International Journal of Oral & Maxillofacial Pathology. 2012;3(2):76-80
Available online at http://www.journalgateway.com or www.ijomp.org
ISSN 2231 – 2250

Case Report

# Adenoid Cystic Carcinoma: A Case Report and Review on Its Histogenesis and Morphogenesis

Rani Hamsa PR, Anu Priya S, Arun Priya S, Thilaga Rani PR

## Abstract

Adenoid cystic carcinoma is a frequently occurring malignant salivary gland neoplasm. It shows insidious and slow growth with high levels of recurrence and distant metastasis. It is presumed to originate from the intercalated duct, being composed of both luminal and myoepithelial cells. Extracellular matrices have been suggested to play an important role in the growth and differentiation of adenoid cystic carcinoma. This paper reports a case of adenoid cystic carcinoma affecting the lip and reviews the diverse theories associated with the genesis of adenoid cystic carcinoma.

**Key words:** Adenoid Cystic;Carcinoma;Cylindroma;Salivary Duct Neoplasms;Myoepithelial Tumour;Extracellular Matrix;Pseudocysts**.**

*Rani Hamsa PR, Anu Priya S, Arun Priya S, Thilaga Rani PR. Adenoid Cystic Carcinoma: A Case Report and Review on Its Histogenesis and Morphogenesis. International Journal of Oral and Maxillofacial Pathology; 2012:3(2):76-80.* 

Received on: 18/01/2012 Accepted on: 17/03/2012

## Introduction

Adenoid cystic carcinoma is a malignant salivary gland neoplasm.[1,2] It is considered to be the second most common malignant salivary tumor, presenting clinically as long-lasting swellings, which can be painful and ulcerated, involving more frequently intraoral minor salivary glands and the submandibular gland.[1,3,4] Microscopically, it is composed of a proliferation of small polyhedral cells with hyperchromatic nuclei, arranged in 3 different patterns: cribriform, tubular and solid. Tumor cells produce a lightly basophilic extracellular secretory material, variably arranged among the neoplastic cells in proliferation. This paper reports a case of adenoid cystic carcinoma affecting the lip and reviews the diverse theories associated with the genesis of adenoid cystic carcinoma.

## Case Report

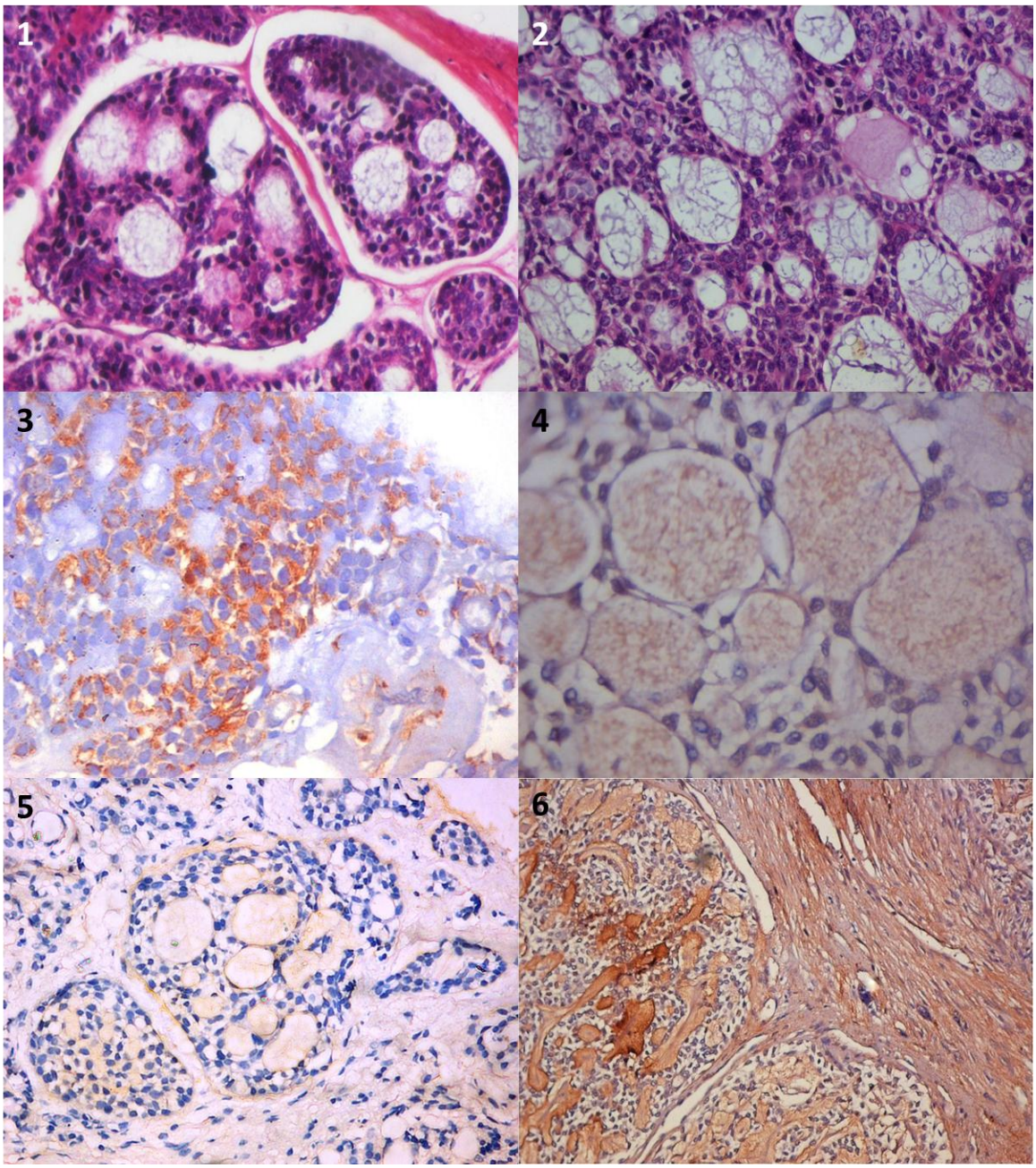
A 65 years old female presented to the dental clinic for evaluation of a mass on the right side of the upper lip. The patient reported that, the lesion initially presented as an asymptomatic nodule approximately 10 years ago, and gradually started increasing in size over the past 5 years. Occasionally, she experienced pain. On examination it was a solitary**,** roughly oval, non-tender, diffuse, firm**,** smooth surfaced swelling measuring about 1 x 1 cm in diameter, extending from the nasolabial fold to the vermillion border of the lip superio-inferiorly, and medio-laterally, 0.5 cm away from the philtrum to the corner of the mouth. Skin over the swelling was not attached to the underlying structures. Complete surgical removal of the lesion was done.

On gross examination, the specimen was oval in shape, pink-tan in color, measuring about 1 x 1 cm in diameter. Histologically, the lesion was composed of discrete sheets, islands, and nests of neoplastic epithelial cells exhibiting cribriform pattern forming duct-like spaces (Figure 1). The tumor cells were polygonal in shape. The duct-like spaces contained abundant eosinoiphilic**,** amorphous**,** mucicarmine and periodic acid schiff (PAS) positive material (Figure 2). The secretory product was positive for laminin (basement membrane molecule). Expression of laminin was seen within the tumor cells (Figure 3), in the pseudocystic spaces (Figure 4), surrounding the tumor islands (Figure 5) and in the intervening stroma (Figure 6). The histological features were suggestive of adenoid cystic carcinoma. There was no clinical evidence of regional nodal involvement or metastatic disease. To our knowledge the patient is currently free of disease two years post operatively.

## Discussion

Adenoid cystic carcinoma is a malignant salivary gland neoplasm. It was initially described by Robin and Laboulbene in 1853.[1,2] In 1856, Theodor Billroth studied its histologic features and described the long

amorphous compartments as cylinders and thus termed it as "Cylindroma".[1,3-5] Until 1940, 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] In 1945, Bauer and Fox suggested the term "Adeno-myoepithelioma" based on their theory that the lesion was histogenetically derived from intercalated duct and myoepithelial cells. In 1953, Foote and Frazell renamed the lesion as Adenoid cystic carcinoma.[3,6] In 1966, Friedmann and Osborn introduced the expression "Cribriform adenocarcinoma" as being more appropriate to its origin, morphology and behavior.[7] It had also been variously referred to as Basiloma, Adenocystic basiloid carcinoma and Adenoepithelioma.[8] J Phlip Sapp et al in 2004 defined adenoid cystic carcinoma as "A malignant salivary gland tumor composed of cuboidal cells in a solid, cribriform (Swiss cheese) or tubular pattern with a predilection for perineural lymphatic spaces".




The photomicrographs of adenoid cystic carcinoma with hematoxylin and eosin staining at X200 (Fig 1) and X400 magnification (Fig 2), along with positive laminin expression showing intracellularly suggesting basement membrane like material (Fig 3), with pseudocyst at X400 magnification (Fig 4), linear staining around the tumor islands at X200 magnification (Fig 5) and in the intervening stroma at X100 magnification (Fig 6).

World Health Organization in 2005 defined adenoid cystic carcinoma as “A basaloid tumor consisting of epithelial and myoepithelial cells in various morphological configurations, including tubular, cribriform and solid patterns. It has a relentless clinical course and usually a fatal outcome”.[10]

Christopher DM Fletcher in 2007 defined Adenoid cystic carcinoma as “An invasive neoplasm composed predominantly of basaloid cells with myoepithelial/basal cell differentiation, accompanied by interspersed ductal structures. It is characterized by cribriform, tubular and/or solid growth pattern and a myxohyaline stroma”.[11]

**Histogenesis of Adenoid Cystic Carcinoma**

Foote and Frazell in 1953 suggested that both ducts and acini are the progenitors of adenoid cystic carcinoma.[12] Friborsky V et al in 1966 proposed that adenoid cystic carcinoma recapitulates the terminal tubule complex stage of development with predominant differentiation of the anlage along the intercalated duct cell line. Using alcian blue, electron microscopy and polarization optics, he concluded that the acellular material was composed of mucopolysaccharides and periodic fibrils of the collagenous type.[13] Hubner et al., in 1971 suggested that adenoid cystic carcinoma originated from the myoepithelial cells which, in addition to myofibrils, contained large amounts of rough endoplasmic reticulum, indicating an intensive synthesis of proteins. They further claimed that the acellular hyaline material was the product of myoepithelium and not of fibroblasts.[13] Tandler in 1971 identified myoepithelial-like cells in association with the ductal lumina, but was not convinced of their role as histogenetic precursors. He was of the opinion that squamous metaplasia is a frequent finding in the tumor cells and the cytofilaments may be tonofilaments rather than myofilament type, the two being indistinguishable.[13]

Thackray AC et al., in 1974 proposed a dual origin of adenoid cystic carcinoma, partly from a population of acinar and ductal cells and partly from myoepithelial cells.[13] Anthony et al in 1975 demonstrated the presence of actomyosin within the component cells of the tumor, suggesting that the tumor cells were myoepithelial in nature.[13] Chisholm DM et al., in 1975 conducted an ultrastructural stereologic analysis of five cases of adenoid cystic carcinoma and demonstrated the presence of 73.0% duct-like cells, 2.5% myoepithelial-like cells, and 1.9% cells of the secretory acinar type. In this study number of myoepithelial cells in the tumor was much lower than the 6.12% value in normal minor salivary glands and he suggested that myoepithelium played an insignificant role in the histogenesis.[13]

Chen et al in 1976 histochemically and ultrastructurally studied the nature of the material contained within the cyst-like tumor spaces. He found the material to be PAS-positive and diastase resistant. The material was Alcian blue, Toludine blue and Mucicarmine- positive, suggesting an acid mucopolysaccharide nature. Ultrastructurally, three zones were easily recognizable: (1) a juxtacellular zone consisting of a network of replicated basal lamina; (2) an intermediate zone of stellate granules; and (3) a central zone of aperiodic filaments and collagen fibers. He concluded that mucoid material present in the cyst-like spaces was identical to that produced by mucous-secretory acinar cells, and, therefore, the tumor cells were epithelial in origin.[13]

Anand P et al., in 1986 conducted an ultrastructural study and identified myoepithelial cells in 9 of 12 cases of adenoid cystic carcinoma. The extent of myoepithelial cell presence in adenoid cystic carcinoma varied from one tumor to another. They were commonly associated with the acinar-intercalated units and tubular-ductal structures and not with the solid areas of tumors. He stated that myoepithelial cells were from two different sources: (1) the original acinar-intercalated ducts; and (2) the proliferation and cytodifferentiation of pluripotential reserve/stem cells.[13]

**Histogenesis of Intraosseous Adenoid Cystic Carcinoma**

A number of theories have been proposed to explain the origin of primary adenoid cystic carcinoma of the mandible. The first hypothesis was based on the work of Gorlin, who in 1957 established the presence of mucous cells in 5.5% of 200 dentigerous cysts. Brown, in a series of 638 cysts, found mucous cells in 42% of dentigerous cysts, in 39.6% of dental cysts, in 20% of lateral periodontal cysts, and in 3.7% of keratocyst. The second hypothesis is based on the description of Stafne in 1969 who

determined the existence of total mandibular inclusions of accessory salivary glands from the submaxillary and sublingual glands. The third histogenetic theory is based on the malignant transformation of an embryologic epithelial remnant included in bone (fissural cyst, or rests of Malassez).[1,4]

**Morphogenesis of Adenoid Cystic Carcinoma**

In 1971, Stuart W. Leafsted et al stated that the architectural arrangement of the tumor appeared to be dependent on the type of tissue invaded by it. When the tumor invaded open spaces and cavity, glandular or solid patterns were predominant, whereas, when it invaded solid tissue, particularly fibroconnective tissue or skeletal muscle; cord-like arrangement was predominant.[8]

Perzin et al in 1978 proposed a hypothesis for the histologic evolution of adenoid cystic carcinoma. They believed that tubular pattern represented the best differentiated form of adenoid cystic carcinoma, where the nests exhibit minimal proliferation of neoplastic cells. The individual units are small and only one to three cells surround a central lumen. As cell proliferation progresses, the units become larger, but the lumens are still maintained, producing a cribriform pattern. The mucinous material within the lumens may eventually be replaced by hyalinization, during the prolonged course, which many of these lesions show. Eventually in some units, cell proliferation becomes more aggressive and lumens are overgrown, thus forming the solid pattern. This progression of cell proliferation may vary in different units, thus producing mixed lesions in which all patterns and transitions between them may be identified.[14]

Jun cheng et al., in 1992 using immunohistochemical stains for basement membrane proteins stated that tumor cells proliferate in strands in which every cell is able to make contact with the basement membrane. These strands grow in various directions and contact each other; the invaginated and enclosed stroma is sometimes isolated from the outer stroma; and the extracellular matrix enclosed by tumor cells, namely a pseudocyst, is formed by secretion and deposition of basement membrane like material by the tumor cells.[15]
Several cytogenetic studies have explored the molecular events in the development and progression of ACC. Persson et al has described a reciprocal t(6;9)(q22-23;p23-24) translocation which results in formation MYB-NFIB fusion oncogene. MYB participates in regulation of cell proliferation, apoptosis and differentiation.

From our understanding of adenoid cystic carcinoma through these theories, we conclude that the component cells such as the ductal and myoepithelial cells might originate from the pluripotent reserve/stem cells and further these myoepithelial cells by producing the basement membrane material form pseudocysts which gives rise to the characteristic cribriform pattern, which is the most commonly encountered histological pattern of adenoid cystic carcinoma. Even this case shows the presence of basement membrane material (positive for laminin) intracellularly, within the pseudocystic spaces, surrounding the tumor islands and in the intervening stroma which supports the above hypothesis.

**Author Affiliations**

1. Dr.Rani Hamsa PR, Professor and Head, Department of Orthodontics, Vyas Dental College and Hospital, Jodhpur, 2. Dr. Anu Priya S, Senior Lecturer, Department of Oral and Maxillofacial Pathology, AECS Maaruti College of Dental sciences and Research Centre, Bangalore, 3. Dr.Arun Priya S, Senior Lecturer, Department of Oral Surgery, K.V.G. Dental College and Hospital, Sullia, 4. Dr.Thilaga Rani PR, Professor and Head, Department of Orthodontics, I.D.E.A.S, Gwalior, India.

**Acknowledgement**

We would like to thank all the staff members of the department of oral and maxillofacial pathology for their support & cooperation.

## References

1. García De Marcos JA, Calderón-Polanco J, Poblet E, Castillo-Pardo De Vera JL, Arroyo-Rodríguez S, Galdeano-Arenas M, et al. Primary adenoid cystic carcinoma of the mandible: Case report and review of the literature. J Oral Maxillofac Surg 2008;66:2609-15.
2. Carrasco-Ortiz D, Aldape-Barrios B. Adenoid cystic carcinoma of the dorsum of the tongue: Presentation of a case. Med Oral Patol Oral Cir Bucal 2006;11:E417-20.
3. Gary L. Ellis, Paul Auclair. Tumors of the Salivary Glands, 4th ed. American Registry of Pathology; 2008.
4. Jehad Al-Sukhun, Christian Lindqvist, Jarkko Hietanen, Ilmo Leivo, Heikki Penttilä. Central adenoid cystic

carcinoma of the mandible: case report and literature review of 16 cases; Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:304-8.
5. Neville, Damm, Allen and Bouquot: Oral and Maxillofacial Pathology, 3rd Edition: Elsevier; 2009.
6. Studart Soares EC, Carreiro Filho FP, Gurgel Costa FW, Maciel Jácome Vieira AC, Negreiros Nunes Alves AP. Adenoid cystic carcinoma of the tongue: case report and literature review. Med Oral Patol Oral Cir Bucal 2008;13(8):E475-8.
7. Noronha Santos Netto JD, Menezes Aguiar Miranda AM, Da Silveira HM, Ribeiro Bartholomeu Dos Santos TC, Pires FR. Fine-Needle Aspiration Biopsy: as an auxiliary diagnostic tool on intraoral minor salivary gland Adenoid cystic carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:242-5.
8. Stuart WL, Gaeta JF, Sako K, Marchetta FC, Shed DP. Adenoid cystic carcinoma of major and minor salivary glands. Am J Surg 1971;122:756-62.
9. Sapp JP, Eversole LR, Wysocki GW. Contemporary Oral and Maxillofacial Pathology, 2nd ed. Mosby; 2003.
10. Barrett W, Speight PM. Perineural invasion in adenoid cystic carcinoma of the salivary glands: a valid prognostic indicator? Oral Oncology 2009;45:936–40.
11. Fletcher DM, Unni KK, Mertens F. World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of Soft Tissue and Bone, IARCPress Lyon; 2002.
12. Tandler B. Ultrastructure of adenoid cystic carcinoma of salivary gland origin. Lab Invest 1971;24:504-12.
13. Chaudhry AP, Leifer C, Cutler LS. Histogenesis of adenoid cystic carcinoma of the salivary glands light and electron microscopic study. Cancer 1986;58:72-82.
14. Perzin KH, Gullane P, Clairmont AC. Adenoid cystic carcinomas arising in salivary glands: A correlation of histologic features and clinical course. Cancer 1978;42:265-82.
15. Jun Cheng. Basement membranes in adenoid cystic carcinoma-An immunohistochemical study. Cancer 1992;69:2631-40.
16. Bhaijee F, Pepper DJ, Pitman KT, Bell D: New developments in the molecular pathogenesis of head and neck tumors: a review of tumor-specific fusion oncogenes in mucoepidermoid carcinoma, adenoid cystic carcinoma, and NUT midline carcinoma. Ann Diagn Pathol. 2011:15(1):69-77.

**Corresponding Author**
Dr.Rani Hamsa PR,
Professor and Head,
Department of Orthodontics,
Vyas Dental College and Hospital,
Jodhpur, India.
Email: ranihamsadr@gmail.com
Ph: +91 9680572715

Source of Support: Nil, Conflict of Interest: None Declared.