Docetaxel-induced hypersensitivity pneumonitis mimicking lymphangitic carcinomatosis in a patient with metastatic adenocarcinoma of the lung

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Docetaxel belongs to the taxane family of anti-cancer drugs, which are commonly used in non-small cell lung cancers. They stabilize microtubules by preventing depolymerization, resulting in cell death. Pneumonitis is an uncommon side effect of docetaxel. We report a case of docetaxel induced hypersensitivity pneumonitis mimicking lymphangitic carcinomatosis in a patient with metastatic adenocarcinoma of the lung.

A 54-year-old man was diagnosed with metastatic adenocarcinoma of the lung in February 2012. He presented with multiple brain metastases which were found to be from his primary lung adenocarcinoma. EGFR (epidermal growth factor receptor) on the cancer cells was wild-type, and ALK (anaplastic lymphoma kinase) was not detected. He received whole brain radiation therapy (3000 cGy) for his brain metastasis. He was subsequently started on cisplatin 75 mg/m² and pemetrexed 500 mg/m² every 3 weeks. He received three cycles of this chemotherapy regimen from April 2012 to June 2012. Repeat imaging at the end of this cycle revealed progression of the disease in his lungs. The chemotherapy was subsequently changed to docetaxel 75 mg/m² every 3 weeks. He received four cycles of docetaxel from July 2012 to October 2012. At this time he presented to the clinic with extreme shortness of breath. On examination, patient had cyanosis; his oxygen saturation was 70% on room air. He had diffuse rales bilaterally on chest examination. He also had a rash on his arms (Figure 1). A chest X-ray (Figure 2) and a CT scan of his chest (Figure 3) were ordered, and patient was admitted to the hospital. He was started on oxygen initially at the rate of 6 L/min via a nasal cannula. He was not able to maintain his oxygen saturation on a nasal cannula, was switched to a non-rebreather mask, and subsequently to non-invasive positive pressure ventilation. He was also started on broad spectrum antibiotics and intravenous steroids. The chest X-ray and CT scan of the chest were read by the radiologist as diffuse interstitial pneumonitis suspicious for lymphangitic carcinomatosis. This was the initial diagnosis for the patient, and given the fact that he had metastatic adenocarcinoma of the lung to begin with and had failed first line chemotherapy, this was thought to be the most likely diagnosis.

During the course of his hospitalization the patient improved significantly and was discharged from the hospital in 10 days. He took steroids for 4 weeks. His repeat CT scan in January 2013 (Figure 4) showed marked improvement in his lung markings. He was initially oxygen dependent but is off oxygen at present. All these changes were attributed to docetaxel and he has been off docetaxel since October 2012 with the latest imaging done in March 2013 revealing slight progression of disease.

DISCUSSION

Docetaxel is a taxane antineoplastic agent with activity against a broad range of cancers. The side effects commonly associated with docetaxel include myelosuppression, alopecia, asthenia, neurosensory problems,
and fluid retention. Hypersensitivity reactions are uncommon with docetaxel partly because docetaxel is mixed in ethanol and water rather than cremophor, and partly because it is given with steroids.\(^1\,\,^2\)

There are several Phase II studies of single-agent docetaxel which report Grade 4 toxicities in individual patients as unexplained pneumonitis,\(^3\) fever, bilateral pneumonia, severe hypoxia,\(^4\) or interstitial pneumonia.\(^5\) More severe cases of interstitial pneumonitis have been reported in patients treated with a docetaxel and gemcitabine combination,\(^6\) and docetaxel administered with concomitant thoracic radiation therapy.\(^7\) However, pulmonary toxicity induced by docetaxel is extremely rare, and only a few cases have been reported in the literature.\(^8\,\,^9\)

The exact mechanism of docetaxel-induced interstitial pneumonitis is not known, but both allergic and the cell-mediated cytotoxic reactions have been suggested.\(^10\) The docetaxel-induced lung toxicity in the cases that have been reported usually occurred after the second to fourth course of chemotherapy, and was usually relieved with corticosteroid therapy.\(^6\) Therefore, the involvement of a cytotoxic T-cell-mediated mechanism is very likely. Interestingly, there

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\(1\) and \(2\) Hypersensitivity reactions with docetaxel

\(3\) - \(5\) Various toxicities reported in Phase II studies

\(6\) - \(9\) Rare cases reported in literature

\(10\) Potential mechanisms suggested
seems to be a positive relationship between the tumor response and the lung injury.

Although pneumonitis secondary to docetaxel is a rare side effect, the mortality rate is high. Oncologists should be aware of this complication. The patients usually present with a high fever, cough, dyspnea, and diffuse lung infiltration. The symptoms develop acutely over 1–2 days and rapidly progress despite empiric antibiotic therapies, and culminate in respiratory failure, which sometimes requires mechanical ventilation. The treatment of choice is the administration of corticosteroid therapy, usually 30–60 mg of prednisone per day for 2–3 weeks, or 60–240 mg per day in more severe conditions such as acute respiratory failure with a slow and careful tapering-off period. Our patient needed non-invasive ventilation and responded well to steroids and antibiotic therapy. His maculopapular rash, possibly from a similar hypersensitivity reaction to docetaxel, also responded well to steroids.

REFERENCES