. Primaryintraosseoussquamouscell carcinoma arising in anodontogeniccyst: a clinicopathologicanalysis of 116 reported cases. J Oral PatholMed. 2011;40:733-8.
5. Baker RD, D'Onofrio ED, Corio RL, Crawford BE, Terry BC. Squamous-cell carcinoma arising in a lateral periodontal cyst. Oral Surg Oral Med Oral Pathol. 1979:47:495-499
6. Makowski GJ, McGuff S, Van Sickels JE. Squamous cell carcinoma in a maxillary odontogenickeratocyst. J Oral Maxillofac Surg. 2001:59:76-80.
7. Chitrapriya Saxena, Pooja Aggarwal, Vijay Wadhwan, Vishal Bansal Primary intraosseous squamous cell carcinoma in odontogenic keratocyst: A rare entity Journal of Oral and Maxillofacial Pathology: Vol. 19 Issue 3 Sep - Dec 2015 page 406
8. Lin YJ, Chen CH, Wang WC, Chen YK, Lin LM. Primary intraosseous carcinoma of the mandible. Dentomaxillofac Radiol 2005;34:112 - 6
9. Schwimmer AM, Aydin F, Morrison N. Squamous cell carcinoma arising in residual odontogenic cyst: report of a case and review of literature. Oral Surg Oral Med Oral Pathol. 1991;72: 218–21.
10. Gardner AF. The odontogenic cyst as a potential carcinoma; a clinico-pathologic appraisal. J Am Dent Assoc. 1969;78:746–55.
11. Jing-Wei Huang, Hai-Yan Luo, Qiong Li, Tie-Jun Li, Primary Intraosseous Squamous Cell Carcinoma of the Jaws. Arch Pathol Lab Med, Vol 133, November 2009 page 1834-1840.
12. Han-Kyul Park, Tae-Seop Kim, Dong-Ho Geum, Sang-Yong Yoon, Jae-Min Song, Dae-Seok Hwang, Yeong-Cheo Cho, Uk-Kyu Kim, Mandibular intraosseous squamous cell carcinoma lesion associated with odontogenic keratocyst: a case report. J Korean Assoc Oral Maxillofac Surg 2015;41:78-83
13. Shear M. Primary intra-alveolar epidermoid carcinoma of the jaw. J Pathol. 1969;97:645–51.
14. Shambhulingappa P, Sheikh S, Puri N, Jindal SK, Primary intraosseous carcinoma of mandible: An update on review of literature with a case report J Clin Exp Dent. 2010;2(2):e91-5.

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