A rare case report of intraosseous adenoid cystic carcinoma of the mandible
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Abstract
Adenoid cystic carcinoma (ACC) is an uncommon malignant tumor of the salivary glands. It generally involves the minor salivary glands, and the hard palate is the most common site. ACC presents as a slow growing mass with mild pain and usually demonstrates perineural invasion. An intraosseous occurrence of ACC is a very rare and when it occurs the mandible is more commonly involved than the maxilla. A Pubmed search has revealed only 26 cases of primary ACC of the mandible until date. Hence, reporting one such rare case of intraosseous ACC in a 49-year-old male patient involving the mandible.

Keywords: Adenoid cystic carcinoma, intraosseous adenoid cystic carcinoma, mandible, salivary gland malignancies

Introduction
The adenoid cystic carcinoma (ACC) is an uncommon malignant tumor of salivary glands arising predominantly from the mucous salivary glands. It constitutes around 5-10% of all salivary gland neoplasms, representing 2-4% of malignant occurrences of the head and neck area. Approximately, 31% of lesions affect minor salivary glands particularly of the palate followed by submandibular and parotid glands. The prominent features of this tumor are slow growth, gradual destruction of surrounding tissues, perineural invasion, and distant metastasis. It rarely arises in an intraosseous location causing bony destruction. The report of 26 cases of primary ACC of the mandible until date in the literature suggests its rarity. The intraosseous ACC affects posterior mandible more common than maxilla. The typical presentation of the intraosseous ACC is pain, swelling and rarely paresthesia and numbness. Intraosseous ACC with perineural invasion behaves aggressively hence en bloc or radical resection of the tumor is the mainstay of the management with the additional post-operative radiotherapy to prevent distant metastasis and recurrence of the lesion. This case report highlights one such rare case of intraosseous ACC affecting the mandible.

Case Report
A 49-year-old male patient presented with a complaint of pain with respect to lower left back teeth region since 2 months and swelling in the same region since 15 days. Pain was secondary in incidence. The primary incidence of pain occurred 6 months back for which he visited a private dental clinic and was diagnosed as chronic pericoronitis with respect to 38, and the tooth was extracted which was uneventful. He was asymptomatic for 4 months and he developed pain 2 months back. The pain was intermittent, localized, dull and moderate in intensity. He noticed an intraoral swelling 15 days back in the same region while brushing the teeth. The swelling was primary in incidence and gradually increased in size. The patient also gave a history of tingling sensation in relation to the left side of the chin since 10 days. No history of trauma and any other associated symptoms.

Past medical and dental history were not contributory except for the extraction of 38. General physical examination showed no gross facial asymmetry. All the vital were in normal limits.

Extra oral examination was non-contributory. Regional lymph nodes were not palpable were also not palpable.
On intraoral examination, a diffuse swelling measuring 3 cm x 2 cm was seen involving the alveolar ridge in relation to 38 [Figure 1] extending buccally from distal aspect of 37 to the retromolar area, lingually extending from distal aspect of 35 to retromolar area anteroposteriorly, and from marginal gingiva to mucolinguual fold superoinferiorly. There was a slit in the mucosa between the buccal and lingual mucosal flaps in the region of 38. The mucosa around this slit appeared keratotic and was of normal in color. On palpation the swelling was tender, soft to firm in consistency with slight lingual cortical expansion, it was compressible but not reducible. No discharge was evident on palpation. There was no mobility or periodontal pockets or tenderness noted it 35, 36, and 37.

Based on the history and clinical findings a provisional diagnosis of chronic osteomyelitis with respect to left posterior mandible was given.

The differential diagnosis of infected residual cyst, keratocystic odontogenic tumor (KOT) ameloblastoma, calcifying epithelial odontogenic cyst (CEOC), and calcifying epithelial odontogenic tumor (CEOT) was considered.

The following investigations were done: Electrical pulp vitality testing in relation to 36 and 37 revealed that the teeth were vital.

The periapical radiograph in relation to 37 and 38 showed an irregular radiolucency [Figure 2] distal to radicular portion of 37 extending anteroposteriorly from the middle 3rd of distal aspect of the distal root of 37 into the ramus of the mandible and superoinferiorly from residual alveolar ridge to the superior boundary of mandibular canal. The borders of the radiolucency were ill defined. The bony trabecule cannot be seen within the radiolucency. Surrounding trabecular pattern appeared normal. There was a vertical bone loss in relation to mesial aspect of 36 and 37, loss of lamina dura at the apical 3rd of roots of 37. The superior boundary of the mandibular canal could not be appreciated.

True mandibular occlusal radiograph did not reveal any changes.

The panoramic radiograph showed diffuse unilocular periapical radiolucency in relation to left body and ramus of the mandible [Figure 3]. It extended from apical region of 37 into the ramus until 1 cm from the sigmoid notch anteroposteriorly and extended from the level of alveolar crest in 38 region until 1 cm above the inferior border of the mandible superoinferiorly and 5 mm from anterior border of ramus until 1.5 cm from the posterior border of the ramus mediolaterally. The borders of the radiolucency were diffuse and ill defined. Bony trabeculae could not be seen within the radiolucency. Surrounding trabecular pattern appeared normal. Superior and inferior boundaries of the mandibular canal could not be appreciated.

Computed tomography (CT) showed an irregular expansile lytic lesion measuring 1.9 cm x 1.2 cm x 3.5 cm involving left ramus of the mandible [Figure 4a and b]. The complete destruction of the medial bony plate of the mandibular ramus was noted. Focal to near total destruction measuring 8 mm was seen in the outer bony plate of the mandible which was consistent with the malignant destruction of left ramus of the mandible.

The radiographic differential diagnosis of chronic suppurative osteomyelitis, central squamous cell carcinoma (SCC), metastatic lesion in the jaw, intraosseous salivary gland tumor were considered.

An incisional biopsy was done with respect to left body of mandible. Microscopically the stained sections revealed islands and cords composed bland looking basaloid cells and angular
cells with areas of cystification giving cribriform (Swiss cheese pattern) appearance [Figure 5]. The cyst-like spaces contained mildly basophilic mucoid material; the background connective tissue was fibrocollagenous with small and medium sized blood vessels. Areas of hyalinization surrounding the islands of tumor cells were also observed. Histopathologic features were suggestive of ACC Grade II which was considered as the final diagnosis.

Before surgery to rule out metastasis of intraosseous ACC to thorax and lung, CT thorax and lung was done which revealed no metastasis.

The patient underwent left hemimandibulectomy with radicular neck dissection followed by mandibular reconstruction using titanium plates and free fibular flap and was treated with external beam radiotherapy with intensity modulated radiotherapy to a dose of 66 Gy/33 fractions for 12 days. The patient is on regular follow-up.

Histopathological examination of the complete excised lesion revealed similar features seen in incisional biopsy.

**Discussion**

The World Health Organization (WHO) defines ACC as a “basaloid tumor consisting of epithelial and myoepithelial cells in various morphological configurations including tubular, cribriform, and solid patterns. These neoplasms belong to the rare group of malignant neoplasms affecting the salivary glands. It has a persistent clinical course resulting in significant morbidity and mortality.”[1]

ACC was first described as “cylindroma” by Theodor Billroth in 1856 based on his observation of specimen in which long amorphous compartments appeared as cylinders on histopathologic examination. Spies, in 1930, were the first to use the term ACC. In 1943, Dockerty and Mayo emphasized the malignant nature of this tumor.[7]

The pathogenesis of central salivary gland neoplasms is unknown. The retromolar mucous gland and sub-mandibular/sublingual salivary glands may get embedded in the lingual cortex during embryological development of jawbones. Some theories propose that the neoplastic transformation of these glands can lead to intraosseous ACC. Furthermore, neoplastic transformation of odontogenic cyst epithelium and sinus epithelium has been suggested as the reasons for the occurrence of these neoplasms.[5,6,10]

ACC is the fifth most common epithelial tumor of the salivary glands and constitutes approximately 6-10% of all salivary gland tumors.[11] The minor salivary glands located in the hard palate is the most frequent site of occurrence, followed by parotid and sub-mandibular glands.[9,11] Lower lip, retromolar-tonsillar pillar region and sublingual gland are less frequently affected.[12] ACC commonly occurs in the 5th decade of life with slight female predilection.[11,12]

Intraosseous ACC is extremely rare. A total of 26 cases of primary ACC of the mandible has been reported in the literature until date.[5] Central lesions have wide age distribution (24-82 years) and occur equally in males and females.[4,13] The

![Figure 4: Computed tomography findings showing an irregular expansile lytic lesion involving the left ramus of the mandible. (a) Sagittal, axial and three-dimensional, and (b) coronal section](image)

![Figure 5: Pictomicrograph demonstrating the Swiss cheese pattern (×40 magnification)](image)
posterior mandible is the most common site of occurrence, however, posterior maxilla can also be involved. Pain and swelling are the most common clinical features with paresthesia and numbness being rare.\textsuperscript{[4]a} The characteristic features include slow growth, gradual destruction of surrounding tissues, perineural invasion, and unpredictable distant metastasis, commonly to lungs and bones.\textsuperscript{[11,14,15]}

In this case, the tumor presented with pain and swelling in the mandibular 3\textsuperscript{rd} molar region in a 48-year-old male patient with tingling sensation in the left chin region. These features are similar to those reported in the literature.

Batsakis\textsuperscript{[12]} proposed diagnostic criteria for primary intraosseous salivary gland neoplasms, which include: (1) Radiographic evidence of osteolysis, (2) presence of intact cortical plates, (3) Presence of intact mucous membrane overlying the lesion, (4) of any primary tumor within major or minor salivary gland, and (5) histological confirmation of the typical architecture and morphological features of a salivary gland tumor.

The present case satisfies all the criteria except for the intact mucous membrane over the lesion. In the reported case, there was a slit like break in the mucosal covering in the region of 38 probably indicative of the previous extraction.

According to Brookstone and Huvos,\textsuperscript{[3,14,16]} lesions that are located within undisturbed, intact cortical bone and overlying periosteum and show no signs of cortical expansion offer the best prognosis and, therefore, suggest Stage I disease. Stage II disease is characterized by lesions surrounded by intact cortical bone that has undergone some degree of expansion. Cortical perforation, breakdown of the overlying periosteum or nodal metastatic spread is categorized as Stage III disease.

The CT scan of the patient revealed destruction of the medial lateral cortical plates of the ramus with the destruction of bone suggestive of malignant tumor. The soft to firm consistency of the lesion on palpation is indicative of extension of the tumor mass into the adjacent soft tissue. According to Brookstone and Huvos, these features are suggestive of a Stage III tumor.

ACC is composed of a mixture of myoepithelial cells and ductal cells that can have varied arrangements. The major histological patterns are cribriform, tubular, and solid. Usually, combinations of the above patterns are seen and the tumor is classified based on the predominant pattern. The cribriform pattern is the most classic resembling Swiss cheese. Histologically, the cribriform or tubular growth pattern is associated with a better prognosis.\textsuperscript{[9]}

The presence of 30-50\% solid areas may indicate an aggressive clinical course with poor prognosis.\textsuperscript{[16]} In this case, cribriform pattern was noted in the incisional biopsy specimen, but the histopathology of the surgical specimen revealed all the three types suggestive of a poor prognosis. There was no evidence of perineural invasion.

Perineural invasion is the characteristic feature of ACC. Although not pathognomonic, it probably results in pain which is a common clinical finding. Perineural invasion occurs through spread along the perineural spaces or within the nerve itself. According to WHO, The influence of perineural invasion on survival has been contradictory.\textsuperscript{[8]}

The clinical differential diagnosis can include infected residual cyst, KOT, ameloblastoma, CEOC, CEOT and radiographically chronic suppurative osteomyelitis, central SCC, metastatic lesion in the jaw, intraosseous salivary gland tumor may be considered. Infected residual cyst can present as pain, and unhealed extraction socket will be evident, but cortical expansion is not a feature. KOT can develop in the 2\textsuperscript{nd} and 3\textsuperscript{rd} decade of life and present with pain and swelling without obvious bony expansion, radiographically they demonstrate a well-defined radiolucent area with smooth and often corticated margins. Ameloblastoma is seen in the age group of 20-50 years, will present as a painless slow growing swelling commonly affecting the posterior mandible with buccolingual cortical expansion radiographically it appears as a multilocular radiolucent with resorption of root and COEC and CEOT are more common in men can present as a slow growing painless mass affecting mandibular in premolar-molar area with 52\% associated with an impacted or unerupted tooth, radiographs reveal a mixed radiolucent radio-opaque lesion with minimal cortical expansion. Central SCC, metastatic lesion of the Jaw and intraosseous malignant salivary gland tumor are more common in men in the 4\textsuperscript{th}-8\textsuperscript{th} decade of life, patient presents with pain, pathologic fracture and paresthesia with normal appearing mucosa. All these lesions may appear as poorly defined radiolucencies with ill-defined borders.

\textit{En bloc} or radical resection of the tumor is the main stay in the management of central salivary gland tumors of the mandible. The tumor has a potential for recurrence irrespective of the treatment modality.\textsuperscript{[3]} Post-surgical radiation therapy results in improved local and regional control.\textsuperscript{[6]}

\textbf{Conclusion}

Although intraosseous ACC arising within the mandible are uncommon, their significance should not be ignored. Because of their unique morphology and clinical behavior, they should be considered in the differential diagnosis of aggressive lesions of the mandible. If intraosseous ACC is suspected, a multidisciplinary approach should be adopted. A long-term follow-up is necessary for intraosseous ACC to detect metastasis and recurrence of the lesion. This case underlines the importance of considering intraosseous malignant salivary gland tumors in the differential diagnosis of poorly defined radiolucencies of the mandible. The early detection will benefit the patient and reduces the morbidity associated with these lesions.

\textbf{Acknowledgment}

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References