Case Report

Sivelestat Improved Oxygenation in a Patient Who Suddenly Developed Hypoxia During Surgical Resection of Perforated Colon

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Abstract

Sivelestat is a potent inhibitor of neutrophil elastase activity. We report a patient who suddenly developed hypoxia during surgery, which improved by the administration of sivelestat. A 72-year-old woman underwent emergency resection of a perforated colon that was capsulated by mesenterium. During the surgical manipulation, the capsule ruptured, causing spillage of dirty discharge into the abdominal space. A few minutes after it ruptured, her oxygen saturation (SpO2) suddenly dropped from 100% to 94%. Ten minutes after it ruptured, administration of sivelestat, 12 mg/hr, was started. Her SpO2 gradually increased and her Arterial Blood Gas (ABG) values improved. After the surgery, she was admitted to the Intensive Care Unit (ICU). There were no remarkable pulmonary complications after extubation. Sivelestat administration was continued for four days. The time course of oxygen desaturation and her blood parameters suggested that systemic circulation of an endotoxin induced the secretion of elastase from neutrophils, which in turn caused sudden desaturation. If the patient had not been treated with sivelestat, there was a high possibility that she could have developed Acute Lung Injury (ALI) due to the hypoxia. When a patient with risk factors for developing ALI develops oxygen desaturation during surgery, administration of sivelestat may improve the patient’s oxygenation and prevent the development of ALI.

INTRODUCTION

Inflammatory mediators generated due to trauma or sepsis may induce the secretion of proinflammatory mediators from inflammatory cells that are abnormally sequestered in the pulmonary microvasculature and cause Acute Respiratory Distress Syndrome (ARDS) [1]. Elastase is a proinflammatory mediator secreted by neutrophils; it causes cell and tissue damage and plays a role in the development of ARDS. Sivelestat which specifically inhibits neutrophil elastase activity, was shown to prevent the development of acute lung injury (ALI) in animal models [2,3]. However, the effect of sivelestat in patients with ARDS is controversial [4,5]. We experienced a patient who suddenly developed hypoxia during abdominal surgery, which improved by administration of sivelestat.

CASE PRESENTATION

A 72-year-old woman with a height of 151 cm and weight of 65 kg, presented to the emergency room with severe lower abdominal pain. Based on the physical examination, panperitonitis due to perforation of the sigmoid colon was suspected. The patient was admitted and emergency resection of the sigmoid colon was scheduled. During the surgical manipulation, the capsule ruptured, causing spillage of dirty discharge into the abdominal space. A few minutes after it ruptured, her oxygen saturation (SpO2) suddenly dropped from 100% to 94%. Ten minutes after it ruptured, administration of sivelestat, 12 mg/hr, was started. Her SpO2 gradually increased and her Arterial Blood Gas (ABG) values improved. After the surgery, she was admitted to the Intensive Care Unit (ICU). There were no remarkable pulmonary complications after extubation. Sivelestat administration was continued for four days. The time course of oxygen desaturation and her blood parameters suggested that systemic circulation of an endotoxin induced the secretion of elastase from neutrophils, which in turn caused sudden desaturation. If the patient had not been treated with sivelestat, there was a high possibility that she could have developed Acute Lung Injury (ALI) due to the hypoxia. When a patient with risk factors for developing ALI develops oxygen desaturation during surgery, administration of sivelestat may improve the patient’s oxygenation and prevent the development of ALI.

Keywords
• Neutrophil elastase inhibitor
• Oxygenation
• Perforated colon
38 mmHg and PaO2 142 mmHg with a tidal volume of 600 ml and a respiratory rate of 10/min (Figure 2). During the surgery, the surgeons confirmed that the sigmoid colon was perforated. However, they observed that the mesenterium covered the perforated colon like a capsule. Although the surgeons carefully manipulated the capsule, the capsule ruptured. Dirty fluid and stool spilled into the abdominal space. The surgeons notified the anesthesiologist that the capsule had ruptured (Figure 2). A few minutes after the capsule ruptured, her SpO2 value suddenly dropped from 100% to 94%. Her ABG values were PaCO2 39 mmHg and PaO2 75 mmHg under 50% of oxygen (Figure 2). Her systolic blood pressure decreased from 140 mmHg to 110 mmHg. We reduced the concentration of sevoflurane from 2.5% to 1%, and this stabilized her hemodynamics at an acceptable level. We suspected that the oxygen desaturation occurred due to the release of an inflammatory mediator such as elastase from neutrophils in the ruptured capsule. Ten minutes after the capsule ruptured, we began to administer sivelestat at 12 mg·hour−1 (Figure 2). Thirty minutes later, the perforated colon was successfully resected (Figure 2). The SpO2 value gradually increased and was 95% at 10 minutes after the start of sivelestat administration. At forty-five minutes after the start of sivelestat administration, the SpO2 value was 99% and her ABG values showed a PaCO2 of 39 mmHg and PaO2 of 120 mmHg (Figure 2). The change in oxygen saturation before, during and after the surgery is shown in Figure 2.

We experienced a patient who suffered sudden oxygen desaturation during surgery, which may have been related to the spillage of dirty discharge into the abdominal space. Before and at the beginning of the surgery, her vital signs and ABG values were relatively stable. However, a few minutes after rupture of the capsule covering the perforation in the colon, her oxygen saturation suddenly decreased. Possible causes of the sudden decrease in SpO2 were pneumothorax, cardiac decompensation, atelectasis and pulmonary embolism. After the surgery, she had relatively stable vital signs and nearly normal chest.

| Table 1: Results of complete blood cell counts before and after the surgery. |
|-----------------|-------------------------------|-----------------|-----------------|-----------------|
| White blood cells (X10³/μl) | 119                          | 54              | 70              | 105              |
| Red blood cells (X10³/μl)    | 371                          | 327             | 318             | 314              |
| Hemoglobin (g/dl)            | 12.1                         | 10.6            | 10.4            | 10.3             |
| Hematocrit (%)               | 34.5                         | 30.8            | 29.9            | 29.1             |
| Platelet count (X10³/μl)     | 20.1                         | 18.4            | 18.3            | 18.3             |

DISCUSSION

We experienced a patient who suffered sudden oxygen desaturation during surgery, which may have been related to the spillage of dirty discharge into the abdominal space. Before and at the beginning of the surgery, her vital signs and ABG values were relatively stable. However, a few minutes after rupture of the capsule covering the perforation in the colon, her oxygen saturation suddenly decreased. Possible causes of the sudden decrease in SpO2 were pneumothorax, cardiac decompensation, atelectasis and pulmonary embolism. After the surgery, she had relatively stable vital signs and nearly normal chest...
did not change the ventilatory settings nor were catecholamines administered during the surgery, and sivelestat dramatically improved oxygenation. In the present case, oxygen desaturation occurred soon after the capsule ruptured. The time course of the development of deoxygenation in the present case was consistent with that in an animal model of lung injury which had been induced by endotoxin administration, in which desaturation began approximately 30 minutes after endotoxin administration [2,6,7] demonstrated that, in trauma patients who developed ARDS, the plasma elastase level had increased immediately after the trauma. The present patient had an elevated white blood cell count (>11000 ml⁻¹) before the surgery. The white blood cell count in the blood sample obtained immediately after admission to the ICU, had decreased to the normal range, although it gradually increased during the next 30 hours. In an animal model of ALI, the neutrophil count in systemic blood samples decreased in the acute phase while the number of polymorphonuclear neutrophils in bronchoalveolar lavage increased [2]. In the present case, considering the time courses of the desaturation and blood parameters, systemic circulation of an endotoxin may have induced the secretion of neutrophil elastase, causing sudden desaturation. This patient was at high risk for developing acute lung injury.

Sivelestat is a potent neutrophil elastase inhibitor. Many animal studies demonstrated that sivelestat can prevent the progression of ALI [2,3,7]. In an animal model of ALI induced by endotoxin administration, pre-emptive administration of sivelestat before administration of endotoxin successfully inhibited the development of ALI [3]. Another animal study showed that sivelestat could inhibit the progression of ALI when administered 2 hours after inhalation of endotoxin [2]. Two studies on human patients reported that sivelestat did not ameliorate ALI, although it should be noted that sivelestat was administered to patients whose lung had already been injured [4,5]. Prior to the surgery, the present patient was not septic and her vital signs were stable. We began to administer sivelestat ten minutes after the onset of hypoxia. The perforated colon, which might have been a source of the assumed chemical mediator, was resected 30 minutes after the capsule ruptured. We started sivelestat administration ten minutes after the capsule ruptured, and there was a dramatic improvement in oxygenation. In a study on patients with Systemic Inflammatory Response Syndrome (SIRS) in Japan, those patients who were treated with sivelestat had a shorter stay in the ICU [8]. The authors of this previous study proposed that sivelestat administration should be started immediately after the development of SIRS. The effectiveness of sivelestat may depend on the timing of administration. The present case suggests that in patients who develop desaturation during surgery, administration of sivelestat may improve the patient’s oxygenation and prevent the development of ALI.

REFERENCES


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