



Fine Needle Aspiration Cytology Diagnosis of Salivary Parotid Basal Cell Adenocarcinoma with Metastasis to the Lung. Report of a Case and Review of the Literature

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Abstract

Basal cell adenocarcinoma (BCAC) is a low-grade malignant counterpart of basal cell adenoma [1]. Literature and case reports involving BCAC are limited as it was newly categorized in the second version of the World Health Organization classification of salivary gland tumors [2]. BCAC has been found to metastasize to cervical lymph nodes as well as to distant sites [8] including the hand [11], manubrium [12], scalp [13] and lungs [14,15]. Metastasis of BCAC to the lung is an uncommon finding with only two reported cases in the literature. This case report describes a 76-year-old female who presented with two right lung masses measuring 1.8 and 1.4 cm respectively. The cytomorphology and immunohistochemistry profile was diagnostic of metastatic basal cell adenocarcinoma, most likely of salivary gland origin. Reporting of this case aims to increase awareness of basal cell adenocarcinoma's potential to metastasize to the lungs while also highlighting the importance of considering this tumor, albeit rare, in the differential diagnosis of metastatic lung masses.

Keywords: Salivary; Metastatic; Basal cell; Adenoma; Adenocarcinoma

ABBREVIATION

BCAC: Basal cell adenocarcinoma, **BCA:** Basal cell adenoma, **US-FNA:** Ultrasound Guided Fine Needle Aspiration, **SGT:** Salivary gland tumors

INTRODUCTION

Basal cell adenocarcinoma (BCAC), also termed basaloid carcinoma, is a low-grade malignant counterpart of basal cell adenoma¹. Literature and case reports involving BCAC are limited as it is a newly categorized entity detailed in the second version of the World Health Organization classification of salivary gland tumors². BCAC is an uncommon entity accounting for only 1-2% of salivary gland carcinomas. Approximately 23% of BCACs arise within preexisting basal cell adenomas [1]. BCACs clinical features include a slow growing tumor most commonly located within the parotid glands and minor salivary glands in adults over the age of 50 [1]. It is locally destructive with a high recurrence rate but

has a favorable prognosis due to its low metastatic potential [1]. BCAC of the salivary gland morphologically resembles benign basal cell adenoma but is distinguishable by its malignant growth characteristics [2]. Treatment of BCAC is guided by its low-grade behavior [3]. The mainstay of treatment is wide local excision [3]. Postoperative radiotherapy is indicated in cases with positive surgical margins or after surgical excision of recurrent tumors [3,4]. We report an uncommon case of basal cell adenocarcinoma with rare metastasis to the lungs. BCAC often proves to be a challenging diagnosis due to its low incidence and limited documentation in the literature. The reporting of this case aims to increase awareness of basal cell adenocarcinoma's potential to metastasize to the lungs and highlight the importance of considering this tumor, albeit rare, in the differential diagnosis of metastatic lung masses.

CASE PRESENTATION

A 76-years-old female with a history of controlled coronary artery disease and hypertension presented with two right lung masses measuring 1.8 and 1.4 cm respectively. Radiographic images were suspicious for malignancy and tissue sampling was recommended for definitive diagnosis. Ultrasound Guided Fine Needle Aspiration (US-FNA) was performed on one of the lung masses. Cytology smears slides and cellblock preparation showed predominately trabecular pattern admixed with focal solid tumor pattern. Islands and clusters of malignant tumor cells were infiltrating the surrounding lung parenchyma (**Figure 1A**). Tumor cells were basaloid-like epithelial cells, some were small cells with small cytoplasm and others with darker nuclei and scattered palisading pattern (**Figure 1B**). Occasional foci showed squamous cell differentiation (**Figure 1C**). Low grade malignant cytologic atypia was noted. Immunohistochemistry studies were performed on cytology cellblock preparation and the tumor

Submitted: 21 May, 2021 | **Accepted:** 22 June, 2021 | **Published:** 27 June, 2021

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Citation: Downing E, Sly M, Barber C, Jahoda J, Steinman C, et al. (2021) Fine Needle Aspiration Cytology Diagnosis of Salivary Parotid Basal Cell Adenocarcinoma with Metastasis to the Lung. Report of a Case and Review of the Literature. SM J Clin Pathol 5: 4.

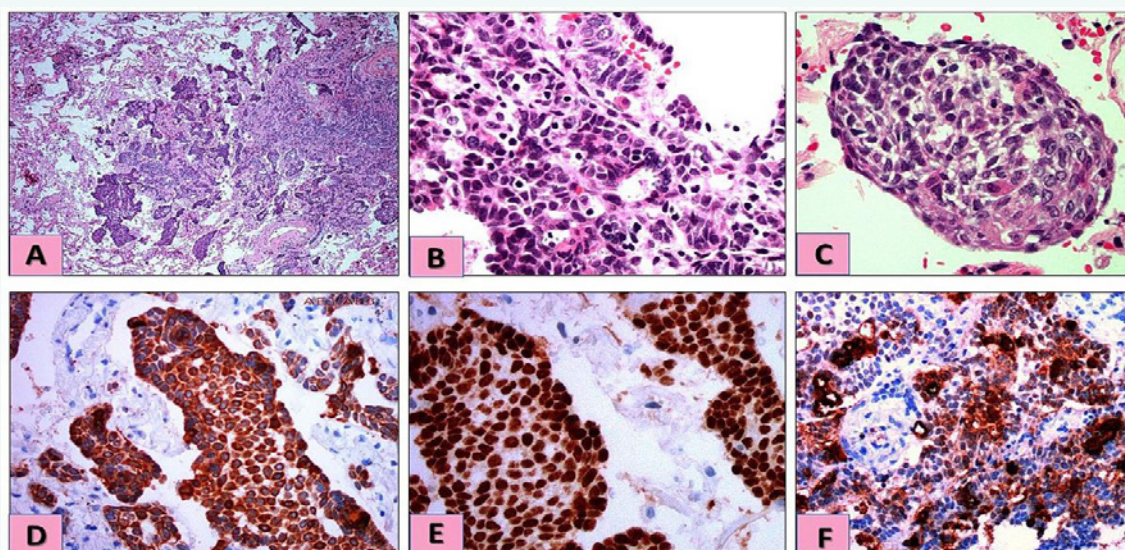


Figure 1 Microscopic description of lung tumor.

A: Tumor masses infiltrating lung parenchyma (H&E stain X20).

B: Tumor cells showing basaloid-like epithelial features, some are small cells with small cytoplasm and others with darker nuclei and scattered palisading pattern (H&E stain X40).

C: Cluster of tumor cells showing focal squamous cell differentiation (H&E stain X40).

D: Tumor cells positive for Cytokeratin AE1/AE3.

E: Tumor cells showing positive nuclear staining with P63.

F: Tumor cells positive for Muc-1.

cells were positive for Cytokeratin AE1/AE3 (**Figure 1D**), High molecular weight cytokeratin 903, Ck5/6 (diffuse pattern), P63 (**Figure 1E**), and Muc-1 (**Figure 1F**). The tumor cells were negative for Chromogranin, Synaptophysin, GFAB, CD117, and Vimentin. The cytomorphology and immunocytochemistry profile was consistent with metastatic basal cell carcinoma possibly of salivary origin.

As the patient recently emigrated from another country, prior history was not available at the time of presentation. With further questioning, the patient gave a vague history of excision of prior tumor from the right neck area. Prior material was obtained, and it was found that the patient presented 5 years earlier with a right parotid palpable 1.2 cm mass that was diagnosed as basal cell adenocarcinoma of the parotid gland. The parotid tumor was described as extending into the extra-parotid adipose tissue, with areas of comedonecrosis, and foci of squamous differentiation. Treatment of the prior tumor included parotidectomy and two excised lymph nodes were negative for metastasis, however, two margins were involved by carcinoma. The excision was followed by radiation.

Comparison of the tumor of current presentation with the prior parotid tumor showed similar cytomorphology and immunohistochemistry profile, and it was determined to be metastasis from the prior BCAC. Surgical excision of the two lung masses was performed with safe margins. Patient showed no further tumor related complications but expired three years later due to cardiac disease complications.

DISCUSSION

Salivary gland tumors (SGT) are rare lesions that have a prevalence of 0.4-13.5 cases per 100,000 people [5]. Specifically, 6% of head and neck cancers and 0.3% of all cancers in the United States are due to malignant SGT [5]. The etiology of SGT remains to be elucidated [5]. Presumed risk factors include cigarette smoking, viral infections, plumbing, rubber manufacturing, woodworking, asbestos mining, nickel exposure, cellular phone use, and a possible genetic predisposition [5]. The only known definitive risk factor is exposure to ionizing radiation [5].

Basal cell adenocarcinoma is a slow growing malignant neoplasm that is typically located in the major salivary glands [3]. It does not have an extensive history in the literature as it has only been classified as a salivary gland tumor by the World Health Organization classification since 1991 [3]. BCAC accounts for approximately 1.6% of salivary gland neoplasms and 2.9% of malignant salivary gland neoplasms [6]. 80% of BCAC are located in the parotid gland, 11% in the minor salivary glands, and 9% in the submandibular glands [7]. BCAC morphologically resembles basal cell adenoma but is distinguishable by its growth features that are specific to malignant neoplasms [2]. The origin of BCAC is still debated, but studies have demonstrated that most arise de novo (77%). In some instances, however, they arose from preexisting basal cell adenomas (23%) [8].

BCAC is predominantly diagnosed in adults between the ages of 40 to 90⁷ and exhibits no gender predilection [1]. Patients often notice a slowly enlarging, nontender mass with



symptom duration ranging from 3 weeks to 7 years prior to initial diagnosis [9]. Interestingly, 10-15% of BCAC cases present along with other cutaneous lesions including eccrine cylindromas and trichoepitheliomas, which suggests the importance of dermatologic examination [9]. BCAC often proves to be a challenging diagnosis due to its low incidence and limited documentation in the literature [10].

The local recurrence rate of BCAC is relatively high at 37% [11]. Recurrence typically occurs anywhere from six months to two years after resection [7]. Despite its relatively high recurrence rate, long term outcomes after undergoing resection are favorable due to the tumor's low rate of distant metastases (4%) and regional lymph node involvement (8%) [11]. BCAC has been found to metastasize to cervical lymph nodes as well as to distant sites⁹ including the hand [11], manubrium [12], scalp [13] and lungs [14,15]. There have only been 2 reported cases of BCAC resulting in death [12]. To our knowledge, our patient is the third documented case of BCAC with metastasis to the lungs.

Primary basaloid tumors of the salivary glands are characterized by "basaloid" epithelial cells with round or ovoid nuclei and an associated thin cytoplasm [7]. The term "basaloid epithelial cells" stems from the fact that myoepithelial, ductal or basal epithelial cells cannot be differentiated from each other based on standard histological evaluation alone [7]. Immunohistochemistry allows for detecting the cell type and improves diagnostic accuracy [7]. Tumors composed of basaloid epithelial cells include benign tumors such as pleomorphic adenomas and basal cell adenomas, and malignant tumors such as undifferentiated small cell carcinoma, adenoid cystic carcinoma, and basal cell adenocarcinoma [7].

Histologically BCAC exhibits multicentric, variable cytologic atypia and mitotic activity [1]. It is typically composed of two cell types, the first of which is small cells with scant cytoplasm in addition to dark nuclei that may demonstrate a palisading pattern [1]. The second type include polygonal cells with clear nuclei and eosinophilic and amphophilic cytoplasm [1]. These tumors are grouped into four histologic growth patterns [1]. BCAC stains positive for CK7+/CK20, p53, HER2, CD117/c-kit, BCL2, PS100, CEA and EMA [1]. Negative stains include GFAP and smooth muscle actin [1].

The diagnosis of BCAC is oftentimes challenging. Clinical examination, magnetic resonance imaging, ultrasonography, and computed tomography are occasionally unable to exclude other tumors of the salivary gland [16]. In addition, microscopic examination of tumor biopsy specimens is oftentimes insufficient to differentiate BCAC from BCA [16]. Examination of semi-serial sections of the excised tumor should be done to look for infiltration of tumor into surrounding normal tissues [17].

The histological differential diagnosis for BCAC includes small cell carcinoma, infiltrating cutaneous basal cell carcinoma, benign basal cell adenoma, and adenoid cystic carcinoma (ACC) [3]. ACC in particular shows vast similarities to BCAC [3]. ACC can be differentiated by its exhibition of cribriform patterns with increased central necrosis along with uniform and

hyperchromatic nuclei [3]. When differentiating ACC from basal cell neoplasms (BCNs) with immunohistochemistry, it was found that CK5/6 immunostaining showed differences in antibody staining location within cells examined [10]. BCN showed a diffuse staining pattern in comparison to only inner luminal staining exhibited in ACC [10]. Other important proteins found to be helpful in differentiating ACC from BCN include β -catenin, CD117, and S100P [10]. Small cell carcinoma exhibits neuroendocrine differentiators including neuron-specific enolase and synaptophysin both distinguishing it from BCAC [3]. Cutaneous basal cell carcinoma shows histological similarities to BCAC however the differentiating factors can be found within clinical history [3].

BCAC and basal cell adenoma (BCA) share histological, clinical similarities, and comparable cytologic and architectural characteristics but differ in their morphological growth features [18]. Both tumors are predominantly located in the major salivary glands and share four histopathologic growth patterns [18]. These growth patterns are solid, trabecular, tubular and membranous [18]. The literature suggests that BCA of the membranous subtype has the highest risk of undergoing malignant transformation into BCAC [18]. BCAC and BCA are derived from similar proliferation of two morphological variants of basaloid cells [18]. The main distinguishing factors between these two tumors are BCAC's malignant growth features that include invasive outgrowth, perineural and vascular involvement, mitotic figures, mild nuclear atypia, and evidence of necrosis [18]. Wilson and Robins claim that local invasion of the surrounding soft tissues and the gland are the best markers for differentiating the basal cell adenoma from basal cell adenocarcinoma [12]. They also found that separating BCAC and BCA based on invasion correlated with the level of mitotic activity, proliferation marker (using Ki-67 antigen expression) and apoptosis marker (caspase 3 expression) suggesting that these findings can support the pathologist's diagnosis of BCAC [12]. The immunoprofiles of BCAC and BCA are very similar and are thus not useful in distinguishing the two [19]. Despite the limited literature on the usefulness of immunohistochemistry in diagnosis of BCAC, our case supports the use of immunohistochemistry and cytomorphology to identify metastatic lesions of BCAC.

Although BCAC is a low-grade malignant neoplasm and has a low rate of metastasis, its locally destructive nature and high recurrence rate, encourages surgeons to perform complete surgical resection of the tumor to avoid future recurrences [20]. The consensus on treatment of BCAC is wide local excision [3]. The use of postoperative radiotherapy is indicated in cases with positive surgical margins or after surgical excision of recurrent tumors [3,4]. Metastases often pose a greater challenge to treat but are not necessarily inoperable [3]. A case of BCAC metastasis to the lung was treated by lobectomy [14]. In our case, the patient underwent resection of the lung metastasis followed by radiotherapy.

The intent of reporting this case is to increase awareness of the potential for basal cell adenocarcinoma to metastasize to the lungs. Furthermore, this case highlights the importance of



considering this tumor in the differential diagnosis for metastatic lung masses. We demonstrate the ability of cytomorphology and immunohistochemistry to identify BCAC as a differential diagnosis in metastatic lung lesions. The aforementioned discussion emphasizing the key distinguishing characteristics of BCAC from mimicking lesions should be considered when forming a diagnosis based on histological and morphological features. This will ultimately provide the patient with timely management and guide appropriate treatment regimens.

ACKNOWLEDGMENT

Special thanks to Erik Sucher, Donya Ahmadian, and Pritam Patel, MD candidates, American University of the Caribbean for their assistance in reviewing the final manuscript.

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