CASE REPORT

Gemcitabine-induced respiratory failure associated with elevated erythrocyte sedimentation rate (ESR)

Sam Davidoff*, Rakesh D. Shah, Talwar Arunabh

Department of Medicine, North Shore University Hospital, 304 Community Drive, Apartment 3D, Manhasset, NY 11030, USA

Received 2 December 2004; accepted 16 August 2005

Summary Gemcitabine is a newer pyrimidine analog used for the treatment of solid tumors. Though generally considered safe, it can cause pulmonary toxicity, which is generally mild and reversible. The purpose of this publication is to document a case of adult respiratory distress syndrome (ARDS) caused by Gemcitabine administration. The patient was noticed to have the extreme elevation of erythrocyte sedimentation rate (ESR) (> 100 mm/h) at the time of diagnosis. We observed excellent response to the corticosteroids. The ESR trended back to normal after the resolution of her symptoms thereby suggesting the utility of monitoring ESR in the diagnosis and management of Gemcitabine-induced pulmonary toxicity.

© 2005 Elsevier Ltd. All rights reserved.

Introduction

Respiratory symptoms as adverse reaction to medication intake are a common phenomenon. Many types of pulmonary problems such as shortness of breath, cough, fibrosis, and pleural effusions are very well documented. However, drug-induced pulmonary edema is relatively rare. Recognition of this is especially problematic in a patient with multiple comorbidities.

We present a case of Gemcitabine-induced pulmonary edema. Throughout the course, the patient was noticed to have an extreme elevation of erythrocyte sedimentation rate (ESR). To our knowledge, this is the first attempt to utilize ESR in the face of Gemcitabine-induced pulmonary edema. The level was monitored. Our implication is that a patient presenting with shortness of breath, bilateral infiltrations on the chest X-ray, leukocytosis, and extreme ESR elevation can at times be exhibiting signs of drug-induced pulmonary toxicity. Along with the overall symptomatology, monitoring the ESR levels can be attempted to observe the response to the ongoing therapy.

KEYWORDS
Gemcitabine-induced lung toxicity; ARDS; Elevated ESR

*Corresponding author. Tel.: +1 516 708 1263.
E-mail address: nsuhdo@yahoo.com (S. Davidoff).
Case presentation

A 60-year-old female was diagnosed with Carcinoma of the right breast in 1998, for which she underwent lumpectomy with subsequent radiation therapy. She was treated with Tamoxifen and remained asymptomatic until July 2003, when she was diagnosed with metastatic disease in the spinal column, liver and contralateral breast. She received five cycles of Vinorelbine from July 2003 to April 2004.

In April 2004, the patient was started on Gemcitabine (1424 mg weekly for 3 weeks of the month). The total of five cycles of Gemcitabine was tolerated well. Her last dose was given 7 days prior to the admission.

The patient was admitted through the emergency room with progressive shortness of breath and non-productive cough for few days. Three days prior to the admission, she was started on Levaquin for presumptive diagnosis of acute bronchitis. Despite that, shortness of breath continued to worsen.

Her physical examination revealed a blood pressure of 170/87 mmHg, and pulse rate of 122 beats per minute, respiratory rate of 32 breaths per minute. The patient’s oxygen saturation was 72% on room air. She was placed on 100% oxygen via facial mask, and the oxygen saturation improved to 91%. Mild jugular vein distention was noticed. Chest examination revealed use of accessory musculature, and bibasilar rhonchi were appreciated on auscultation. There were no audible heart murmurs. Abdominal and neurological exams were unremarkable. Examination of the extremities did not show any edema. Distal pulses were palpable.

The chest radiograph (Fig. 1) at the time of admission revealed diffuse, bilateral, multifocal opacities indicative of air space disease without significant pleural effusion. There was no cardiomegaly.

Laboratory examination demonstrated leukocytosis of 17,300 cells/mm³ (neutrophils 80%, lymphocytes 16%, eosinophils 1% and monocytes 3%), mild anemia (hemoglobin of 10.1 g/dL and hematocrit of 29.5%) and platelets of 167,000/μL. Arterial blood gas analysis while the patient was on FiO₂ of 100% demonstrated pH 7.44; pCO₂ 42 mmHg; pO₂ 64 mmHg. Patient’s blood, sputum and urine samples were sent for cultures. A CT scan of the chest (Fig. 2) showed extensive ground-glass opacities throughout both lungs, more so in both upper lobes. Interlobular septal thickening and small bilateral pleural effusions were also seen.

The patient was initially treated with Albuterol and Ipratropium given via hand-held nebulizer and intravenous Lasix 40 mg. Levaquin 500 mg orally per day was continued for possible Community acquired pneumonia. Because of the lack of improvement, Levaquin was discontinued on the 2nd day of hospitalization and the patient was started on Vancomycin 1 g/day intravenously and Ceftazidime 2 g every 12 h intravenously. The patient underwent bronchoscopy but broncho-alveolar lavage did not reveal an infectious cause of the pulmonary process. Repeated microbiological evaluation of the blood was also negative. She continued to remain hypoxemic and her ESR was found to be 128 mm/h. As the diagnosis of Gemcitabine related pulmonary toxicity was entertained, the patient was started on Solu-Medrol 40 mg intravenously every 12 h.
There was a significant clinical response to the steroids. The patient’s dyspnea improved. She was able to maintain adequate oxygenation (oxygen saturation of 94% while being supplemented with oxygen via nasal canula at the rate of 4 L/min). On the 5th day of the steroid therapy, the patient’s oxygen saturation was stable at 96% on 2 L/min of oxygen via nasal canula. On the 8th day of the steroid treatment, the oxygen saturation was 94–96% without any supplementation. The repeat CT scan of the chest also showed almost complete resolution of the infiltrates seen on the first CT scan of the chest (Fig. 3). As the clinical symptomatology improved, the ESR showed a downward trend. Four day after starting the steroids, the ESR was 89 mm/h; and on the 10th day of the treatment, it went down to 59 mm/h. A total 14-day course of steroids was given. Ten days after the discontinuation, the ESR was found to be 41 mm/h and pulmonary function test did not reveal significant abnormalities.

Discussion

Gemcitabine-induced pulmonary toxicity can cause respiratory dysfunction. Only a few cases of adult respiratory distress syndrome (ARDS) due to Gemcitabine have been reported. The onset of the pulmonary toxicity cannot be predicted and the time course of this complication is variable. There seems to be no relationship between the dose and the severity of the pulmonary insult. Past history of radiation therapy to the chest and older age seem to be the predisposing factors. Most commonly reported symptom is dyspnea, occurring in about 8% cases. ARDS associated with Gemcitabine is rare with the incidence of 0.002%. The exact mechanism of the severe lung damage is not clear but autopsy reports describe diffuse alveolar damage as the pathological manifestation of the acute respiratory failure.

The underlying pathological mechanism of pulmonary insult can be to be two-fold. Commonly, Gemcitabine simply causes hypersensitivity reaction, which is self-limited and improves with the discontinuation of the drug. However, it seems that Gemcitabine is capable of inducing direct endothelial damage to the pulmonary vasculature that can be severe enough to result life-threatening non-cardiogenic pulmonary edema. Therefore, early initiation of the corticosteroids and a diuretic agent can be life saving after the infectious etiology of the process is excluded.

Etiology of progressive hypoxemia and bilateral infiltrates on chest X-ray in a patient receiving Gemcitabine is complex and timely recognition of the problem quite often presents a challenge and remains a diagnosis of exclusion. Even though some patients respond well to withholding of the drug and watchful waiting, the rapidity of the development of respiratory failure underscores the need for highly efficient work-up.

Elevation of ESR is known to be associated with drug toxicity syndromes. To our knowledge, this is the first report that describes ESR elevation in association with Gemcitabine-induced pulmonary edema. In addition, we were able to observe that improvement in the clinical picture correlates with changes in ESR. Therefore, we suggest that in the appropriate clinical setting, elevated ESR, and worsening hypoxemia with bilateral infiltrates on chest X-ray, Gemcitabine-induced pulmonary toxicity should be considered in the differential diagnosis. Serial measurement of the ESR may be attempted to monitor clinical response to treatment.

References


