Mechanical Ventilation Due to Severe Bronchospasm After Cisplatin-Etoposid Infusion

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Abstract

Cisplatin and vepeside are reported as chemotherapeutic agents causing hypersensitivity reactions. However, severe bronchospasm leading to intubation and mechanical ventilation is uncommon. We report a 69-year-old woman who experienced severe bronchospasm after cisplatin-etoposide therapy. Bronchospasm did not resolve despite intensive medication and was relieved only after application of invasive mechanical ventilation

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Introduction

Hypersensitivity reactions are potential side effects of chemotherapy, sometimes causing life-threatening complications. Cisplatin and etoposide are reported as chemotherapeutic agents causing hypersensitivity reactions. However, severe bronchospasm leading to intubation and mechanical ventilation is uncommon (1-10). Invasive mechanical ventilation can be life saving by allowing time for the drugs to be effective. We report a case of severe bronchospasm occurring after cisplatin and etoposide infusion which required invasive mechanical ventilation.

Case Report

A 69-year-old woman who was diagnosed as small cell carcinoma was seen by the Oncology Department. The patient was diagnosed as lung adenocarcinoma two years ago and had received cisplatine-vinorelbine therapy. No complications were noted except vomiting. There was no history of aspiration during vomiting. The patient was accepted to be in complete remission following this therapy. She was a non-smoker and had been on medication for hypertension for the past five years. She had a history of urticaria following antibiotics and no other history of an atopic disorder.

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The patient was started on cisplatin-etoposide combination therapy on an ambulatory basis. She was premedicated with dexamethasone. On the first two days of the therapy no complication occurred. On the third day, the patient complained of shortness of breath soon after the therapy was administered. There was no history of aspiration. Physical examination revealed ronchi. No urticaria or rash was observed. Chest radiographs did not reveal any infiltrate. The patient was referred to the Pulmonology Department. Bronchodilators, steroids and antihistaminic drugs were administered. Although partial relief was achieved initially, the patient deteriorated and was transferred to the respiratory intensive care unit. APACHE II score was 25 at admission to the respiratory intensive care unit. Arterial blood gas analyses at admission to ICU revealed moderate hypoxemia and hypocapnia (PaO_2=52, SaO_2=85.6%, $PaCO_2$=27.9, pH=7.36, HCO_3=20). At the 20th hour of admission to the Pulmonology Department the patient was intubated due to development of hypotension which was refractory to dopamine and which worsened the existing tachypnea and tachycardia. Results of arterial blood gas analyses before intubation were: $Pa0_2$=52.5, SaO_2=81.6%, $PaCO_2$=44, pH=7.24, HCO_3=17.4. Pressure controlled mode was applied. During the initial 24 hours a total of 240 mg methyl-prednisolone was prescribed. After the first 12 hours of mechanical ventilation sedative therapy was stopped. Weaning was started after 24 hours and the patient was extubated successfully at the end of 48 hours. After extubation noninvasive positive pressure ventilation through face mask was applied for a short period. The second day 100 mg methyl-prednisolone was ordered and afterwards the steroid dosage was tapered each day. The tracheal aspirate cultures did not reveal any organisms or eosinophils. The chest radiographs in the respiratory intensive care unit did not reveal any pathology. All the respiratory complaints resolved and the patient was discharged on the 7th day.

Discussion

Bronchospasm due to cisplatin or etoposide has been reported on several occasions (1-3,9,10). Hudson et al reported that 23 out of 45 patients with Hodgkin's disease developed a hypersensitivity reaction to etoposide (1). Among these 23 patients only 5 had bronchospasm which was reversed with medication. Severe bronchospasm requiring mechanical ventilation is rare.

Hypersensitivity reactions to etoposide were initially thought to be uncommon, but recent reports have revealed that it may have been underreported (2). The underlying mechanisms for hypersensitivity reactions have not been identified yet. Some studies explain this entity with type I and some explain it with type II reaction and some others believe that nonspecific histamine release could be the underlying mechanisms (3). However, bronchospasm is believed to occur as a result of type I hypersensitivity reaction. Eschalier et al have reported that in anesthetized dogs, histamine levels have increased after etoposide infusion (4). Hypotension occurred after etoposide whereas no such effect occurred after cisplatine. Also in Eschalier's study, cardioaccelerator activity of vepeside has been noted which was compatible with our patient's physical findings at admission to RICU (respiratory intensive care unit). Kellie et al have observed that most of the reactions occurred after the infusion was complete (2).

In our patient, it has not been possible to identify the etiologic agent since both drugs can cause hypersensitivity reactions. If we assume that the reaction was due to vepeside, then probably type 1 hypersensitivity reaction or nonspecific histamine release should be taken into account because our patient did not have a history of etoposide medication.

The frequency of life-threatening hypersensitivity reactions due to cisplatin was reported as 5% (5). In patients with a history of prior cisplatine therapy, an immunologically mediated anaphylactic reaction was reported as the cause of this complication (4). Although it has not been shown that cumulative doses cause anaphylaxis, most reactions occur after several cycles (6,7). Likewise our patient had received cisplatin two years ago. A case of anaphylactic shock after cisplatin infusion has been reported by Carlucci et al (5). Also the anaphylactoid reaction occurring in workers exposed to platinum revealed that Ig E mediated hypersensitivity could be the mechanism (8).

Our patient developed a very serious hypersensitivity reaction which required invasive mechanical ventilation, but as mentioned above, it is hard to decide which drug caused this complication. The atopic status of our patient and the combined use of cisplatin and etoposide may have been the cause of this severe reaction. No matter which drug is responsible for this complication, we draw attention to the fact that hypersensitivity reactions to these drugs, although not very common, can be life threatening.

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