Oral Pathology

Adenoid Cystic Carcinoma of Palate: A Case Report and Overview

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Abstract

Adenoid cystic carcinoma (AdCC) is a rare malignant salivary gland tumor of epithelial origin and accounts for 10% of all salivary gland neoplasms and 1% to 2% of all head and neck malignancies. It is the fifth most common malignancy of salivary gland origin. Cribriform, tubular and solid are the three recognized histopathological patterns. It is a slow-growing tumor, but the long-term prognosis is poor with a 15-year survival rate of less than 50%. An accurate pathological diagnosis of AdCC is essential if patients are to receive timely and appropriate treatment. Present article describes a case of a 80 year old female patient with Cribriform type of AdCC on palate.

|| Key Words

Cribriform, Malignancy, Palatal tumor, Salivary gland neoplasms, Survival rate

|| Introduction

Salivary gland tumors are a diverse group of lesions and they show great morphologic variations. These neoplasms may arise not only from the major salivary glands, but also from any of the numerous intraoral minor salivary glands. Hence, we can expect tumors originating from the accessory glands in the lip, palate, tongue, buccal mucosa, floor of the mouth and retromolar area.[1] Adenoid cystic carcinoma (AdCC) is the fifth most common malignancy of salivary gland origin. It is a slow growing malignant salivary gland tumor which was first described by three Frenchmen (Robin, Lorain, and Laboulbene) in two articles published in 1853 and 1854. Billroth (1859) coined the term, "cylindroma" for AdCC because of its cribriform appearance formed by tumor cells with cylindrical pseudolumina or pseudo spaces.[2] Spies is credited for the term adenoid cystic carcinoma, in a discussion of tumors, cutaneous and non-cutaneous, of the basal cell variety in 1930.[3] AdCC progresses slowly with wide perineural invasion. Lymphatic spread to the neck remains rare. Haematogenous dissemination, on the other hand, occurs often in the course of the disease.[4]

|| Case Report

A 80-year-old female patient reported to our institute and she was referred to the Department of oral Pathology and Microbiology with the chief complaint of pain since 8-10 months and swelling in upper right back region of jaw since 6-7 months. Pain was dull aching in nature, the intensity of which gradually increased over a period of time. Patient visited a private dental clinic, where she was prescribed analgesics (Details of medication not available). Pain relived temporarily after taking medication, then it again aggravated after which the patient visited to our institute. Patient was apparently alright 10 months before, then she developed a peanut size swelling in right palatal region which gradually increased to the present size. Patient gave history of hypertension for 2 years and was under medication for the same and was operated for hernia 12 years back. On extraoral examination (Fig.1) no relevant findings were observed. Intraoral examination (Fig.2) on inspection showed a solitary swelling on palatal aspect measuring 5*3 cm extending from permanent maxillary right canine to permanent maxillary second molar region. The swelling was well demarcated, dome shaped with posterior part of swelling showing erythematous surface. On palpation swelling was tender and firm to hard. Grade II mobility and deep pockets were present i.r.t. permanent maxillary second molar. On temporomandibular joint (TMJ) examination adequate mouth opening, and no tenderness and deviation was seen. Lower right submandibular lymph node was palpable, mobile and tender on palpation.

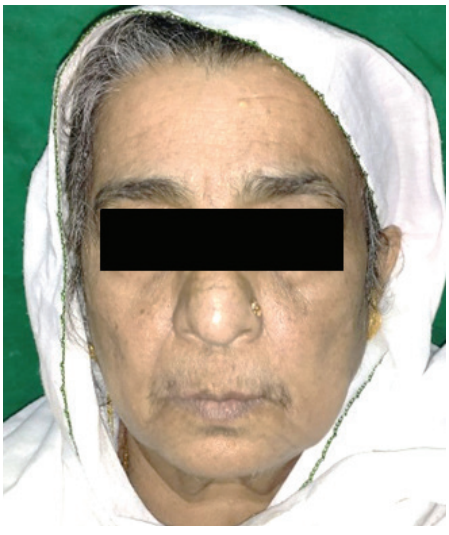

Fig.1: Extroral clinical photograph

(A 80-year-old female patient complained of pain and swelling in upper right back region of jaw since 7 months.)

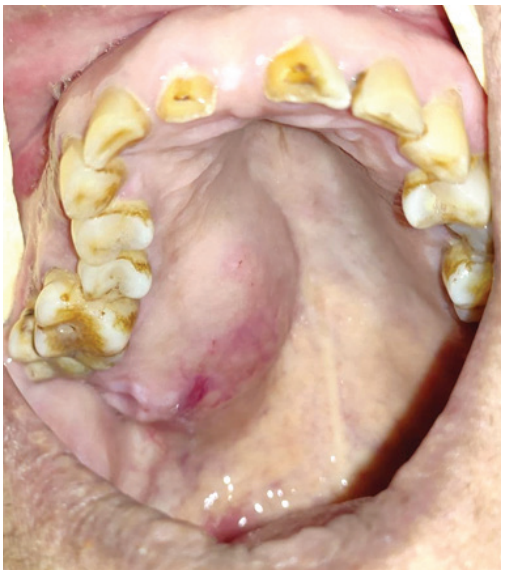

Fig.2: Intraoral clinical photograph

(A diffuse, tender, firm to hard swelling with smooth overlying surface on palatal aspect i.r.t. 13,14,15,16 and 17 measuring 5*3 cm.)

Patient was advised orthopantomogram (OPG), which showed (Fig. 3) arc shaped bone loss at maxillary right first and second molar region, with loss of right maxillary tuberosity. Computed tomography (CT) was advised to check the extent of lesion, which showed (Fig. 4 and 5) approximately 2.1*2.6*2.2 cm sized (AP*ML*SI) [AP- Anteroposterior, ML- Mediolateral, SI- Superoinferior] well defined soft tissue density lesion with epicenter around right half of palate and floor of right maxillary sinus causing erosion with scalloping of right hard palate, right sided superior alveolar arch (around right upper molar teeth) and floor of right maxillary sinus. It showed superior extension via pterygopalatine canal reaching up-to pterygopalatine fossa with its mild widening. Routine blood investigation performed showed all the parameters within normal range. Based on the clinical findings a provisional diagnosis of benign salivary gland tumor was given. Differential diagnosis included pleomorphic adenoma, peripheral ameloblastoma and peripheral giant cell granuloma.

Incisional biopsy was advised to the patient. On histopathological examination H & E-stained section showed single bit of tissue consisting of surface epithelium, connective tissue stroma, salivary gland tissue and nerve tissue. Lesional area separated from

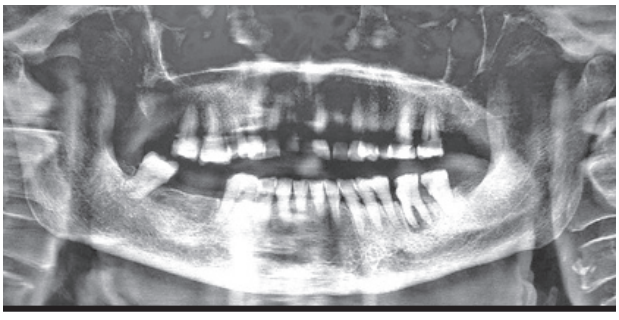

Fig.3: Orthopantomogram

(Well defined radiolucency extending from distal aspect of permanent maxillary first molar to maxillary tuberosity)

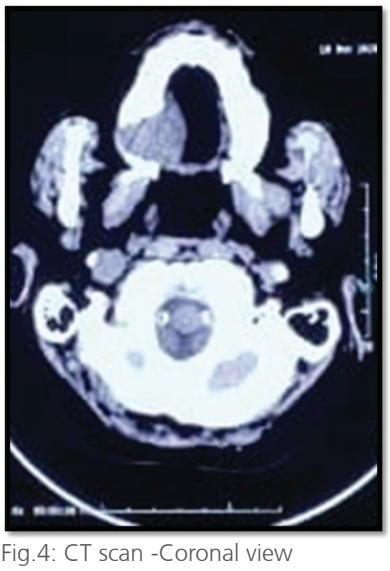

Fig.4: CT scan -Coronal view

(well defined soft tissue density lesion with epicenter around right half of palate and floor of right maxillary sinus causing erosion with scalloping of right hard palate, right sided superior alveolar arch and floor of right maxillary sinus.)

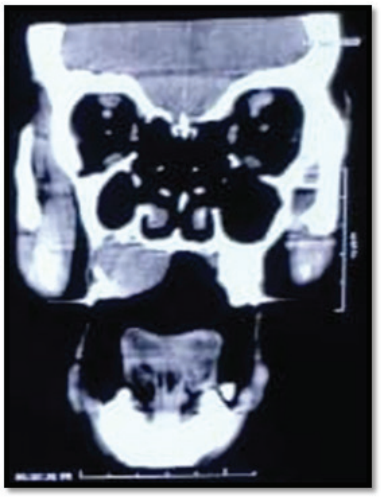

Fig.5: CT scan -Axial view

(Superior extension via pterygopalatine canal reaching up-to pterygopalatine fossa with its mild widening. It is further extending via right pterygomaxillary fissure and peeping into right maxillary fat pad into right infratemporal fossa and medially peeping into sphenopalatine foramen.)

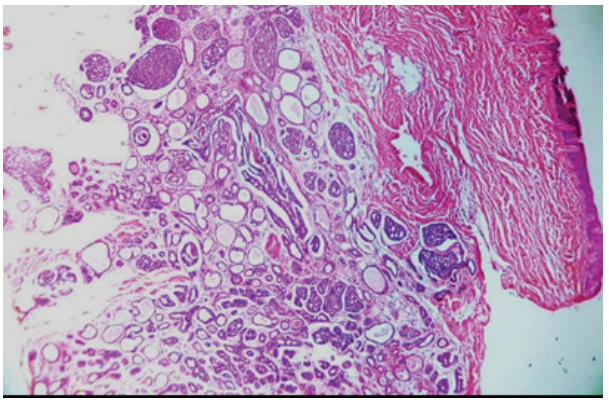

Fig.6: H & E-stained section (4X)

(Surface epithelium, connective tissue stroma, salivary gland tissue and nerve tissue)

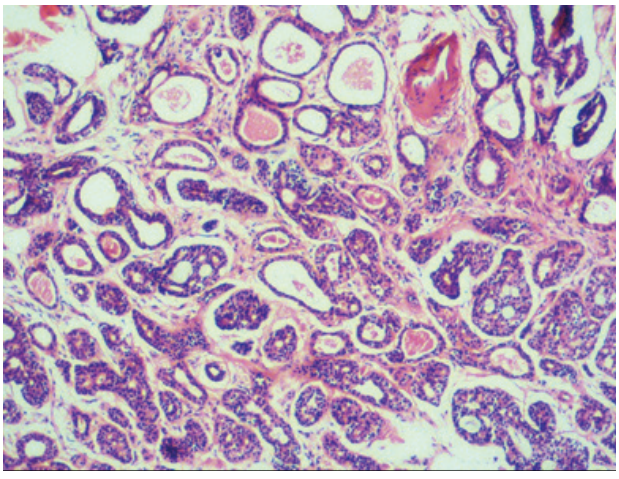

Fig.6: H & E-stained section (10X)

(Lesional area consisted of epithelial cells proliferating in cribriform pattern. Multiple duct like or tubular structure consisting of homogeneous eosinophilic material and lined by one to two layers of cuboidal to flattened epithelial cells were noted)

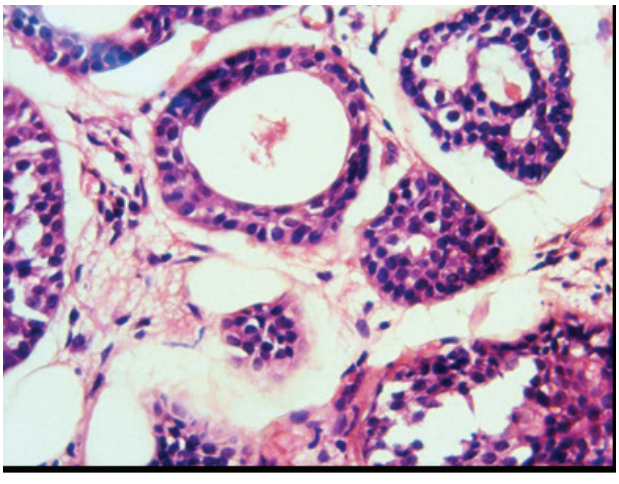

Fig.6: H & E-stained section (40X)

(Islands composed of basaloid cells with microcystic spaces. Duct like structures and islands are surrounded by fibrous and hyalinized band of connective tissue stroma.)

overlying stratified squamous epithelium by a fibro cellular band of connective tissue stroma. Epithelial cell nests formed multiple cylindrical cysts like patterns resembling a Swiss cheese or honey comb pattern. Multiple duct like or tubular structure consisting of homogeneous eosinophilic material and lined by one to two layers of cuboidal to flattened epithelial cells were noted. Few islands composed of basaloid cells with microcystic spaces were seen. Duct like structures and islands were surrounded by fibrous and hyalinized band of connective tissue stroma. Endothelial lined vascular channels and adipose tissue was also seen. Based on histopathologic finding and correlation of clinical and radiographic features, final diagnosis of Adenoid cystic carcinoma was given.

|| Discussion

Adenoid cystic carcinoma is a rare malignant salivary gland tumor of epithelial origin and accounts for 10% of all salivary gland neoplasms and 1% to 2% of all head and neck malignancies.[5] The World Health Organization (WHO) defines AdCC as a "Basaloid tumor consisting of epithelial and myoepithelial cells in various morphological configurations including tubular, cribriform, and solid patterns."[6] It is one of the most common malignant tumors of the minor salivary and most common site is the minor salivary glands of the oral cavity (31% of lesions affect minor salivary glands, particularly the palate).[7]

In parotid gland AdCC is relatively rare (2-3 % of all tumors) and in submandibular glands it constitutes for 12-17 % of all tumors and is the most common malignancy. Some investigators have found female predilection in AdCC. It is rare in people less than 20 years and mostly found in middle aged population.[8] Although almost any site with a secretory gland component and has been reported in sites such as breasts, uterine cervix, esophagus and lungs, etc.[9] In many cases the tumor goes unnoticed because of slow clinical course and an indolent growth pattern. After perineural invasion, depending on location of invaded local nerves and structures varying symptoms can be seen.[10] The most common site of distant metastasis is the lung, followed by bone with other common sites including the liver and the brain.[11,12]

AdCC arises from ductal and myoepithelial cells and shows 3 distinct histologic patterns: tubular, cribriform, and solid. The cribriform pattern is the most commonly occurring (46.3%), followed by the solid (38.3%) and tubular (14.9%) patterns.[13,14,15] In cribriform pattern the epithelial cells are arranged in multiple cylindrical spaces, having a pseudo cystic appearance, containing a hyaline material. The tubular type is made up of ducts that can be formed by one or two layers of cells similar to the myoepithelial cells. The solid variant is composed of solid epithelial islands with central

areas of necrosis; the cells are small, basophilic and hyperchromatic with a densely granulated nucleus and scarce mitotic figures.[16] Szanto et al. gave grading for AdCC based on percentages of each pattern in the lesion. Grade I tumors contain only the tubular or cribriform growth pattern, grade II tumors contain cribriform or tubular growth with less than 30% solid component, and grade III tumors contain more than 30% solid component. Grading can be difficult as 1 tumor may show varying degrees of more than 1 subtype.[17]

Many immunohistochemical markers have been studied as potential prognostic indicators in AdCC. Smooth muscle actin, S100, and smooth muscle myosin heavy chain highlights cells showing myoepithelial differentiation surrounding the pseudocysts. Strong positivity for c- KIT (CD117) regardless of grade is seen in almost all neoplastic cells in the solid pattern, all cells surrounding pseudocysts in the cribriform pattern, and all luminal cells in the tubular pattern.[18] Increased expression Ki-67 is seen with increasing amounts of solid (grade III) component. p53 may show increased staining in areas of high-grade transformation. Increased p53 expression may also be an independent marker of poor prognosis.[19]

Many researchers have studied genetic alterations in AdCC. One of the studies found that MYB-NFIB fusion and associated gene alterations could help in predicting perineural invasion in AdCC tumors of HN. They quoted that the participation and fusion of other genes.

without the involvement of MYB in AdCC could be a related cause for the other subset of non-MYB AdCC.[20] Also, tumor DNA studies have suggested that agents that inhibit signalling through the Notch, protein kinase A, or FGF-IGF-PI3K pathways or block the epigenetic effects of chromatin remodelling might also be active in ACC.[21]

The differential diagnosis of AdCC includes tumors such as polymorphous adenocarcinoma, basal cell adenoma, basal cell adenocarcinoma, pleomorphic adenoma, epithelial myoepithelial carcinoma, basaloid squamous cell carcinoma, HPV related multiphenotypic sinonasal carcinoma.

Pleomorphic adenoma can be identified by the presence of mesenchymal, especially cartilaginous, differentiation in the stroma. Expression of glial fibrillary acidic protein and CD57 could be reliably used in cell block preparations to differentiate pleomorphic adenoma from AdCC.[22]

Basal cell adenoma can be differentiated by the presence of a capsule and lack of stromal and perineural invasion. Basal cell adenocarcinoma may be more difficult to differentiate with solid AdCC; however, lack of clear cytoplasm and hyperchromatic, angulated nuclei with the presence of peripheral palisaded nuclei in the former may aid in diagnosis. It is characterised by mutation of wnt/ beta catenin pathway leading to abnormal nuclear accumulation of beta catenin by immunohistochemistry.[23]

Polymorphous adenocarcinoma occurs almost exclusively in the minor salivary glands and histopathologic features are also overlapping with ACC such as ductal, tubular, and even cribriform growth. Perineural invasion is also common. However, the presence of cuboidal or columnar cells containing pale and ovoid nuclei with eosinophilic cytoplasm is in contrast with the hyperchromatic and angulated cells of AdCC.[24]

Epithelial-myoepithelial carcinoma can be differentiated by the presence of larger clear cells, absence of isomorphic cytological features, pseudocyst containing basal lamina material, typically contains compact branching tubules and shows positivity for PAS stain. It is characterised by HRAS mutation and lacks fusion involving MYB, NFIB or MYBL1.[25]

Salivary duct carcinoma can be identified by the presence of larger tumor cells with greater cytoplasm and increased mitotic figures, comedonecrosis. Intermix of ductal/ myoepithelial cells is absent.[23]

The basaloid squamous cell carcinoma does not show cribriform pattern and basophilic mucinous substance is seen. Mixture of small dark and large pale cells respectively without uniformity in architecture is seen. HPV related multiphenotypic sinonasal carcinoma shows positivity for high-risk HPV negative for MYB-NFIB fusion.[26]

Possible treatments of AdCC include four different modalities: surgical therapy, radiotherapy, chemotherapy and combined therapy (surgery and radiotherapy, radiotherapy and chemotherapy). The treatment of choice is radiotherapy and chemotherapy

in most of the cases.[27] Only surgical removal or radiotherapy in isolation may fail to eliminate the possibility of recidivation in surgical margins. Avery et al. and Miglianico et al. recommended postoperative radiotherapy, as radiation produces tumor regression and relieves symptoms.[28] The role of chemotherapy for AdCC is still controversial. Studies have shown consistently low response rates to chemotherapy for AdCC. This lack of a response is believed to reflect the slow growth rate of AdCC.[29] Few studies have demonstrated higher survival rates for AdCC than for SCC, based on overall survival and recurrence free survival, and have reported 5-year survival rates for AdCC ranging between 66 and 92%.[30] Some investigators have quoted that the histological subtypes with low malignancy levels (tubular and cribriform) have a better prognosis compared to those with a high-degree of malignancy (trabecular and solid).[31]

|| Conclusion

AdCC is a rare malignancy of salivary glands and is different from other malignancies because of its tendency for perineural invasion and histopathological variants reported. Clinical documentation of such cases is required in order to better understand and learn more about tumors of salivary glands. Optimal treatment of AdCC still has not been completely established. Tumor staging and grading with detection of perineural invasion and margin status are important prognostic tools. Proper physical examination accompanied by surgery and radiation and careful attention to quality-of-life issues are the pillars of management of this malignancy.

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