The use of Thyroid Transcription Factor 1 and Napsin A immunohistochemistry in differentiating primary versus metastatic adenoid cystic carcinoma in the lung

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Clinical Presentation

Case 1: A 42 year old woman presented for routine surveillance computed tomography (CT) scan and positron emission tomography (PET) scan. She has a history of right maxillary sinus adenoid cystic carcinoma (T4, N0, M0), initially treated with resection in Thailand and right breast invasive duct carcinoma treated with right mastectomy and radiotherapy in 2016. The CT and PET scan noted two small 3mm and 5mm nodules in the lingula of the left upper lobe in 2017 which was kept under observation. Repeat PET scans in November 2018 showed the two nodules had mild FDG avidity but had increased in size to 8mm and 10mm. The patient remained systemically well. Initial investigation with a CT guided fine needle aspiration (FNA) of the left upper lobe lesion was performed and a follow up lung wedge resection was done. The findings of both are discussed below.

Case 2: An 81 year woman presented to the emergency department with chest pain and palpitations in November 2018. She has a past history of right submandibular mastectom and radiotherapy in Thailand and right breast invasive duct carcinoma (T4, N0, M0), which was excised in 2005. A number of studies have evaluated the expression of TTF-1 and/or napsin A in primary lung tumours.1 Adenoid cystic carcinoma (ACC) frequently originates from the salivary glands of the head and neck, and has a propensity for multiple and late distant metastases with the lung being the most commonly involved organ.2 Primary lung ACC shows histomorphological features identical to ACC at other anatomical sites. Hence, it is challenging to distinguish primary lung ACC from metastatic carcinomas to the lung. There are clinical features that can be helpful, such as site of tumour and number of lesions. Primary lung ACC is more likely to arise in a central tracheobronchial location while evidence of multiple lesions and/or peripheral locations are more suggestive of a metastatic source.3,4 However, neither of these criteria are definitive.

Cytological Findings

Case 1: FNA left upper lobe lung mass produced highly cellular smears with cohesive and dispersed basophilic cells. They show cribriform architecture with basaoid cells surrounding rounded globules of acellular metachromatic magsnom colour material on Diff-Quik staining (Figure 1). The cell block contained similar material and immunohistochemistry (IHC) shows positive staining for thyroid transcription factor 1 (TTF-1) and napsin A in the luminal component, p40 positive staining in the basaoid component (Figure 2).

Case 2: Left upper lobe lung mass core biopsy showed an infiltrative lesion comprised of cribriform structure with the dual population of luminal and apical cells. The cribriform spaces are filled with basement membrane material. The luminal cells showed positive staining for CD31, S100 and CK5, while the apical cells were positive for p40. The luminal cells showed patchy positivity for TTF-1 and napsin A (Figure 4).

Discussion

Primary ACC of the lung is a rare malignancy and accounts for 0.04% to 0.2% of all primary lung tumours.5 Adenoid cystic carcinoma (ACC) frequently originates from the salivary glands of the head and neck, and has a propensity for multiple and late distant metastases with the lung being the most commonly involved organ.6 Primary lung ACC shows histomorphological features identical to ACC at other anatomical sites. Hence, it is challenging to distinguish primary lung ACC from metastatic carcinomas to the lung. There are clinical features that can be helpful, such as site of tumour and number of lesions. Primary lung ACC is more likely to arise in a central tracheobronchial location while evidence of multiple lesions and/or peripheral locations are more suggestive of a metastatic source.7,8 However, neither of these criteria are definitive.

Thyroid transcription factor 1 (TTF-1) is a highly conserved homeodomain-containing transcription factor that is expressed in thyroid, lung, and kidney tissues. It is a highly sensitive and specific marker for thyroid and lung tumours, and it is minimally expressed in other solid tissues.9 In addition, An et al. also looked at expression of TTF-1 and napsin A in metastatic ACCs which included 10 cases of metastatic ACC to lung, from primary head and neck sites. They demonstrated that 50% of metastatic ACCs to lung showed positive immunostaining for TTF-1 and napsin A. Furthermore, the primary tumours in these cases were negative for TTF-1 and napsin A. It has to be noted that due to the rarity of the disease, overall case numbers are small and different TTF-1 clones and immunostaining protocols were used in the reported studies. In particular, the reported TTF-1 clones used in the studies were also different to the SP141 clone (Ventana) we used in our cases. Overall, the current literature shows that positive expression for TTF-1 and napsin A in primary lung ACC is low (overall expression approximately 8%), with a higher percentage of metastatic ACCs to lung expressing TTF-1 and napsin A. This expression profile is in keeping with our two cases of metastatic ACC to lung.

ACCs have also been reported to contain a tumour-type specific t(6;9)(q22-23;p23-24) translocation, which generates a fusion of the MYB proto-oncogene to the transcription factor NFIB.10 Further studies have shown MYB-NFIB fusion or MYB-translocations in approximately 33-46% of salivary ACCs.11 This translocation, however, does not appear specific to salivary gland neoplasms, they do not appear to differentiate between a primary salivary versus lung origin.

Conclusions

Primary lung adenoid cystic carcinoma is a rare malignancy, TTF-1 and napsin A positive immunostaining is more likely to be seen in metastatic, rather than primary lung ACC, based on the current published literature and as shown in our cases.

References


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