

# Two rare primary tumours of the thymus with differential immunohistochemical characterisation and a potential new entity

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## Abstract

Adenoid cystic carcinoma (ACC) is a rare and aggressive biphasic malignant tumour with both ductal and myoepithelial components. Though mostly considered a tumour of the salivary gland (accounting for 10% of all salivary tumours) its exocrine origin means that it is rarely also described at other sites with exocrine glandular components such as the respiratory tract, breast, skin, and lacrimal glands. Thymic carcinoma with adenoid cystic carcinoma-like features (TCACC) is an extremely rare thymic adenocarcinoma variant that has been described nine times in the literature to date. Until now, primary ACC in the thymus is yet to be described. We present two recent cases for comparison - the first is a classic example of a primary ACC of the lung; the second is a proposed case of primary ACC of the thymus - and consider the morphological, immunohistochemical, and genetic similarities, differences, as well as difficulties in diagnosis.

**Keywords** Adenoid cystic carcinoma; CD117 MYB gene rearrangement; MYB gene rearrangement; primary thymic carcinomas

## Case 1

A 53-year-old female presented to A&E with chest pain. A CT thorax revealed a left upper lobe lung lesion compressing the bronchus. Biopsy showed a neoplasm with tubular spaces and a double layer of monotonous, basaloid cells (Figure 1). Pulmonary adenoid cystic carcinoma (pACC) was diagnosed.

pACC is rare, contributing to 0.04–0.2% of all primary lung tumours<sup>1</sup> and is thought to arise from glands in the submucosa of the bronchi. Appearing in the 4<sup>th</sup>–6<sup>th</sup> decades of life, more often in

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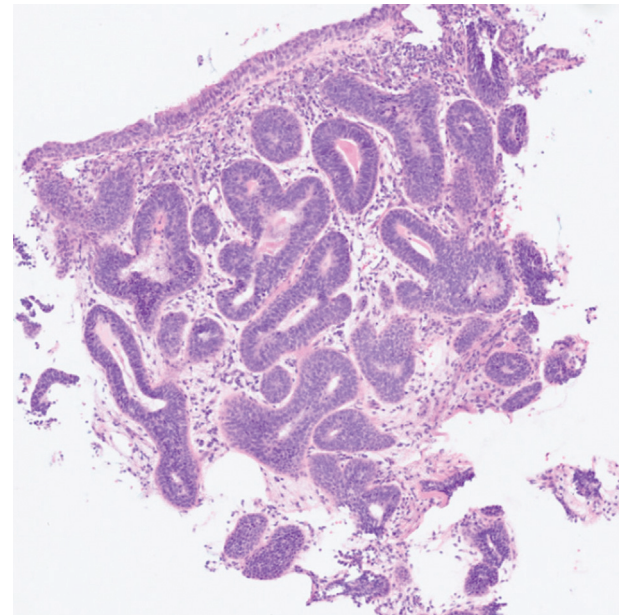
women, and not associated with smoking, it can display a variety of morphological patterns including cribriform, tubular and solid.

Immunohistochemical staining (Table 1) in pACCs typically shows luminal glandular cytokeratin and peripheral myoepithelial staining (Figure 2). CD117 is very useful to the diagnosis with its location interestingly being linked to prognosis (Figure 3).<sup>2</sup> MYB oncogene translocation resulting in MYB-NFIB fusion oncoprotein is reported in up to 90% of ACCs, though the level is lower in pACC at 41%<sup>3,4</sup> and sensitivity of this 6q23.2-q23.3 rearrangement for ACC is close to 100%.

Keeping these features in mind, we now consider a second case – possibly representing an entity not yet described in the literature; primary ACC of the thymus (ptACC).

## Case 2

A 57-year-old male truck driver presented to A&E with chest pain and shortness of breath. CT and PET imaging revealed a 5.8 cm x 4.9 cm irregularly-shaped mass in the mediastinum, with no lymphadenopathy or other PET uptake in the salivary glands or

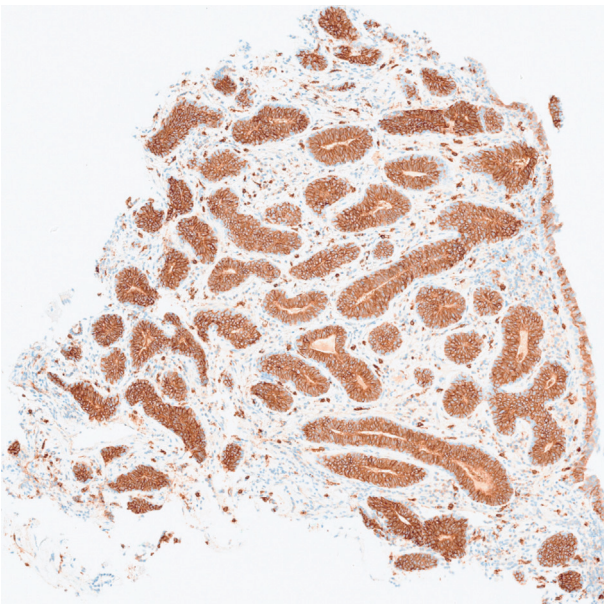


**Figure 1** Case 1. Primary ACC of the lung. Haematoxylin and eosin. Biopsy showed a neoplasm comprising tubular, gland-like spaces and a double layer of monotonous, polyagonal, basaloid cells.

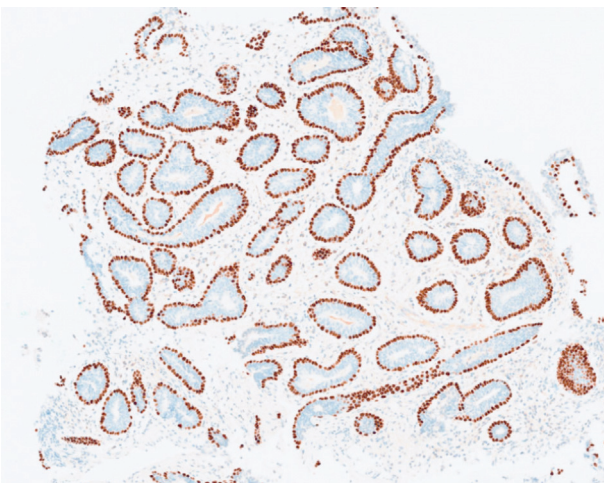
## Ancillary tests

	Classical ACC (most commonly salivary, followed by lung)	Primary TCACC (rare, 9 cases in the literature)	Case 2 (?ptACC)
CD117 (c-kit)	✓ (strong, either luminal, or both luminal and basal)	✗/(✓ normally negative, but inconsistency remains in the limited literature)	✓
Myoepithelial component (SMA, S100, calponin, p40/56)	✓	✗	✓
CK7	✓ (salivary, lung)	✓	✗
CK20	✗	✗	✓
TTF1	✓ (lung)/✗ (salivary)	✗	✗
MYB rearrangement	✓ (60–90%)	✗	✗
PAS positive material	✓	✗	?

Table 1



**Figure 2** Case 1. Primary ACC of the lung. Case 2. Thymic tumour. There is strong diffuse CD117 positivity, which is classical for ACC.



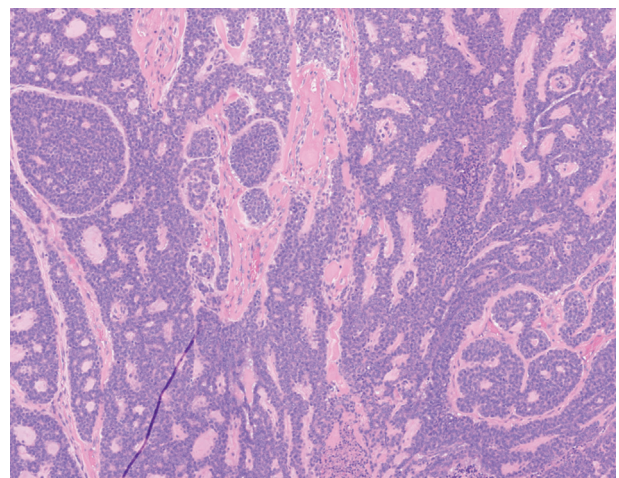
**Figure 3** Case 1. Primary ACC of the lung. P60 highlights peripheral myoepithelial component surrounding the glandular epithelial spaces. P40, CK5/6 also had a similar staining pattern.

soft tissues of the neck, effectively ruling out metastasis from any of these sites.

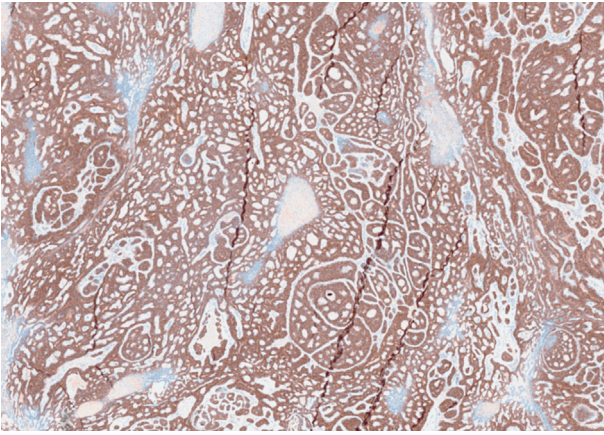
An intact encapsulated lesion was removed. Microscopically the specimen was composed of nests, cords, and islands of basaloid cells with largely cribriform architecture and focal solid areas (<30%) (Figure 4). The cribriform spaces contained a pale myxoid material, and in places cords of tumour cells were associated with a hyaline basement-membrane-like material. The stroma had a fibromyxoid quality. Some residual thymic tissue was seen at the edge of the tumour.

Tumour cell immunohistochemistry showed strong positivity for both CK20 and CD117 (Figure 5). Surrounding the tumour islands peripherally, was staining for a myoepithelial component (CK5/6, p40/63, SMA) (Figure 6). Patchy positivity with S100 in both myoepithelial and epithelial components. The tumour was negative for CD5, TTF1, and CK7 as well as for MYB gene rearrangement at 6q23.2-q23.3.

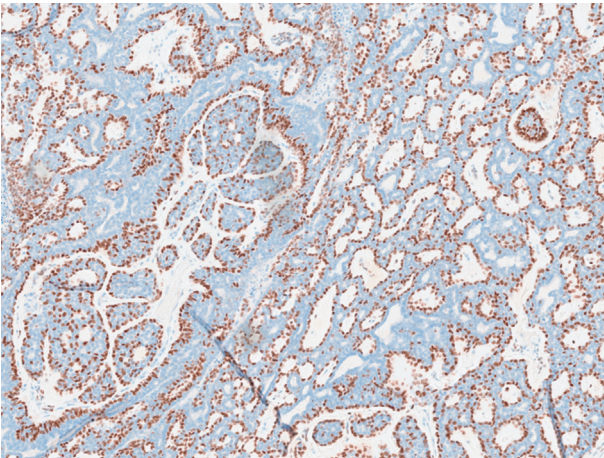
Morphological features were strikingly suggestive of a classical adenoid cystic carcinoma, with immunohistochemical markers also in favour of this diagnosis (positive CD117 and myoepithelial markers). Absence of alternative PET tracer uptake supports a thymic primary, and we therefore suggest that this is a



**Figure 4** Case 2. Thymic tumour. Haematoxylin and eosin. Islands of tumour with focal tubular and cribriform architecture surrounded by fibromyxoid stroma. Cords are associated with a hyaline-basement-like material.



**Figure 5** Case 2. Thymic tumour. There is strong diffuse CD117 positivity. This marker is positive in adenoid cystic carcinoma. The WHO defines TCACC as negative for this marker.



**Figure 6** Case 2. Thymic tumour. There is positive staining for peripheral myoepithelial markers. This image shows p60.

ptACC, which has never previously been reported in the literature.

## Discussion

We present these two cases together to illustrate the difficulties when a possible new entity (case 2, ptACC) shares similarities with an already rare tumour (Case 1, pACC) and even rarer tumours (TCACC).

Primary thymic carcinomas are rare and heterogeneous tumours. Initially, it was suggested that Case 2 represented Thymic Carcinoma with Adenoid Cystic Carcinoma-Like Features (TCACC), a primary thymic carcinoma of which there have only been 9 cases in the literature to date<sup>5</sup> (a surgical description of the tumour in case 2 has been published elsewhere<sup>5</sup>). Current understanding of TCACC is derived from these few case reports, and the WHO now includes TCACC in their most recent

classification<sup>4</sup> and outlines their immunohistochemical and morphological appearances that differ from classical ACC despite some of the nine aforementioned case studies not meeting these criteria. Unlike ACC, TCACC should not have a myoepithelial component and be negative for CD117 (Table 1).

Our tumour in Case 2, a confirmed primary of the thymus, has a morphology that could be in keeping with TCACC but immunohistological staining that is more suggestive of classical ACC.

## Conclusion

These cases highlight the importance of immunohistochemistry, imaging modalities, histological examination and genetic analysis in classifying rarely seen tumours. ACC has many typical features, but as none of these are altogether sensitive and specific, a certain amount of caution should be applied when assessing unusual-appearing variants which could represent, for example, TCACC. We also propose a new entity of ptACC, and suggest that some of the previous TCACC case studies have shown immunological and histological deviation that could more accurately place them in this third group. Alternatively, either TCACC or ACC is more heterogeneous than originally thought. ◆

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## Practice points

- Primary ACC is a rare tumour commonly associated with the salivary glands but can also occur in other organs with exocrine features such as the lung, breast, and skin
- This tumour has a number of different histological appearances but is characterized by a biphasic glandular and myoepithelial cell component which can be stained for immunohistochemically
- Primary ACC has not previously been described in the thymus but a recently described entity, TCAAC, can appear similar on first examination. TCAAC does not contain a myoepithelial cell component

**Self-assessment questions**

**1. What combination of immunohistochemical and genetic result would be most suggestive of an ACC?**

- a. Positive CD117 staining. Positive for MYB 6q23.2-q23.3 rearrangement
- b. Positive CD117 staining. Negative for MYB 6q23.2-q23.3 rearrangement
- c. Negative CD117 staining. Positive for MYB 6q23.2-q23.3 rearrangement
- d. Negative CD117 staining. Negative for MYB 6q23.2-q23.3 rearrangement

Answer: a

**2. In which organs have primary ACCs been previously definitively described?**

- a. Salivary glands, thymus, lung, skin.
- b. Salivary glands, breast, skin, lacrimal glands, lung.
- c. Salivary glands, lung, lacrimal glands, breast, vagina.
- d. Salivary glands, breast, skin, lungs, seminal vesicles.

Answer: b

**3. MYB 6q23.2-q23.3 rearrangement is found in what proportion of primary ACCs?**

- a. 0%
- b. 10–20%
- c. 30–60%
- d. 60–90%
- e. 80–100%

Answer: d