Section: Pathology

Original Research Article

CLINICOPATHOLOGICAL AND IMMUNO-HISTOCHEMICAL EVALUATION OF ADENOID CYSTIC CARCINOMA AT DIVERSE ANATOMICAL SITES

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ABSTRACT

Background: Adenoid cystic carcinoma (ACC) is a rare malignant epithelial tumour that is most commonly found in the salivary glands but can also occur at extra-salivary locations. It can present clinically in many ways, leading to diagnostic difficulties despite the characteristic histopathological features.

Case Presentation: This case series describes ACC of the nasal cavity, base of tongue, lung, and breast. The age of the patients ranged from 38 to 76 years. Clinical, radiological, histopathological and immunohistochemical data were analysed. All cases showed the typical tubular and cribriform patterns on histological examination, with pseudocystic areas containing hyaline basement membrane–like material. The nasal cavity lesion had invaded the perineurium, and the tongue lesion had invaded skeletal muscle. CD117 and p63 were consistently positive by immunohistochemistry. The pulmonary case was negative for Napsin A, confirming primary pulmonary ACC. The breast tumours were triple negative and showed the typical morphological characteristics of ACC.

Conclusion: ACC is consistent in its histomorphological and immunohistochemical features across different anatomical locations. Its characteristic tubular and cribriform architecture is essential for accurate diagnosis, particularly at unusual sites, and is confirmed by CD117 and p63 immunostaining. Pathological examination and long-term follow-up are important because of the potential for local recurrence and delayed metastasis.

Keywords: Adenoid cystic carcinoma; CD117; p63; immunohistochemistry; cribriform pattern.

INTRODUCTION

Adenoid cystic carcinoma (ACC) is a rare malignant epithelial tumour that tends to arise in the secretory glands and makes up about 10% of all salivary gland tumours. Clinically, ACC grows very slowly but relentlessly and has a remarkable tendency for invasion of perineural tissues, resulting in local recurrence, and for haematogenous metastasis to distant organs with high frequency over time.[1,2]

The histological features of ACC are a biphasic population of luminal ductal cells and outer modified myoepithelial cells organised in three distinct growth patterns: cribriform, tubular, and solid. The cribriform variant is the most distinctive, showing a characteristic “Swiss cheese” appearance. Besides the salivary glands, ACC may arise at extra-salivary anatomical locations containing secretory glandular tissue, such as the respiratory tract, lacrimal glands, oesophagus, breast, skin, and lower female genital tract. The clinical course and prognosis differ considerably depending on the predominant site and growth pattern.[3]

Immunohistochemistry (IHC) is a valuable tool for definitive diagnosis and for distinguishing ACC from its mimics on the basis of its dual cell morphology.[4] In normal ducts, immunoreactivity for cytokeratin 7 (CK7) is usually seen in ductal cells, while immunoreactivity for smooth muscle actin (SMA), p63, and S100 is usually seen in myoepithelial cells. Moreover, strong and diffuse expression of CD117 (c-KIT) and nuclear staining of MYB — an oncoprotein resulting from the gene fusion between the MYB and NFIB genes — are highly sensitive diagnostic benchmarks.[3,5]

Extra-salivary ACC is rare, and site-specific standardised protocols are lacking, making management difficult. The present case series discusses the diverse clinicopathological features, architectural patterns, and immunophenotypes of adenoid cystic carcinoma at uncommon and atypical locations, with the aim of improving diagnostic accuracy.

Case Presentations

Case 1 — Adenoid Cystic Carcinoma of the Nasal Cavity

A 76-year-old female presented with a long-standing history of progressive nasal obstruction associated with intermittent episodes of epistaxis. Computed tomography revealed a soft tissue mass occupying the right nasal cavity. Histopathological examination demonstrated a biphasic neoplasm composed of epithelial and myoepithelial cells arranged predominantly in tubular and cribriform patterns. Numerous pseudocystic spaces containing eosinophilic secretions and hyaline basement membrane–like material imparted the characteristic "Swiss cheese" appearance. Perineural invasion was identified, supporting the infiltrative nature of the lesion. Based on the morphological findings, a diagnosis of adenoid cystic carcinoma of the nasal cavity was established (Figures 1, 4, and 5).

Case 2 — Adenoid Cystic Carcinoma of the Base of Tongue

A 75-year-old male presented with progressively worsening dysphagia and discomfort during swallowing. Biopsy from the lesion at the base of the tongue revealed overlying pseudoepitheliomatous hyperplasia with an underlying infiltrative neoplasm composed of basaloid cells arranged in tubular and cribriform patterns. Tumour infiltration into the adjacent skeletal muscle fibres was evident. The neoplastic cells exhibited minimal cytological atypia and low mitotic activity. Immunohistochemical evaluation demonstrated diffuse positivity for CD117 and p63, confirming the dual epithelial–myoepithelial differentiation characteristic of adenoid cystic carcinoma (Figures 2, 4, and 5).

Case 3 — Primary Pulmonary Adenoid Cystic Carcinoma

A 38-year-old male presented with persistent cough and occasional breathlessness. Radiological imaging revealed a mass lesion involving the right lower lobe of the lung. Bronchoscopic biopsy showed a neoplasm composed of basaloid cells arranged predominantly in a cribriform architecture with multiple pseudocystic spaces containing basophilic mucoid material. Immunohistochemical analysis demonstrated strong positivity for CD117 and p63, while Napsin A was negative, thereby excluding primary pulmonary adenocarcinoma and supporting a diagnosis of primary pulmonary adenoid cystic carcinoma (Figures 3, 4, and 5).

Case 4 — Adenoid Cystic Carcinoma of the Breast

A 52-year-old postmenopausal woman presented with a painful lump measuring 2.5 × 2 cm in the upper outer quadrant of the left breast, of six months' duration. Mammography categorised the lesion as BI-RADS 4. Fine-needle aspiration cytology revealed basaloid epithelial cells associated with hyaline globules, raising suspicion for adenoid cystic carcinoma. Lumpectomy specimen examination showed a well-circumscribed grey-white tumour measuring 2.5 cm in greatest dimension. Histologically, the tumour exhibited a combination of cribriform and tubular growth patterns with characteristic pseudocystic spaces containing eosinophilic hyaline basement membrane–like material. Immunohistochemistry demonstrated a triple-negative phenotype (ER−, PR−, HER2−) with diffuse CD117 positivity and peripheral p63 staining. The lesion was diagnosed as Grade 1 adenoid cystic carcinoma of the breast (pT2N0). The patient remained free of recurrence and metastasis during 24 months of follow-up.

Case 5 — Adenoid Cystic Carcinoma of the Breast

A 61-year-old woman presented with a gradually enlarging right breast lump measuring 4 × 3 cm over a period of one year. Radiological evaluation revealed a suspicious breast lesion, and cytological examination suggested a malignant epithelial neoplasm. Modified radical mastectomy was subsequently performed. Gross examination demonstrated a firm grey-white tumour measuring 4 cm. Microscopic evaluation revealed classical cribriform and tubular patterns admixed with focal solid areas. Multiple pseudolumina containing eosinophilic hyaline globules were present. Immunohistochemical analysis showed a triple-negative phenotype with strong CD117 expression in luminal epithelial cells and p63 positivity in abluminal myoepithelial cells, confirming the diagnosis of adenoid cystic carcinoma of the breast (pT2N0).

Overall Summary of the Case Series

This case series highlights the clinicopathological and immunohistochemical spectrum of adenoid cystic carcinoma of the nasal cavity, base of tongue, lung, and breast. Although the presentations and locations differed, all cases shared similar histomorphological characteristics, including tubular and cribriform architecture, pseudocystic spaces filled with hyaline basement membrane–like

material, and a characteristic biphasic cellular composition.

Immunohistochemically, CD117 and p63 were reliable and useful diagnostic markers, enabling confident diagnoses and differentiation from morphological mimics. The series underscores the need to be aware of the different presentations of ACC and the key role of histopathological examination and immunohistochemistry in diagnosis, especially at rare locations.

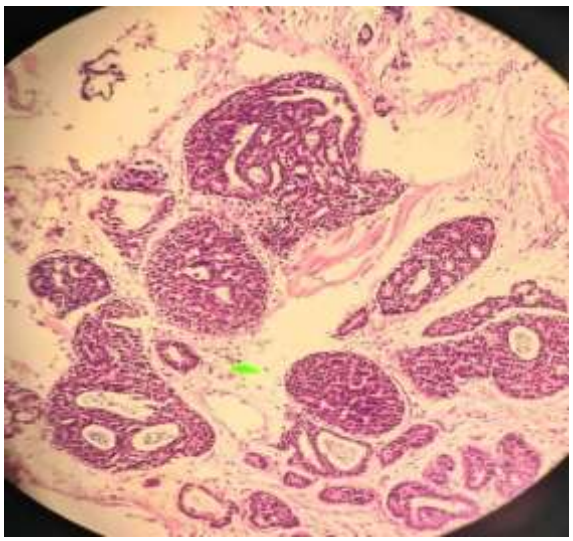

Figure 1: Adenoid cystic carcinoma of the nasal cavity (H&E, ×20)

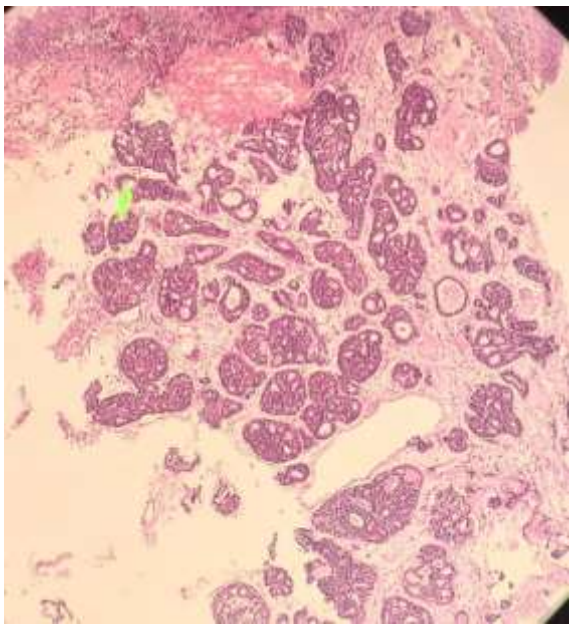

Figure 2: Adenoid cystic carcinoma of the base of tongue (H&E, ×10)

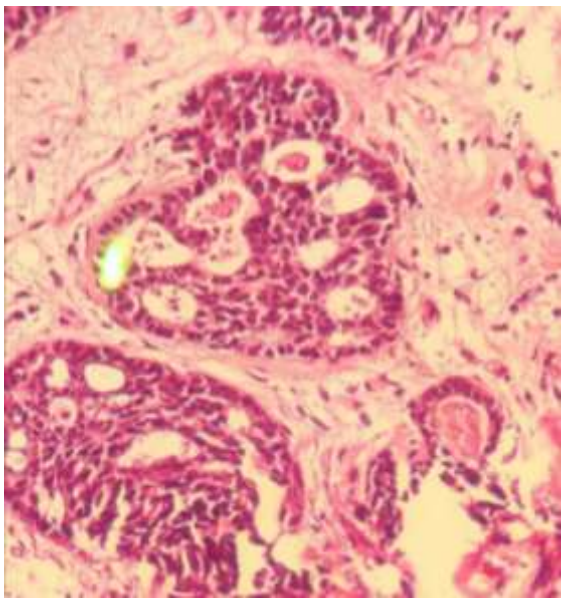

Figure 3: Primary pulmonary adenoid cystic carcinoma (H&E, ×40)

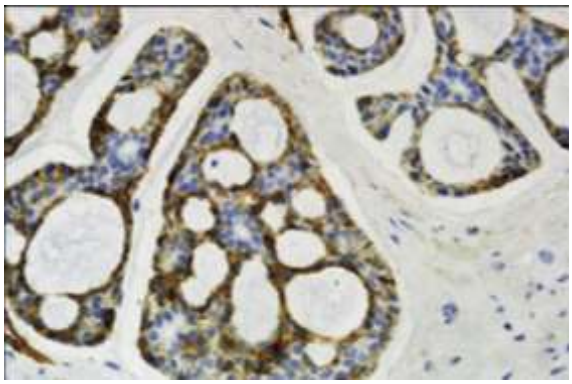

Figure 4: CD117 showing strong positivity in luminal cells (IHC, ×10)

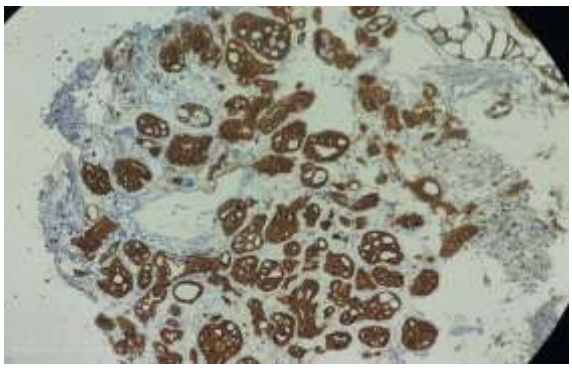

Figure 5: p63 showing strong positivity in myoepithelial cells (IHC, ×10)

DISCUSSION

Adenoid cystic carcinoma (ACC) is a rare malignant tumour that typically occurs in the salivary glands but may also be found at other sites, such as the sinonasal tract, tongue, lung, and breast. Although slow growing, ACC is locally invasive, has a high rate of recurrence, is often metastatic in the late stages, and is known to spread perineurally. This

case series highlights the clinicopathological and immunohistochemical features of ACC at various locations, showing that the tumour has similar morphological features and immunophenotype across all organs.[6,7] The typical features of ACC — tubular and cribriform patterns with eosinophilic or basophilic material in pseudocystic spaces — were seen in all cases in our series. The tumours were biphasic, with luminal epithelial and abluminal myoepithelial cells. Previous studies have suggested that the cribriform and tubular subtypes are more frequent and carry a more favourable prognosis than subtypes with a solid component.[6,8]

Perineural invasion was common in the present study; it is known to play a major role in local recurrence, skull base invasion, and therapeutic failure in sinonasal adenoid cystic carcinoma. Because of its ability to spread along nerves, sinonasal ACC is often diagnosed at a late stage, and careful imaging and pathological evaluation are essential.[9,10] Despite low mitotic activity, the lesions infiltrated the surrounding skeletal muscle. Although biopsies may show bland cytological features, ACC can behave aggressively, underscoring the importance of recognising infiltrative growth patterns for prognosis. Long-term monitoring is important because distant metastases may occur years after treatment.[7,11]

Primary pulmonary ACC is a rare malignancy that makes up less than 1% of all lung cancers. It has a histology comparable to that of salivary gland ACC and requires immunohistochemical studies for diagnosis. Primary pulmonary ACC was confirmed by positivity for CD117 and p63 and negativity for Napsin A, results similar to those reported in previous studies.[11,12] ACC of the breast is very rare, accounting for less than 0.1% of all breast carcinomas. In this study, the breast tumours showed both classical cribriform and tubular architecture and were triple negative. Compared with classic triple-negative breast cancers, breast ACC generally carries a good clinical prognosis, with lower rates of lymph node involvement and favourable long-term outcomes; none of the patients showed recurrence during follow-up.[13,14]

Immunohistochemistry played a crucial role in confirming the diagnosis in all cases: CD117 (c-KIT) was positive in luminal epithelial cells and p63 was positive in peripheral myoepithelial cells in every case. This dual staining highlights the biphasic nature of ACC and aids in differentiating it from similar histological entities such as polymorphous adenocarcinoma and invasive cribriform carcinoma. CD117 and p63 are expressed uniformly across a variety of anatomical locations, underscoring their role in common pathology.[15,16]

The present case series demonstrates that ACC may develop at multiple anatomical sites and present in different ways, yet all cases share the same histomorphological and immunohistochemical characteristics. Awareness of these features is essential at atypical locations. Early diagnosis, appropriate surgical management, and long-term follow-up are crucial because of the risk of local recurrence and late metastasis.[6,7,13]

CONCLUSION

This series emphasises the clinicopathological and immunohistochemical uniformity of adenoid cystic carcinoma across various locations. The cribriform and tubular patterns were characteristic, and CD117 and p63 staining allowed accurate diagnosis in all cases. Understanding these diagnostic features is crucial for differentiating ACC from its mimics, especially at rare sites. The infiltrative growth and the risk of late recurrence and metastasis require early diagnosis, prompt therapy, and long-term follow-up.

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