CASE STUDY

Cytologic diagnosis of adenoid cystic carcinoma of the breast metastatic to the lung by bronchial cytology: a case report

Sharda Lallu, Sarla Naran and Peter Bethwaite
Anatomic Pathology, Wellington Hospital and University of Otago, Wellington

ABSTRACT
The application of bronchial washings, brushings, trans-bronchial fine needle aspiration cytology in the detection of respiratory tract cancer is now routine. A pulmonary metastasis from a breast adenoid cystic carcinoma is very uncommon. We document a case of pulmonary metastasis of adenoid cystic carcinoma in the breast in a 59 year old female on bronchial brushings, washings and trans-bronchial fine needle aspiration with subsequent histologic confirmation. The patient’s history and the cytdiagnostic features, including cribriform, epithelial clusters, epithelial balls, branching epithelial cylinders and cellular hyaline mucoid globules, led to the correct diagnosis. This case is of interest because of rare occurrence of lung metastasis of the breast adenoid cystic carcinoma, diagnosed on bronchial washings, brushings and trans-bronchial fine needle aspiration cytology.

Key words: Adenoid cystic carcinoma, breast, metastasis, lung, bronchial cytology, fine needle aspiration.


INTRODUCTION

Adenoid cystic carcinoma (ACC) arising in the breast is an uncommon primary tumour accounting for 0.1% of all breast malignancies. In comparison to other sites, ACC of the breast has a good prognosis and shows low incidence of spread to regional lymph nodes. A proportion of these tumours are complicated by local recurrence or metastatic spread to distant sites (1,2). The mean time span between the initial mastectomy and distant metastasis is 6.8 years (3). Morphologic features of cytology and histologic appearances of ACC in the breast are similar to the ACC of other anatomical sites such as salivary glands, lacrimal glands, lung, nasal cavity, skin, trachea, uterine cervix, prostate glands, oesophagus and Bartholin’s gland (4-5). ACC was previously termed cylindroma, initially described by Billroth in 1856 with the first description of breast ACC, credited to Geschickter in 1945 (6-9). ACC has previously been reported as negative for the receptors ER and PR (1,8) as seen in our case in the primary breast ACC. In this study we report a case of ACC of the breast metastatic to the lung after 9 years following mastectomy and clearance of lymph nodes, diagnosed by bronchial washings, brushing and trans-bronchial FNA in a 59 year old female. Metastatic ACC was confirmed on bronchial biopsy and she was treated with radiotherapy. Six years later the patient came back with metastasis of ACC to the scalp, which was excised.

CASE REPORT

A 59 year old female smoker presented with shortness of breath, cough, increasing hemoptysis, weight loss, lethargy, night sweats and fevers. Chest x-ray showed nodular opacity adjacent to the right hilum, which may represent a cluster of smaller nodules, each measuring approximately 1.4 cm in diameter, a lung lesion in the apical segment of the right lower lobe and also an abnormality in the mediastinum and lesions in the thoracic cavity. The possibilities were either metastatic disease from the previous breast cancer or a primary lung malignancy with metastasis to the mediastinum. The lungs otherwise appeared clear with no evidence of failure. She had asthma as a child and breast cancer was diagnosed in 1998.

Bronchoscopy was performed and revealed some irregular mucosa in the apical segment in the right lower lobe. The bronchial washings, brushing and trans-bronchial FNA were performed via the bronchoscope for cytology examination and diagnosed as suspicious for metastatic ACC. A subsequent bronchial biopsy was negative, therefore repeated bronchoscopy was done for cytology and histology. Bronchial biopsy confirmed the diagnosis of metastatic ACC. The patient completed radiotherapy to the right hilum/mediastinum. One year later the patient came back with hip pain. Chest x-ray revealed radiation pneumonitic changes of her right lung and no metastases seen in her left hip. Six years later she presented with a painful tender mass to her left frontal scalp and excision of this mass showed metastatic ACC. On a bone scan there was definitively a L4 lesion and increased activity bilaterally in the sacrum. She also had abnormal increased activity in the proximal left femur and proximal humerus which looked most consistent with metastatic disease. On CT scan of the chest the right lower lobe was completely collapsed with a mass obstructing the bronchus and was most likely a recurrence of ACC. CT scan of the abdomen and pelvis showed multiple bilateral soft tissue lesions arising from the kidneys and were most likely deposits of cancer.

MATERIALS AND METHODS

Bronchial washings, brushings and trans-bronchial FNA samples were collected in 30% ethyl alcohol in physiologic saline and filter preparations were made on size 5 μm Sartorius AG-Cellulose Acetate filters (Sartorius, Germany) using the cytosieve method and stained by the Papanicolaou method. The remainder of the sample was spun down and from the sediment a cell block was made and fixed in 10% formalin, routinely processed and stained with hematoxylin-eosin (H & E). The cell block preparation was insufficient.

CYTOLOGIC FINDINGS

Papanicolaou stained filters from all samples showed many cohesive three dimensional clusters of uniform cells with bailing effects and smooth border (Figures 1a and 1b), cystic spaces,
cribriform clusters, branching cylinders and solid clusters with ciliated bronchial cells in the background. The cribriform clusters were relatively large and contained round pale areas corresponding to the “cystic” spaces (Figures 2a and 2b). Another characteristic finding was the presence of pale blue or pale purple hyaline globules associated with small nests of tumour cells. Naked globules were also identified. Tumour cells exhibited a delicate cytoplasm. The nuclei were relatively uniform with a finely granular, evenly distributed chromatin and cystic spaces containing cyanophilic amorphous material.

Figure 1a and 1b: Filter preparation showing three dimensional clusters of uniform cells with balling effect and smooth border (Papanicolaou stain X 400)

HISTOLOGIC FINDINGS

H & E stained sections showed fragments of respiratory epithelium in which there were islands of atypical cells comprising angulated nuclei and forming variably sized well demarcated lumen, with features consistent with metastatic ACC. Sections from scalp excision biopsy showed skin with fatty subcutis, the typical structure of scalp. The dermis was extensively infiltrated by ACC, showing perineural infiltration focally (Figure 3).

Figure 3: Scalp excision biopsy showing skin with fatty subcutis, the typical structure of scalp and the dermis was extensively infiltrated by ACC, with perineural infiltration focally (haematoxylin-eosin X 100)

DISCUSSION

Adenoid cystic carcinoma (ACC) of the breast is rare, accounting for less than 0.1% of all breast cancers. This variant of adenocarcinoma is typically seen in salivary glands but has been reported in other organs including breast, skin, lung, cervix, larynx, prostate and Bartholin gland. Unlike ACC in the salivary gland, ACC of the breast has a good prognosis, with axillary metastasis being rare. Distant metastasis, usually to the lungs, can occur without positive axillary nodes and local recurrence is more likely (1). Axillary metastasis has been reported in rare cases suggesting that distant metastases predominantly develop by a hematogenous dissemination (10).

The extra-mammary tumours are highly fatal due to frequent metastases and extensive local invasiveness, with an overall 5 year survival rate of 40%. ACC of the breast is much less malignant than histologically identified neoplasms in other sites possibly due to the factors such as the relatively small size of these tumours when first noticed in the breast and their location, which enables total excision (5). ACC has previously been reported as negative for ER and PR. One review of the literature, however, found that more than half of ACCs of the breast were positive for at least one of these receptors. Despite the relative ER-PR negativity of this special type of breast carcinoma, the prognosis is good. It is believed that the tumour is ER negative not a result of poor differentiation, but possibly due to preserved polarity and differentiation of the component epithelial and myoepithelial cells (1).
ACC of the breast, occur predominantly in woman aged 60 to 66 year and mean age is 64 and may be bilateral. It tends to develop in the peri areolar area. Cytology and histological appearances of ACC of the breast are similar to the adenoid cystic carcinoma of other anatomic sites. Recent reports describe characteristic features on cytology to enable preoperative diagnosis comprising cellular aspirate with tightly cohesive aggregates of cells with enclosed spheres and interconnecting cylinders of acellular material. The principal cell type represent the epithelial cells and minor proportion of cells are ovoid to spindle shaped with hyperchromatic nuclei, representing myoepithelial cells. Another characteristic features is the numerous bare nuclei in the background.

The histological features of ACC of the breast are the intercellular cystic spaces lined by basement membrane material and biphasic cellularity with myoepithelial cells intermixed with epithelial cells (2). In addition, the arrangement of tumour cells around cores or spheres of homogenous acellular material and the presence of cystic spaces with cyanophilic amorphous material with positivity of mucin is a very valuable feature in the diagnosis of this rare variant of breast carcinoma (4). In exfoliate specimens of the respiratory tract, the cytodiagnosis of ACC may be difficult due to the frequent intact mucosa overlying the tumour, which prevents exfoliation of the tumour cells. The tendency of the exfoliated tumour cells lose their orientation in relationship to the cystic spaces and the often bland appearance of individual tumour cells may be difficult to discern among the normal or reactive respiratory tract epithelial cells (11, 12).

The differential diagnosis of pulmonary ACC includes reserve cell hyperplasia, where there are sheets of compactly arranged small cells with scant cytoplasm, round nuclei and a high nuclear/cytoplasmic ratio. The presence of attached columnar cells will favor a diagnosis of reserve cell hyperplasia and the presence of tubular and cribiform structures militates against a diagnosis of reserve cell hyperplasia. The tumour cells in carcinoind usually display uniform, small cells with rounded nuclei and a stipped chromatin with marked cell dissociation. Bare nuclei are uncommon. The nuclear features seen in carcinoind are different from those in ACC and the presence of mucoid globules within glandular structures favors a diagnosis of ACC. Small cell carcinoma is composed of small cells with nuclear molding, stipped chromatin, traumatic nuclear streaking and scant cytoplasm. In contradistinction, the neoplastic cells in ACC do not show nuclear molding and lack traumatic artifacts, they are composed of cells with dark nuclei. Acellular balls of basement membrane material within the cell clusters are not seen in small cell carcinoma. In well-differentiated adenocarcinoma, the glandular structures are usually seen cytologically without solid cores of pseudocyst material and the cells are usually larger and the cytoplasm more prominent than in ACC. Also, the nuclei are usually eccentric with a prominent nucleolus (11-14).

Before making a diagnosis of primary ACC or metastatic ACC, clinical and radiological correlation is essential. In our case a known history of primary ACC of the breast helped in making a definitive diagnosis. This report illustrates the biologic behavior of which this tumour is capable. Progression was extremely slow. Signs of metastases did not appear until nine years after removal of the primary tumour and the patient survived for six years after metastases in the lung.

ACKNOWLEDGMENTS

The authors acknowledge Louise Goossens for her photographic assistance and Ian Tompson for formatting images.

# REFERENCES


# AUTHOR INFORMATION

Sharda Lallu, BSc CFIAC, Cytotechnologist
 Sarla Naran, BSc CFIAC, Cytotechnologist
 Peter Bethwaite, MB ChB PhD FRCPA FFSc (RCPA), Pathologist and Senior Lecturer

1Department of Cytology, Anatomic Pathology, Wellington Hospital, Wellington
 2Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago, Wellington

Correspondence and reprint requests: Dr Peter Bethwaite, email: pbb@apath.co.nz

Copyright: © 2015 The authors. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.