CASE REPORT

ADENOID CYSTIC CARCINOMA INVOLVING THE MAXILLARY SINUS, ORBIT AND PALATE: A CASE REPORT WITH REVIEW OF LITERATURE

Dr. Neha Shah*, Prof. (Dr.) J.G.Ray,**

Abstract

Salivary gland neoplasms form a diverse group of tumours with different histological characteristics and clinical behaviour patterns. Adenoid cystic carcinomais a relatively rare malignant salivary gland tumourcomprising less than 1% of all malignancies of head and neck. It has a deceptively benign histologic appearance. The clinical course is characterized by indolent, locally invasive growth with high propensity for local recurrence and distant metastasis.Though the combination of surgery and postoperative radiation therapy has improved loco-regional control of the disease yet late local recurrence and distant metastasis rates remain high and may occur decades after initial diagnosis. So, long term follow up of such patients is essential.

We present a case of Adenoid cystic carcinoma affecting the orbit, maxillary sinus, and palate of a 35 year old female patient with a brief literature review and highlight the importance of histopathology in making correct diagnosis.

Key Words: Adenoid cystic carcinoma, orbit, maxillary sinus, palate, malignant tumour, minor salivary gland

INTRODUCTION

Adenoid cystic carcinoma (ADCC) is a rare malignant salivary gland tumor comprising less than 1% of all malignancies of head and neck. It is the 5th most common malignancy of salivary gland origin, representing 5-10% of all salivary gland neoplasms.[1,2] It can arise in any salivary gland site, but approximately 50-60% develops within the minor salivary glands.[1,3] Among the major salivary glands, parotid is the most common site followed by submandibular gland whereas for the minor salivary glands, palate is the most common site followed by nose and paranasal sinuses.[2,4] Less common sites include lower lip, retromolar tonsillar pillar area, sublingual gland, buccal mucosa and floor of the mouth.[2] Besides oral cavity, ADCC has been reported to occur in lacrimal gland, ceruminous gland, esophagus, bronchus, lung, breast, skin, uterine cervix, ovary, Bartholin gland and prostrate.[4-6]

It affects a wide age range with a peak incidence in the fifth and sixth decade.[5,7,8] There is slightly more propensity for occurrence in females than males by ratio of 3:2. [6] It is characterized by a slow and indolent growth generally in sub mucosal localization, making these tumors hard to diagnose.[9] Histologically, three variants of ADCC are recognized: cribriform, tubular and solid.[1-9] Cribriform, being the most common and solid being the least common form.[1,2,4,8] Perineural invasion is common though lymph node involvement is rare.[4,7] The differential diagnosis of ADCC includes polymorphous low grade adenocarcinoma (PLGA), basal cell adenoma (BCA), basal cell adenocarcinoma (BCAC), basaloid squamous cell carcinoma (BSC) and pleomorphic adenoma.

The clinical behaviour of ADCC is a paradox: Firstly, tumor growth is slow, but its clinical course is relentless and progressive. Secondly, operative intervention is usually feasible, but multiple local recurrences are the rule.

ABOUT THE AUTHORS

*** Senior Lecturer,** Department of Oral & Maxillofacial Pathology, Gurunanak Institute of Dental Sciences & Research, Kolkata
****Professor and Head,** Department of Oral & Maxillofacial Pathology, Dr. R. Ahmed Dental College & Hospital, Kolkata

Figure 1. Extra-oral photograph showing diffuse swelling in the middle third of face on right side.

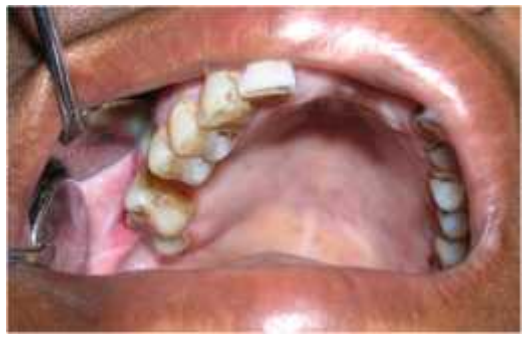

Figure 2. Intraoral photograph showing obliteration of buccal vestibule in relation to 15, 16, 17 and 18 and smooth surfaced swelling on right side of palate with respect to 15, 16, 17 and 18.

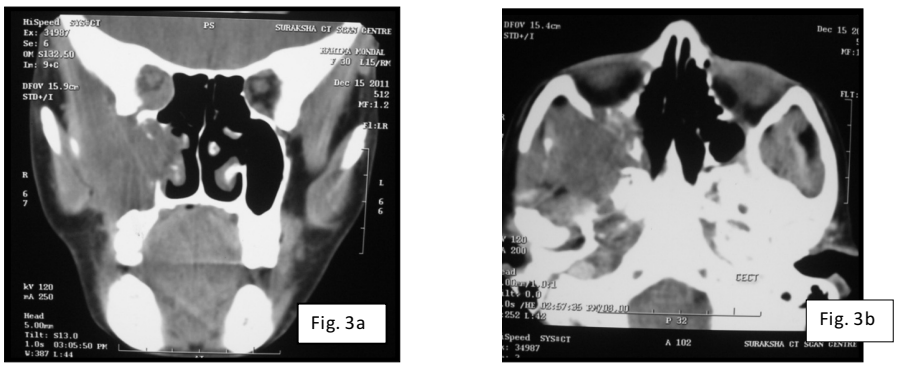

Figure 3a & 3b. Computerized Tomography of face showing expansile lytic mass within the right maxillary sinus invading ipsilateral masticator space and orbit.

Thirdly, metastatic spread to regional lymph nodes is uncommon, but distant spread to the lungs and bones is frequent. Lastly, 5-year survival rates are optimistically high, but 10- to 20- year survival rates are dismally low. [3,8]

Radiological investigations, especially CT scans are important to delineate the tumour, to plan extent of surgery and to look for recurrences during follow up postoperatively. [1]

The choice of therapy is affected by site, stage, histologic grade, and biologic behaviour of the ADCC. [3] The primary treatment of ADCC of head and neck is surgery with wide margins followed by radiotherapy. [1,6,7,9]

Here, we present a case of adenoid cystic carcinoma involving the orbit, maxillary sinus and palate with a brief literature review on its clinical presentation, histopathological features and differential diagnosis.

CASE REPORT

A 35 year old female patient reported to the Department of Oral and Maxillofacial Pathology at Dr. R. Ahmed Dental College and Hospital with a chief complain of pain in right side of face since 2 years. The patient gave a history of trauma 1 year back following which the pain increased. There was also a history of pus discharge from right nostril along with impaired vision and difficulty in seeing with the left eye. Dental history revealed extraction of upper right first molar 5 years back and upper right and left central incisor 7-8 months ago.

Extra-oral examination revealed a solitary, diffuse swelling in the middle third of the face on the right side, measuring roughly 3.0 cm x 2.0 cm. [Fig. 1] The overlying skin was intact and smooth. The swelling was firm and tender on palpation. There was puckering of cheek on the right side. The left eye was partially open.

Intra-oral examination revealed missing 16, 11 and 21. There was presence of a diffuse swelling involving the maxillary right buccal vestibule with respect to upper right second molar, first molar and second premolar measuring about 1.5 cm x 1.0 cm. Obliteration of buccal vestibule in relation to 18, 17, 16 was present. There was presence of another swelling on the right side of palate in relation to

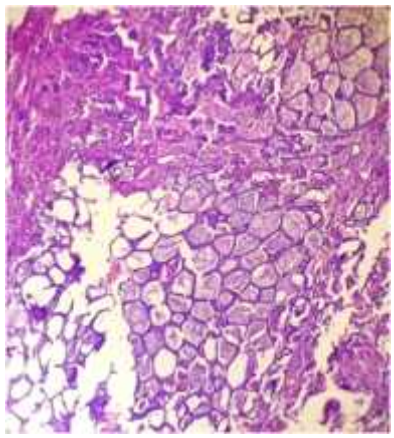

Figure 4. H&E stained section showing mixed arrangement of tumour cells comprising chiefly of cribriform pattern. (10x view)

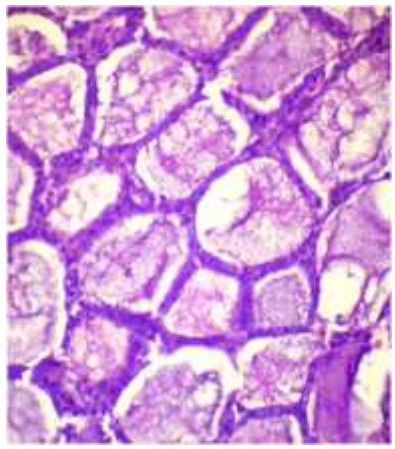

Figure 5. H&E stained section showing tumour composed of basaloid cells with angulated, hyperchromatic nuclei and scanty cytoplasm. The pseudo cysts contain hyaline material. (40x view)

18,17,16 and 15 measuring about 1.5 cm x 1.0 cm. Both the swellings were smooth surfaced without any ulceration and were firm and tender on palpation both buccally and palatally . There was presence of indentation of 18 on the adjacent buccal mucosa. [Fig. 2]

Computerised Tomogram revealed expansile lytic mass within the right maxillary sinus invading ipsilateral masticator space and orbit. [Fig. 3a,3b] A provisional diagnosis of malignancy was made and the patient was referred to the Department of Oral and Maxillofacial Surgery for incisional biopsy. Incisional biopsy was performed from the representative site under local anesthesia and submitted to our department for histopathologic evaluation.

Section stained with haematoxylin and eosin revealed the presence of tumour cells with deeply stained basophilic nuclei arranged in mixed pattern comprising chiefly of cribriform variant. [Fig. 4] Under higher magnification we observed the presence of basaloid cells with small, angulated, hyperchromatic nuclei and scant, clear to eosinophilic cytoplasm. The pseudo cysts contained hyaline material. [Fig.5] The connective tissue stroma was dense fibrous and hyalinized. Based on histopatholgy, a diagnosis of Adenoid Cystic Carcinoma was made and the patient was referred to the Oncology department of N.R.S Medical Hospital where radical surgery was performed followed by radiotherapy. The patient was kept on periodic follow up.

DISCUSSION

Adenoid cystic carcinoma (ADCC) is a malignant salivary gland tumour that was originally described by three Frenchmen Robin, Lorain and Laboulbene in 1853.[3,4,8] Since its first description, this neoplasm underwent numerous name changes before being given its current name by Spies in 1930.[3,5] In 1859, Billroth suggested the name cylindroma attributing to its cribriform appearance formed by tumor cells with cylindrical pseudolumina or pseudospaces.[1,2,8] Until 1940s, the tumor was thought to be a benign variant of the mixed salivary gland tumor. In 1943, Dockerty and Mayo emphasized the malignant nature of this tumor.[4] Conley and Dingman described ADCC as "one of the most biologically destructive and unpredictable tumours of the head and neck."[3,8]

ADCC is thought to arise from the mucous-secreting glands derived from the foregut that is the parotid, submandibular, sublingual glands and the mucus glands throughout the upper respiratory tract.[3,8] Electron microscopy and immunohistochemical analysis have shown that the tumour cells arise specifically from cells showing either epithelial or myoepithelial differentiation. [3,5,8]

Clinically, it is characterized by an initial period of slow and indolent growth that is usually asymptomatic. In most cases the tumour goes unnoticed until it has invaded local nerves and structures causing varying symptoms depending on location.[5] Tumours of the parotid present with trismus whereas ulceration of the overlying mucosa is usually seen in tumours of minor salivary glands.[4]

Histologically, the tumour is composed of basaloid cells with small, angulated, hyperchromatic nuclei and scant, clear to eosinophilic cytoplasm arranged into 3 prognostically significant patterns: cribriform, tubular, and solid.[1,4,5,8]

In the cribriform pattern, epithelial cells are arranged in multiple cylindrical spaces, having a pseudo cystic appearance, and many of these pseudo cysts contain 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 and few mitotic figures.[8]

Generally, all three patterns are observed in most tumours as was seen in our case and the tumour is classified according to the histologic pattern that predominates. Histological typing is helpful to predict prognosis of the tumour.[2,6,8] ADCC is graded according to Szanto, et al. as cribriform or tubular (grade I), less than 30% solid (grade II) or greater than 30% solid (grade III).[2,3,5,8] It has been reported that tubular pattern (well differentiated) has best prognosis and solid pattern (poorly differentiated) has worst prognosis.[2,3,5,6] Grading can be difficult as one tumour may show varying degrees of more than one subtype. Hence, several authors have reported that staging using the American Joint Committee on Cancer tumour stage to be more predictive of prognosis and distant metastasis.[5]

ADCCs of the minor glands have been reported to have worse prognosis than those of the major salivary glands.[2,3] Tumors in the submandibular gland have a poorer prognosis than those in the parotid.[4] Tumours involving the nose, paranasal sinuses and maxillary sinus have the worst prognosis as they are usually detected with higher stages at the time of diagnosis.[2,3] Tumors of minor salivary glands usually have the tendency to infiltrate extra glandular soft tissues and bone thereby allowing increased dissemination of the tumour.[2] Bone involvement and failure of primary surgery are associated with poor prognosis.[4]

Immunohistochemical studies have shown that the pseudocysts are positive for periodic acid schiff reagent (PAS) and Alcian blue and contain basement membrane components such as type IV collagen, heparin sulfate and laminin isoforms. Epithelial cells are positive for carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA). Duct lining cells are positive for C-kit (CD117) and myoepithelial cells are positive for S-100 protein, calponin, p63, smooth muscle actin and myosin. Expression of S-100, glial fibrillary acidic protein (GFAP) and neural cell adhesion molecule (NCAM) have been correlated with the presence of perineural invasion. p53 mutations appear to be involved with tumour progression and recurrence.[2] Strong c-KIT expression 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. Increased expression of the cellular proliferation marker Ki-67 and p53 have been seen with increasing amounts of solid (grade III) component and has been shown to correlate with worse prognosis. Thus, Ki-67 and p53 may be useful adjunct in assignment of tumour grade and prognosis.[5]

The differential diagnosis of ADCC includes tumors that also exhibit tubular and cribriform structures such as polymorphous low-grade adenocarcinoma (PLGA), tumors with basaloid cellular morphology such as basal cell adenoma (BCA), basal cell adenocarcinoma (BCAC) and basaloid squamous cell carcinoma (BSCC), and tumors with a dual population of ductal and myoepithelial cells such as pleomorphic adenoma (PA).[5]

A polymorphous architecture characterizes PLGA whereas ADCC has a more limited range of histologic patterns. Foci of papillary growth and areas of single cell infiltration are characteristic of PLGA. Basophilic pools of glycosaminoglycans are seen in ADCC but not in PLGA. PLGA shows uniform cell population with cytologically bland, round or oval vesicular nuclei and pale eosinophilic cytoplasm whereas cells in ADCC have clear cytoplasm, angular, hyperchromatic nuclei and may show mitotic activity.[2,5] The Ki-67 index is reported to be 10 times higher in ADCC compared to PLGA. Smooth muscle markers of myoepithelial differentiation are positive in ADCC but negative in PLGA. Though PLGA may form solid areas, they lack the overall high-grade feel associated with ADCC.[1,2,4] Although both ADCC and PLGA show neural invasion, in PLGA this is often associated with a striking whorling arrangement of single-file cords of cells or small ducts, and is seen predominantly within, or very close to, the main tumor mass.[4]

Occasional foci in pleomorphic adenoma can resemble ADCC but the presence of typical myxochondroid matrix and plasmacytoid or spindle shaped cells helps to differentiate between the two.[1,2,4] Expression of GFAP and CD57 is positive in pleomorphic adenoma and negative in ADCC.[5]

Cribriform structures may sometimes be observed in BCA and such cases can be differentiated from ADCC on the basis of presence of capsule and lack of stromal and perineural invasion in BCA.[5] Further, lack of clear cytoplasm, hyperchromatic, angulated nuclei along with presence of peripheral palisaded nuclei and focal squamous differentiation with whorling pattern in BCAC may aid in diagnosis and differentiation from solid ADCC.[2,5]

BSCC can resemble solid variants of ADCC but typically involves the hypopharynx and larynx, which are uncommon sites for ADCC. Both can show islands with cribriform configurations, hyaline material surrounding tumor nests, and solid areas with comedonecrosis, but BSCC also has evidence of squamous differentiation and usually involves the overlying mucosa.[4] The basement membrane material secreted by BSCC tends to dissect between tumour cells rather than form crisp cribriform spaces seen in ADCC. Focal keratinization, attachment to rete pegs, and presence of surface dysplasia or carcinoma in situ helps to distinguish it from ADCC. Furthermore p63 staining is diffuse in BSCC compared to ADCC.[2]

The combination of surgery and postoperative radiation therapy improves loco-regional control of the disease. Despite this achievement, late local recurrence and distant metastasis is high and may occur decades after initial diagnosis.[5] Radiotherapy is mandatory when disease-free margins cannot be obtained surgically and when there is locally advanced disease or high-grade histological findings.[7] The 5-year survival rate after effective treatment is 75%, but long-term survival rates are low (10 years-20% and 15 years-10%).[2] Distant metastasis may occur in 40-60% of the case and been reported mainly in the lungs, liver, bones and rarely in kidney and brain.[4] The course of disease is usually fulminant if metastases occur in bone, especially the spine.[5] The main prognostic factors are site, clinical stage, and histologic pattern along with primary lesion size, presence or absence of metastasis, invasion of nerves and margin status.[2,4,5,8] Hence, long-term follow up of patients is mandatory because of the indolent but infiltrative nature of ADCC associated with late recurrence and distant metastasis.[2,7-9]

CONCLUSION

ADCC is an uncommon salivary gland malignancy. It is unique for its slow, indolent clinical course, peculiar histopathological features, tendency for perineural invasion, local recurrence and distant metastasis. Histopathology plays a very important role in the identification of these tumours hence, extensive knowledge and expertise in pathology is essential for making accurate diagnosis and planning treatment.

REFERENCES

1) Singla N, Rathod G, Singla D. Adenoid cystic carcinoma of the parotid gland: A case report and review of literature. International Archives of Integrated Medicine. 2015; 2(4): 182-186.

2) Sirisha N, Chundru V, Amudala R, Thankappan P, Nagaraju DC. Adenoid cystic carcinoma of palate: A case report and review of literature. Dent Res J. 2013; 10(2): 274–278.

3) Bradley JP. Adenoid cystic carcinoma of the head and neck: a review. CurrOpinOtolaryngol Head Neck Surg. 2004; 12: 127-132.

4) Barnes L. Surgical Pathology of the Head & Neck. 3rd ed. Vol.1, Ch-10, India: Replika Press Pvt. Ltd.; 2009. Pg. 552-557.

5) Jaso J, Malhotra R. Adenoid Cystic Carcinoma. Arch Pathol Lab Med. 2011; 135: 511-515.

6) Mitra S, Kundu S, Pattari KS, Ghosal GA. Metastatic Pleural Effusion: A Rare Presentation of Salivary Gland Adenoid Cystic Carcinoma. Indian J Chest Dis Allied Sci. 2011;53:107-110.

7) Tincani JA, Negro DA, Araujo PCP et al. Management of salivary gland adenoid cystic carcinoma: institutional experience of a case series. Sao Paulo Med J. 2006;124(1):26-30.

8) Sekar B, Dominic A, Murali S. Adenoid Cystic Carcinoma of Palate - A Case report with Review of Literature. JIADS. 2010; 1(4): 55-58.

9) Monteiro D, Lino J, Bernardo T, Fernandes J, Monteiro E. Adenoid Cystic Carcinoma of the Head and Neck: Epidemiology and Predictors of Prognosis. International Journal of Otolaryngology and Head & Neck Surgery.2013; 2: 165-173.