LETTERS TO THE EDITOR

Bronchiolitis Obliterans Organizing Pneumonia Induced by Chemotherapy

To the editor: Bronchiolitis obliterans organizing pneumonia (BOOP) is a clinicopathologic syndrome recognized in the 1980s as a distinct disorder with characteristic features. Symptoms are usually subacute, with fever, nonproductive cough, malaise, mild dyspnea, and anorexia. The diagnosis of BOOP requires the presence of a combination of pathological, clinical, and radiological features. Typical imaging features are multiple patchy alveolar opacities varying from areas of ground glass density or consolidation. Distribution is peripheral and bilateral. Histology shows intra-alveolar buds of granulation tissue and bronchiolar lesions (when present) consisting of similar buds of granulation tissue inside the airway lumen.[1,2]

BOOP may be idiopathic (cryptogenic organizing pneumonia) or secondary to various underlying conditions. Infection (bacterial, viral, parasitic, or fungal), various drugs, and inflammatory and/or systemic disorders including cancer are known causes of BOOP.[3]

We report the case of a lung cancer patient presenting with BOOP after chemotherapy with paclitaxel and gemcitabine.

A 69-year-old woman was diagnosed 10 months earlier with stage IV lung adenocarcinoma. She received 6 cycles of chemotherapy with paclitaxel (100 mg/m^2 on days 1 and 8), gemcitabine (1000 mg/m^2 on days 1 and 8), and carboplatin targeted to an area under the plasma concentration curve of 5 (day 1) scheduled every 3 weeks, achieving partial response. She then continued therapy with 2 substances (paclitaxel and gemcitabine) at the same doses every other week, with standard corticosteroid and antihistamine premedication.

Six weeks into the second regimen (3 doses of gemcitabine) with no signs of toxicity, she complained of dry cough, dyspnea, asthenia, and fever. Chest radiographs showed bilateral interstitial infiltrates that worsened in a few days with hypoxemia requiring oxygen therapy. Serologic tests for *Legionella, Mycoplasma, Coxiella, Chlamydia,* adenovirus, cytomegalovirus, and influenza A virus were negative. A high-resolution computed tomography scan of the lungs revealed bilateral interstitial infiltrates predominating in the right lung and patches of ground-glass attenuation.

Fiberoptic bronchoscopy was performed with bronchoalveolar lavage (BAL) and transbronchial biopsy. Microbiological examination of the BAL for microorganisms, acid-fast bacilli, and detection for *Pneumocystis carinii* were negative, as was cytological examination for malignancy. A cell count showed 2×10^9/L cells, 3% neutrophils, 55% lymphocytes and 42% macrophages. Immunocytometry of BAL cells showed: 90% CD3, 65% CD4, 33% CD8, 6% CD57/CD8 (NK).

A histopathological pattern consistent with BOOP was revealed on examination of the transbronchial biopsy, with no evidence of malignancy.

The patient started corticosteroid therapy and clinical improvement followed rapidly within 24 hours. After 3 weeks of treatment a new chest radiograph showed complete resolution of the lung infiltrates. Corticosteroids were tapered off until cessation with no further evidence of relapse.

Lung toxicity with paclitaxel as a single agent has not been defined, although lung toxicity with gemcitabine has been widely described. Dyspnea is reported to occur in fewer than 10% of patients, many of whom have lung cancer, with serious dyspnea occurring in 5%.[4] Severe lung toxicity and death after gemcitabine has also been reported.[5] Patterns of lung toxicity with gemcitabine range from mild dyspnea, to acute hypersensitivity reaction with bronchospasm, to fatal acute respiratory distress syndrome.

Cytosine arabinoside (ara-C) is another nucleoside analog with structural similarities to gemcitabine that has clearly been associated with acute or subacute lung toxicity, the most frequent manifestations being noncardiogenic pulmonary edema with progression to acute respiratory distress syndrome. Ara-C has been reported as a cause of BOOP in patients, most of whom had acute leukaemia.[6]

A search on MEDLINE for organizing pneumonia and paclitaxel or gemcitabine yielded no other reports of BOOP related to the use of either of these drugs.

Since paclitaxel is rarely associated with lung toxicity, the known association between gemcitabine and pulmonary toxicity, as well as the association between BOOP and ara-C (structurally similar to gemcitabine) helped us to establish the diagnosis of BOOP induced by gemcitabine after we had ruled out other known causes of BOOP.

Gemcitabine is widely used as a single agent or in combination with other drugs in chemotherapy for a variety of tumors including lung, breast, ovarian, and pancreatic cancer. Thus, a high index of suspicion is needed when a patient in chemotherapy develops dyspnea, especially if either gemcitabine or ara-C is included in the regimen. Early recognition of BOOP or other signs of pulmonary toxicity associated with chemotherapy will allow appropriate treatment, including withdrawal of the drug and the initiation of corticosteroid treatment. Death can be avoided in many cases.

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