February 2012 Pulmonary Case of the Month

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History of Present Illness
A 49 year old female was seen for fever and shortness of breath in December 2011. She has a history of right infiltrating ductal breast cancer diagnosed in 2001 at age 38. Treatment included mastectomy with negative lymph nodes, followed by 4 courses of doxorubicin and cytoxan. She did well until March 2010 when erythema was noted over her right chest. Biopsy showed adenocarcinoma consistent with breast carcinoma. The biopsy was “triple negative”, i.e., negative for estrogen receptors, progesterone receptors and Her2. PET scan demonstrated multiple positive lymph nodes in the mediastinum, supraclavicular area and bone metastases. She received radiation to her chest wall and chemotherapy most recently gemcitabine, carboplatin and iniparib. In October 2011 brain metastases were noted and she was started on stereotactic brain radiation and dexamethasone.

Past Medical, Family and Social Histories
She had a prothrombin mutation noted and was begun prophylactically on warfarin in 2010.
There was a family history of breast carcinoma.
She was a non-smoker with no unusual exposures.
Current medications include omeprazole, metoprolol, and warfarin.

Physical Examination
She was receiving oxygen at 3 L/min by nasal cannula. Temperature was to 37.9°C. She had bilateral crackles on chest auscultation, most prominent at bases. Physical Examination was otherwise noncontributory.

Initial Laboratory Evaluation
Hemoglobin/Hematocrit 11.8 g/dL/33.9%
White blood count 5.1 X10⁹/L
Platelets 64 X 10⁹/L
INR 1.58

Chest CT scan
Chest CT scan is in figure 1.
Figure 1. Selected images from the admission CT scan. The CT scan was interpreted as showing diffuse groundglass opacities and scattered centrilobular nodules.

Which of the following diagnosis are consistent with the patient’s presentation and CT scan?

1. Pulmonary edema
2. Bacterial pneumonia
3. Fungal pneumonia
4. Drug reaction
5. All of the above
Correct!
5. All of the above

Groundglass opacities are nonspecific and the differential is large including acute process such as pulmonary edema, infectious pneumonitis, and noninfectious pneumonitis. Chronic process may also present with groundglass opacities including interstitial diseases, bronchoalveolar carcinoma and numerous other causes such as organizing pneumonia, alveolar proteinosis and chronic eosinophilic pneumonia.

Hospital Course
She was empirically started on broad spectrum antibioitics. Cocci serology and PCR of a nasal swab for influenza and mycoplasma antibodies were negative. Because no diagnosis was apparent, bronchoscopy with bronchoalveolar lavage (BAL) was done. The fluid was slightly hemorrhagic and did not clear with repeated lavage. Smears and cultures of the BAL fluid were negative. The BAL fluid was also negative for Aspergillus antibody and PCR for pneumocystis and legionella.

The patient continued to have low-grade fever and oxygen requirements increased. For this reason a VATS lung biopsy was performed. The results are present in Figure 2. Special stains for organisms were all negative.
Figure 2. Low power views (Panels A & B) and high power view (Panel C) of H&E stained VATS lung biopsy. The biopsy was described as fibrinous acute lung injury with increased alveolar macrophages, scattered multinucleated giant cells and increased extravascular tissue eosinophils.

Which of the following are consistent with the clinical course and lung biopsy?
1. Pulmonary edema
2. Bacterial pneumonia
3. Metastatic breast cancer
4. Drug toxicity
5. Bronchoalveolar carcinoma
Correct!

4. Drug toxicity

Although the pathology is nonspecific it is consistent with drug toxicity. There was no evidence of infection or cancer on the biopsy.

Which of the following is most appropriate?

1. Stop gemcitabine
2. Stop carboplatin
3. Stop iniparib
4. Stop corticosteroids
Correct!

1. Stop gemcitabine

Of the agents the patient was receiving, gemcitabine is the drug most commonly associated with pulmonary toxicity and the most likely agent. Treatment of drug induced lung disease involves stopping the offending agent. Although no randomized trial has been performed, corticosteroids are often added and anecdotally may hasten resolution of the lung toxicity. This was done in this case and the patient had marked clinical improvement a month later. We speculate the delay in symptoms between her last gemcitabine therapy and her symptoms might have been due to the corticosteroids she was receiving for her brain metastasis.

Acute dyspnea with infusion of gemcitabine occurs in about 10% of subjects. There appear to be three types of gemcitabine lung toxicity:

1. Capillary leak syndrome
2. Diffuse alveolar damage
3. Alveolar hemorrhage

The frequency of lung toxicity is relatively low at about 0.27% of patients receiving the drug. Reduction in DLco within 2 months of treatment has been reported in 24% of patients, but this is often self-limited. The reduction in DLco appears to be more frequent in women, older age, and those with a low baseline DLco. Some cases of pulmonary fibrosis are reported, but are rare. Factors increasing the risk of lung injury include other chemotherapy (including paclitaxel) and chest radiation. The mortality rate with acute pneumonitis is up to 20%, but rapid response to steroid therapy has been reported.

Iniparib is a poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitor. A recent phase 2 trial in metastatic “triple negative” breast cancer reported 123 patients given iniparib with or without gemcitabine/carboplatin. Iniparib improved survival from 7.7 months to 12.3 months. Dyspnea was reported, but no severe pulmonary complications from iniparib were reported in this study.

References