A case of small cell cancer of the breast in a male with synchronous stage IV non-small cell lung carcinoma

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Abstract

Extrapulmonary small cell carcinomas (EPSCC) are extremely rare. Most reports indicate success with therapy directed at the tumor as if it was pulmonary small cell carcinoma Primary small cell carcinoma of the breast is an uncommon form of EPSCC. Differentiating between a primary small cell carcinoma of the breast from metastatic disease to the breast is very important. According to the literature, there have been approximately 70 cases reported worldwide. Of these cases, only two cases are documented in men. Prognosis is varied and depends on stage of disease at presentation. A combination of surgery, chemotherapy and/or radiation is required to adequately treat patients with small cell carcinoma of the breast. We present a case of a male patient diagnosed with stage IV non-small cell lung carcinoma first and then subsequently diagnosed with a concurrent small cell carcinoma of the breast responding to treatment with concurrent chemotherapy and radiation.

Introduction

Extrapulmonary small cell carcinomas (EPSCC) are extremely rare. The most frequent sites of origin documented in the literature include the female genital tract (vagina, cervix), gastrointestinal tract (pancreas, cecum, stomach, esophagus), genitourinary tract (bladder, kidney), and head and neck.[1-3] The tumors are equivalent to the pulmonary component in terms of morphology and clinical behavior. Most reports indicate success with therapy directed at the tumor as if it was a pulmonary small cell carcinoma.[4-6] Some reports indicate success with surgery for local disease that is amenable to surgery. However, there are no guidelines or treatment options clearly defined for EPSCC.

Primary small cell carcinoma of the breast (PSCCB) is an uncommon form of EPSCC. Differentiating between a primary small cell carcinoma of the breast from metastatic disease to the breast is very important. Therefore, a non-mammary site must be excluded. The tissue must also be examined for an in-situ component as this would favor breast as the primary site.

According to the literature, there have been approximately 70 cases reported worldwide of primary small cell carcinoma of the breast.[7-15] Of these cases, there are only two cases documented in men.[6,8]

We present a case of a male patient diagnosed with stage IV non-small cell lung carcinoma first and then subsequently diagnosed with a concurrent small cell carcinoma of the breast.

Case Report

A 61 year old Caucasian male was transferred from an outside facility for respiratory failure and acute renal failure. On arrival, the patient had been intubated at the outside facility so he was moved to the intensive care unit. Two days after admission, hemoptysis was noted from the patient's endotracheal (ET) tube. A computed tomography (CT) scan of the chest was performed and demonstrated a left upper lobe bronchial obstruction with associated atelectasis, bilateral pleural effusions and mediastinal lymphadenopathy (LAD). The obstruction at the time was assumed to be related to an endobronchial malignancy due to fullness of the hilum per radiology. A bronchoscopy was performed the next day. This documented an endobronchial mass in the posterior segment of the right upper lobe, a mass obliterating the entire orifice of the posterior left upper lobe with active bleeding. Biopsies were obtained from the lung masses as well as bronchial washings from both lungs. Pathology revealed a non-small cell lung carcinoma (NSCLC) with squamous cell type from the right upper lobe biopsy and atypical squamous metaplastic mucosa with fibrin material from the left upper lobe biopsy.

One week later, the patient underwent a video-assisted thoracoscopic surgery (VATS) procedure with pleural stripping and drainage of the right sided effusion to check for a source of malignancy. Cytology of the effusion was negative for any malignant cells. Pleural biopsy demonstrated fibrinopurulent exudate, marked inflammation, necrosis and hemorrhage without any evidence of malignancy.

CT scans of the abdomen, pelvis and head were performed for staging of disease. A chronic, left atrophic kidney was found but otherwise scans were negative for malignancy. A bone scan was also performed and was negative for metastatic lesions.

He was extubated successfully and continued on hemodialysis for his renal failure thought to be related to hypotension and one working kidney. At discharge, he was transferred to a rehabilitation facility with an appointment for a local oncologist near his home to begin treatment.

Approximately one month after discharge, he returned to our hospital for hemoptysis. A repeat CT scan of the chest was done and showed no change in the size of the mass documented in the left upper lobe but did show improvement in the consolidation and atelectasis documented two months prior. It also revealed gynecomastia of the right breast without obvious masses. The patient had a biopsy by interventional radiology (IR) of the lingula. Pathology showed a non-small cell lung cancer of squamous cell type. After almost complete resolution of the patient's hemoptysis, a bronchoscopy was repeated due to a positive biopsy of the right upper lobe on previous admission but no mass documented on CT scan of the chest. Repeat bronchoscopy demonstrated sharp carina, irregularity of the anterior segment of the right upper lobe, and abnormal mucosa of the left main bronchus towards the lingula. Biopsies were taken of the abnormal mucosa of the left upper lobe and bronchoalveolar lavage (BAL) was taken of the right upper

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lobe. An endoscopic bronchial ultrasound (EBUS) was performed as well and a biopsy was taken of an L4 lymph node that was enlarged on visualization. Pathology demonstrated non-small cell carcinoma squamous cell type of the biopsies of the left upper lobe irregularity and a negative cytology of the BAL from the right lung.

The patient was discharged home and had decided to continue further follow up with our office for treatment. Given the delay in treatment, a PET scan was ordered prior to beginning treatment. PET showed a left pulmonary hilar lesion with an SUV of 18.8 (Figure 1), a right precarinal lymph node with calcification and SUV of 4, right breast retroareolar uptake with an SUV of 2.8 (Figure 2) and an atrophic left kidney. On questioning, the patient had complaints of a right breast mass for approximately one week. On examination, a mass could be felt in the right breast in the retroareolar region and was approximately 3 cm in size. Before treatment could begin for his lung cancer, a biopsy of this mass was obtained in IR. Pathology from this biopsy demonstrated a neuroendocrine carcinoma with a Nottingham score of 8 (glands = 3, nuclei = 2, mitoses = 3), grade III. The tumor consisted of sheets of crowded cells with hyperchromatic, pleomorphic nuclei with high nuclear cytoplasmic ratio (NC ratio), scant cytoplasm, easily seen mitoses (Figure 3). Immunohistochemical staining results showed: CD56 - strong positive, synaptophysin - strong positive, p63 - moderately positive, nuclear, diffuse, CK5/6 - negative and TTF-1 - negative. These results were most consistent with a high grade small cell carcinoma of the breast. This biopsy was compared to the patient's previous biopsies and there was no resemblance noted in any of the samples. No in-situ component was identified in the biopsy specimen. In light of the PET scan being negative for any other metastatic sites of disease, this was labeled as a primary small cell carcinoma of the right breast with a simultaneous diagnosis of Stage IV NSCLC of the lung.

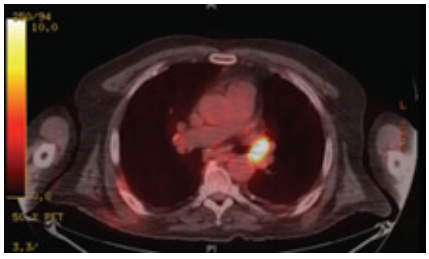

Figure 1. PET scan showing the hypermetabolic lesion in the left pulmonary hilar area with SUV of 18.8 that was not apparent on computed tomography after diagnosis.

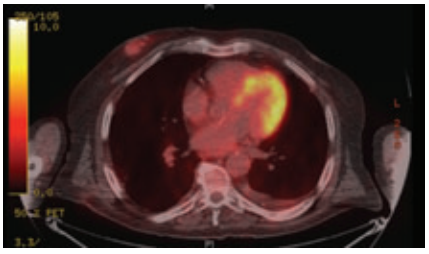

Figure 2. PET scan showing the right retroareolar breast mass with SUV of 2.8 that was discovered while the patient was being treated for his NSCLC of the lung.

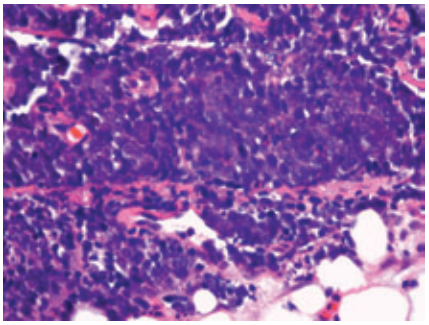

Figure 3. H&E stain showing sheets of crowded cells with hyperchromatic, pleomorphic nuclei with high NC ratio, scant cytoplasm, easily seen mitoses.

The patient received radiation therapy (RT) to the right breast concurrently with chemotherapy using carboplatin and etoposide. He completed RT to the right breast in one month with a total dose of 5000 cGy and a tumor boost to the right breast of 1000 cGy in 5 days. Due to hemoptysis at presentation and recurrence at a future date, it was decided to give RT to the left upper lobe of the lung to prevent further and possible fatal hemoptysis. He completed this radiation in 56 days with a total dose of 6660 cGy. As of now, the patient has completed 5 cycles of carboplatin/etoposide and is doing well. CT scan of the chest has shown resolution of the breast mass and volume loss of the left upper lobe without malignancy or new disease. The breast mass has resolved on examination.

Discussion

PSCCB is an extremely uncommon form of EPSCC. They are extremely rare. According to the literature, there have been approximately 70 cases reported worldwide of primary small cell carcinoma of the breast.[7-15] Of these cases, two cases have been documented in men.[6,8]

Differentiating between a primary small cell carcinoma of the breast from metastatic disease to the breast is very important. Therefore, a non-mammary site must be excluded. PSCCB can only be diagnosed after all other sources of possible malignancy are excluded clinically and radiographically, or if there is an in-situ component seen histologically in the breast tissue as this would suggest a primary breast origin. Based on its clinical similarity to pulmonary small cell carcinoma, this type of tumor is considered extremely aggressive.

Once diagnosed, treatment options are highly varied and are not currently standardized.[1,4-7] According to our literature review, no one treatment is recommended over another. Numerous cases were amenable to surgery as the disease was localized to the breast with some patients receiving adjuvant chemotherapy and/or radiation therapy if a lumpectomy was performed.[7,13,15] Other clinicians treated their patients with chemotherapy standardized for small cell lung carcinoma using cisplatin/etoposide, carboplatin/etoposide, fluorouracil/epirubicin/cyclophosphamide, or docetaxel/carboplatin.[7,10-12] Some physicians used concurrent chemotherapy and radiation with cisplatin and etoposide.[14,15]

Our patient was treated with carboplatin and etoposide concurrently with RT to the right breast as this would treat his small cell carcinoma of the breast, but also have activity against his stage IV non-small cell lung cancer. He was not considered for surgery due to his concurrent lung cancer. Resolution of disease in his breast was documented after three cycles of carboplatin and etoposide and completion of RT clinically and radiographically.

Conclusions

Prognosis for PSCCB is varied and depends on the stage of the disease at presentation. A combination of surgery, chemotherapy and/or radiation is required to adequately treat patients with small cell carcinoma of the breast. We recommend future randomized clinical trials to evaluate the most efficacious treatment regimen for these patients and long term follow up to help determine the course of the disease.

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