

# Adenoid cystic carcinoma of minor salivary glands: A Diagnostic Challenge

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## ABSTRACT

*Adenoid cystic carcinoma most often presents a diagnostic and treatment challenge owing to the rarity of occurrence. Most findings reported in literature about adenoid cystic carcinoma are actually based upon studies of small number of patients and there is a dire need for further studies regarding its clinical behavior, treatment modalities and prognosis.*

**Keywords:** Minor salivary gland neoplasm, Palatal tumors, Adenoid cystic carcinoma, adenocarcinoma

## INTRODUCTION

Adenoid cystic carcinoma is first described by Billroth in 1859 as malignant salivary gland tumor<sup>1</sup>. He described it as cylindroma due to its cribriform appearance of tumor cells which was attributed to cylindrical pseudolumina or pseudospaces of tumor cells. However term “adenoid cystic carcinoma” was first coined by Ewing in 1954. Adenoid cystic carcinoma is a relatively rare malignant salivary gland tumor comprising less than 1% of all malignancies of head and neck. It is the 5<sup>th</sup> most common malignancy of salivary gland representing 5-10% of all salivary gland neoplasms<sup>2,3</sup>. The parotid gland is most common site of occurrence followed by submandibular glands. More than 55% of cases of adenoid cystic carcinoma have been reported in parotid gland and submandibular gland. The adenoid cystic carcinoma involving minor salivary gland is less common than major salivary gland. Palate is most common site of occurrence in 50% cases of adenoid cystic carcinoma involving minor salivary glands. The adenoid cystic carcinoma accounts for 8.3% of minor salivary gland tumors and 17.7% of malignant minor salivary gland tumors of palate. The other sites of occurrence is lower lip, retromolar area, tonsillar pillar area, sublingual gland, buccal mucosa and floor of the mouth.<sup>3</sup> However adenoid cystic carcinoma can involve nose and paranasal sinuses also<sup>4</sup>. Clinically tumor is often most deceptive due to its small size and benign growth having extensive subclinical invasion and marked tendency for early metastasis which have unpredictable prognosis<sup>5</sup>. Histologically adenoid cystic carcinoma has three patterns, cribriform type, tubular type and solid type. The cribriform type is most common while solid type is the least common. It is well established and reported that most of adenoid cystic carcinoma do not occur in

“pure” form i.e histologically adenoid cystic carcinoma has not typical presentations of cribriform, tubular or solid types. In most of adenoid cystic carcinoma all three patterns can be observed. The main reason for this histological typing is to assess the prognostic difference between histologic types. Tubular pattern is believed to have the best prognosis compared to the cribriform pattern and solid pattern<sup>6</sup>. Szanto et al.<sup>7</sup> graded adenoid cystic carcinoma as cribriform or tubular (grade I), less than 30% solid (grade II) or greater than 30% solid (grade III).

## DISCUSSION

Adenoid cystic carcinoma most often presents a diagnostic and treatment challenge owing to the rarity of occurrence. Most findings reported in literature about adenoid cystic carcinoma are actually based upon studies of small number of patients and there is a dire need for further studies regarding its clinical behavior, treatment modalities and prognosis<sup>8</sup>. Adenoid cystic carcinoma may occur at any age however patients between age group of 24 to 78 years are most predilected. The adenoid cystic carcinoma involving major salivary glands have high incidence in younger age group (mean 44 yrs) than those involving minor glands (mean 54 yrs). The females are more affected than males (1.2:1). The characteristic clinical finding occurring in early course of the disease is pain which precedes the noticeable swelling<sup>9</sup>. The major cause of intense pain is neurotropism of neoplastic cells of adenoid cystic carcinoma. The minor salivary glands of palate in greater palatine foramen area is most predilected site of occurrence for adenoid cystic carcinoma. The most common malignant neoplasm of minor salivary glands is mucoepidermoid carcinoma (21.8%) followed by polymorphous low grade adenocarcinoma(7.1%). The adenoid cystic

carcinoma is the third most common malignancy (6.3%)<sup>10,11</sup> affecting minor salivary glands. Adenoid cystic carcinoma of the minor salivary glands have been reported to have worse prognosis than those of the major salivary glands<sup>12,13</sup>. The adenoid cystic carcinoma 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<sup>14</sup>.

The lymph node involvement is uncommon (< 5% of cases) in adenoid cystic carcinoma and is usually due to contiguous spread rather than lymphatic permeation or embolization<sup>15</sup>. The differential diagnosis of adenoid cystic carcinoma includes polymorphous low grade adenocarcinoma, basal cell adenoma, mixed tumor and basaloid squamous cell carcinoma. Histologically the cribriform pattern of adenoid cystic carcinoma can also be seen in basal cell adenoma, mixed tumor and polymorphous low grade adenocarcinoma. So histological distinction is quite challenging. Adenoid cystic carcinoma has a more limited range of histologic patterns with no more than three patterns, basophilic pools of glycosaminoglycans, clear cytoplasm, angular, hyperchromatic nuclei and may show mitotic activity. However polymorphous low grade adenocarcinoma is characterized by polymorphous architecture, foci of papillary growth, areas of single cell infiltration, uniform cell population with cytologically bland, round or oval vesicular nuclei and pale eosinophilic cytoplasm. The Ki-67 index is reported to be 10 times higher in adenoid cystic carcinoma compared to polymorphous low grade adenocarcinoma. Smooth muscle markers of myoepithelial differentiation are positive in adenoid cystic carcinoma but negative in polymorphous low grade adenocarcinoma<sup>16</sup>. Few foci in pleomorphic adenoma can resemble adenoid cystic carcinoma but the presence of typical myxochondroid matrix and plasmacytoid or spindle shaped cells helps in its differentiation<sup>17</sup>.

Cribriform structures may sometimes be observed in basal cell adenoma and such cases can be differentiated from adenoid cystic carcinoma on the basis of gradual structural alteration from areas typical of basal cell adenoma. The peripheral palisading and focal squamous differentiation with whorling pattern present in basal cell adenoma are not usually encountered in adenoid cystic carcinoma<sup>18</sup>. The chromosomal aberrations of 6q, 9p and 17p12-13 have been reported in adenoid cystic carcinoma. Hypermethylation of the promoter region of the p16 gene in adenoid cystic carcinoma is associated with higher histologic grades of malignancy<sup>19</sup>. The adenoid cystic carcinoma has multidisciplinary treatment approach including surgery, radiotherapy, chemotherapy and combined therapy. The surgical approach involves excision

with the widest possible surgical margins as tumor cells infiltrate beyond the clinical and radiographic margins. The radiotherapeutic approach can involve neutron therapy which helps in achieving reasonable local control as a primary therapeutic modality. However adoptive immunotherapy along with chemoradiotherapy has recently shown promising results. The expression of E-cadherin is used as prognostic marker for adenoid cystic carcinoma while degree of metastasis is determined by count of high argyrophilic nuclear organizing regions<sup>6</sup>. The determining factors in prognosis of adenoid cystic carcinoma is its anatomic location, primary lesion size, presence or absence of metastasis at the time of diagnosis, perineural invasion and histological variant<sup>20</sup>. Distant metastasis is reported to occur in 25%-50% cases of adenoid cystic carcinoma. The most common site for metastasis is lung<sup>21</sup>. Post-treatment the reported 5-year survival rate is 75%. However long-term survival rate is comparatively low (10 years in 20% cases and 15 years in 10% cases).

## CONCLUSION

Adenoid cystic carcinoma is rather an uncommon salivary gland malignancy. It is unique for its peculiar histopathological features and tendency for perineural invasion. Lesions involving the sinus tend to have a poor prognosis due to its infiltrative growth and distant metastasis. Long-term follow-up of patient at regular intervals is mandatory.

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