Rapidly Progressive Aerogenous Spread in Lepidic Predominant Adenocarcinoma (Formerly Bronchioloalveolar Adenocarcinoma) with Rapid Death

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Abstract

Lepidic predominant adenocarcinoma (formerly included under the heading of bronchioloalveolar adenocarcinoma) can rarely present with a pneumonitic presentation with rapid dissemination and respiratory failure due to aerogenous spread. Here we present two cases of rapidly fatal lepidic predominant adenocarcinoma each with a pan-pneumonitic presentation. In each case, the patient presented with pneumonia-like symptoms and, despite intervention, died within the span of three months. Autopsies revealed diffuse lepidic predominant adenocarcinoma with extensive micropapillary metastatic spread. The cause of death for each was respiratory failure due to aerogenous dissemination. The rarity of this presentation makes it suitable for further analysis.

The International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society set out new standards for the diagnosis of lung adenocarcinomas in 2011 for the purpose of standardizing diagnoses. This collaboration created five new subtypes instead of the past common diagnosis of “mixed type bronchioloalveolar adenocarcinoma.” The two cases presented here are presumed to fall under the new heading of nonmucinous lepidic predominant adenocarcinoma, although it should be noted that both contain evidence of other subtypes as well.

Aerogenous spread leading to respiratory failure in bronchioloadenocarcinoma is documented in the literature but still only rarely mentioned. Most of the cases of aerogenous spread of adenocarcinoma concern elderly males who were either smokers or had some other lung insult before the rapid adenocarcinoma was discovered. Additionally to our knowledge, this is the first paper published reporting this anomaly since the reclassification of lung adenocarcinomas in 2011.

We present two cases of presumed lepidic predominant adenocarcinoma (formerly bronchioloalveolar carcinoma), both presenting with rapid dissemination with respiratory failure and metastatic disease leading to rapid death.

Case One:

Patient History

The first case is a 56-year-old, African American female who was admitted to the hospital for respiratory distress and suspected pneumonia. No previous medical record was known.

Hospital Course

Patient A was admitted to the hospital on 6/28/2011 and was transferred to another area hospital where she received a lung wedge resection for areas of consolidation of the lower left lobe. The wedge resection showed evidence of TTF-1 positive adenocarcinoma. The patient
suffered progressive respiratory distress until her death on 7/7/11, nine days after her initial presentation.

Diagnosis

Upon autopsy, Patient A was determined to have died from respiratory failure secondary to pulmonary carcinomatosis. Her lungs showed diffuse pulmonary adenocarcinoma with both micropapillary and bronchioloalveolar subtypes. Upon sectioning, the lungs revealed white-tan irregular nodularity diffusely spread throughout all lobes of both lungs with bilateral consolidation. Metastatic adenocarcinoma was found in the adrenals, thyroid, liver, and hilar lymph nodes. Grossly, the liver parenchyma contained multiple well-circumscribed tan-brown nodules.

Histology confirmed diffuse lepidic spread of adenocarcinoma with accompanying invasive micropapillary adenocarcinoma. The lepidic spread lead to aerogenous dissemination, leading to a rapid death by respiratory failure that mimicked pneumonia.

Case Two:

Patient History

The second case concerns a 71-year-old woman with Type II diabetes mellitus who was being treated with Byetta and had recently undergone a voluntary hip replacement. Upon follow-up for the successful replacement, multiple masses were found in her lungs and bones.

Hospital Course

Patient B died two months after the lung masses were originally found. A pleural biopsy demonstrated poorly differentiated adenocarcinoma, positive for pancytokeratin, cytokeratin 7, CEA, B72.3, and BerEP4.

Diagnosis

At autopsy, Patient B was found to have died from respiratory failure, secondary to carcinoma of the lung. Lung sectioning revealed bilateral diffuse consolidative gritty white nodules that filled 70% of the lung parenchyma. Both lungs and all lobes were involved. Bilateral pleural adhesions were noted, and the pleural surface had multiple tumors. Metastatic mucinous adenocarcinoma was found in the adrenals with heavy periadrenal soft tissue involvement. A colloid nodule was located in the thyroid. There were multiple bone metastases. Figure 1 demonstrates slices of each lung. Multiple small, yellow/tan nodules covering almost the entire surface of the parenchyma are noted.
Histology showed mixed lung adenocarcinoma with extensive lepidic spread and invasive mucinous/colloid type, as indicated in Figure 2. The lepidic spread was determined to have led to aerogenous dissemination, leading to respiratory failure.

**Figure 1:** Multiple small nodules are diffusely present throughout the lung parenchyma in Case Two.
Discussion

Although adenocarcinoma is the most common lung cancer in nonsmoking women and its numbers have been increasing over the past several years, the complication of rapidly progressive death due to respiratory failure brought about by aerogenous spread of lepidic-predominant adenocarcinoma is still somewhat of an anomaly. Aerogenous spread leading to respiratory failure in bronchioloalveolar adenocarcinoma is present in only four published cases. Within those cases, only one concerned respiratory failure within a few months of initial diagnosis, and that particular study focused on an elderly male. Most of the cases present in the literature concerning aerogenous spread of adenocarcinoma focus on elderly males who were either smokers or had some other lung insult (such as tuberculosis) before the rapid adenocarcinoma was noted. Additionally to our knowledge, this is the first paper published reporting this anomaly since the reclassification of lung adenocarcinomas in 2011.

The International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society released a reclassification of lung adenocarcinomas in 2011, making the term bronchioloalveolar adenocarcinoma obsolete. Instead, BAC has been reclassified into five subcategories. The cases presented here are best typified by the new category of lepidic predominant nonmucinous adenocarcinoma, with a micropapillary pattern present as well. The lepidic predominant subtype would normally have close to a 100% five-year survival rate; however in these cases, the rapid dissemination with respiratory failure and metastatic disease was rapidly fatal.
The diffuse, pneumonitic presentation of lepidic predominant adenocarcinoma is a well-known, if rare, variation. Research suggests that this form might be treated with tyrosine kinase inhibitors of epidermal growth factor receptor. However in the cases presented here, the disease was so rapid that no successful intervention could be made, even if the clinician was able to correctly diagnose a pneumonia presentation as underlying carcinoma.

Aerogenous spread has itself been extensively studied. One theory is that an increased number of neutrophils promotes tumor shedding and thus aerogenous spread. This pattern has been observed in the micropapillary subtype. Of note, histology on Patient A revealed a micropapillary pattern in addition to the major finding of lepidic spread. However, a micropapillary subtype was not observed in Patient B, suggesting that while the subtype may increase the odds of aerogenous spread, it is not essential.

As the incidence of adenocarcinoma of all types continues to rise, the number of cases with the unusual presentation of rapid death due to aerogenous spread should increase. Although this will likely present clinically as a pneumonia-like illness, with advances in molecular testing and coordination between clinicians and pathologists, early diagnosis should be possible. With further advances, what is now a rapid death sentence may become as practical to manage as its more common counterparts.
References:


