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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, the patient was admitted to the Intensive Care Unit (ICU). Her trachea was extubated 30 hours after admission to the 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. She had no remarkable past medical history, and chest roentgenogram revealed no remarkable abnormalities (Figure 1). Her body temperature was 38.0. A complete blood cell count before the surgery revealed an elevated white blood cell count (Table 1). In the operating room, her vital signs were as follows: systolic blood pressure, 155 mm Hg; heart rate, 98 b·min^{-1}; and SpO2, 95%. Her left radial artery was secured for continuous blood pressure monitoring. Her arterial blood gas (ABG) values in room air were as follows: PaCO2, 35mmHg; PaO2, 64 mm Hg; SpO2, 95%; hemoglobin (Hb), 10.9 g·dl^{-1}; and base excess (BE), 1.0 mmol·l^{-1}. Anesthesia was induced by 0.1 mg fentanyl and 80 mg propofol. Ten mg vecuronium was administered to facilitate tracheal intubation. Anesthesia was maintained by sevoflurane, 1.5%-4.0%, and a mixture of 50% oxygen with air with incremental administration of fentanyl. At the beginning of surgery, her vital signs were stable and the SpO2 was 100%. Her ABG values were PaCO2

38 mmHg and PaO2 142 mmHg with a tidal volume of 600 ml and a respiratory rate of 10min^{-1} (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

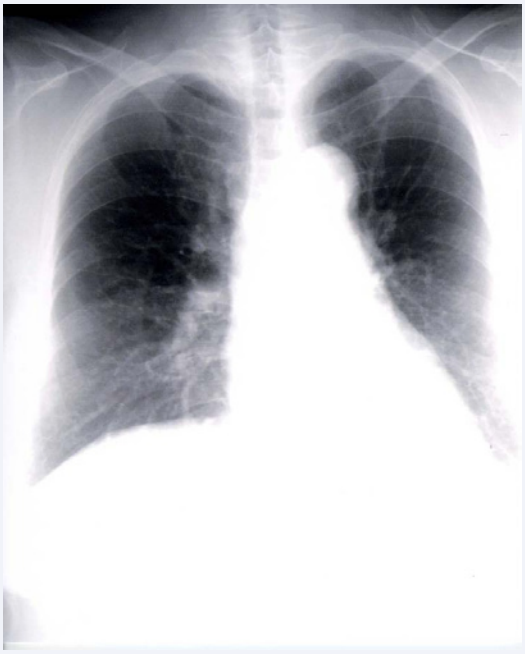

Figure 1 Chest roentgenogram obtained before surgery. No pulmonary abnormalities are seen.

Table 1: Results of complete blood cell counts before and after the surgery.

	Before surgery	Admission to ICU	6 hours after admission to ICU	30 hours after admission to ICU
White blood cells (X10^2/μl)	119	54	70	105
Red blood cells (X10^4/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 (X10^4/μl)	20.1	18.4	18.3	18.3

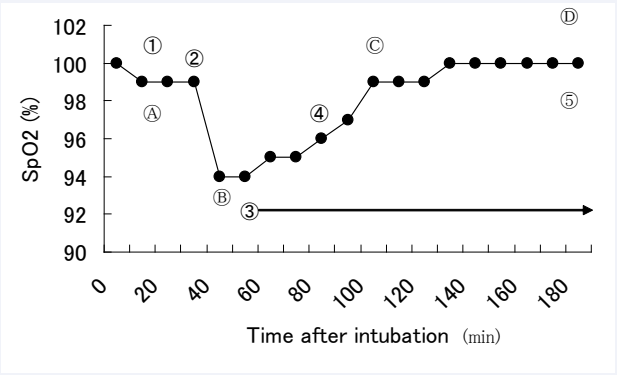

Figure 2 Change in oxygen saturation before, during and after the surgery.
①Start of surgery
②Perforation of capsule
③Start of administration of sivelestat
④Resection of colon
⑤End of the surgery
Ⓐ,Ⓑ,Ⓒ,Ⓓ: the times at which arterial blood samples were obtained. The results of ABG analysis are shown in the text.

(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 mm Hg and PaO2 of 120 mm Hg (Figure 2). The change in oxygen saturation before, during and after the surgery is shown in Figure 2. At the end of the surgery which occurred 140 minutes after rupture of the capsule, her ABG values were PaCO2 37.9 mm Hg, PaO2 205 mmHg, BE -1.4 mmol·l^{-1}, and Hb 9.9 g·dl^{-1}with a tidal volume of 600 ml and respiratory rate of 10min^{-1}, with 50% oxygen (Figure 2). The duration of anesthesia was 275 min, and the total volume of fluid infused was 3100 ml. Four packs of fresh frozen plasma were administered during the surgery. During the anesthesia, total blood loss was 500 ml and urine output was 300 ml. The patient was admitted to the Intensive Care Unit (ICU) after the surgery. Blood examination performed upon arrival at the ICU revealed that her WBC count had decreased to the normal range (Table 1). Chest roentgenograms obtained just after the patient arrived at the ICU and at 6 hours after arriving at the ICU revealed no signs of ALI (Figures 3 & 4). In the ICU, the patient's breathing gradually stabilized. Eighteen hours after admission to the ICU, her trachea was extubated. Sivelestat administration was continued for 4 days after the surgery. There were no respiratory complications after the surgery.

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

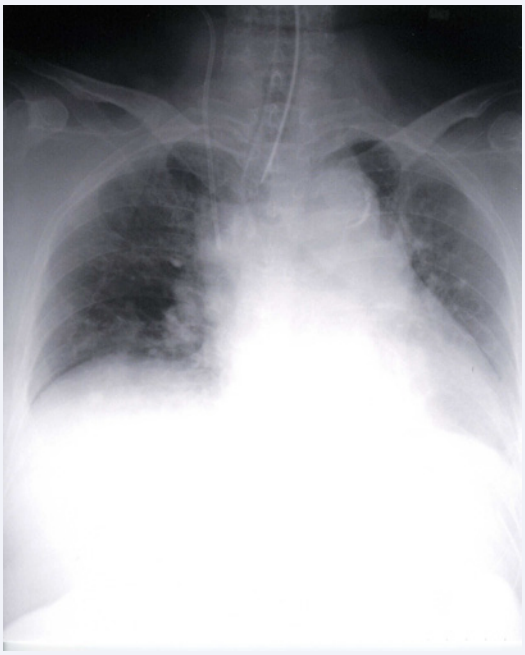

Figure 3 Chest roentgenogram obtained just arriving at the ICU. There are no signs of ALI.

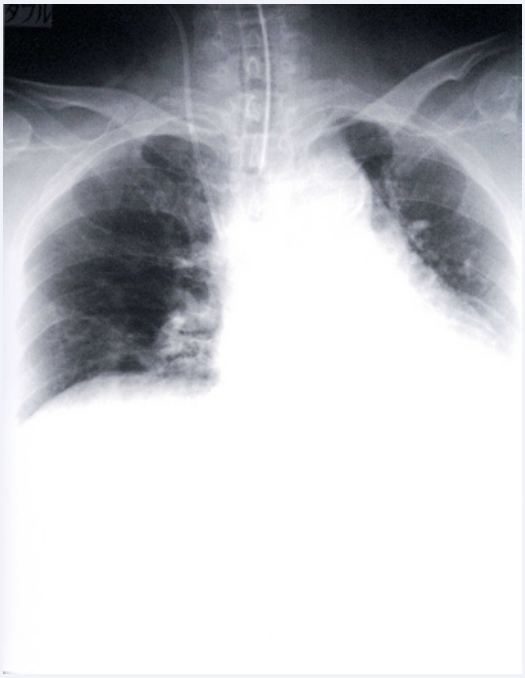

Figure 4 Chest roentgenogram obtained 6 hours after arriving at the ICU. There are no signs of ALI.

roentgenograms, ruling out the possibility of pneumothorax and cardiac decompensation. Therefore, the development of atelectasis or pulmonary embolism may have caused oxygen desaturation. Because the time course of the desaturation seemed to be related to the occurrence of rupture of the capsule, we suspected that desaturation occurred due to the appearance of an inflammatory mediator or neutrophils in the circulation. We 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 (>11000μl^{-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

1. Ware LB, Matthay MA. The acute respiratory distress syndrome. N Engl J Med. 2000; 342: 1334-1349.

2. Kawabata K, Hagio T, Matsumoto S, Nakao S, Orita S, Aze Y, et al. Delayed neutrophil elastase inhibition prevents subsequent progression of acute lung injury induced by endotoxin inhalation in hamsters. Am J Respir Crit Care Med. 2000; 161: 2013-2018.

3. Nishina K, Mikawa K, Takao Y, Maekawa N, Shiga M, Obara H. ONO-5046, an elastase inhibitor, attenuates endotoxin-induced acute lung injury in rabbits. Anesth Analg. 1997; 84: 1097-1103.

4. Kadoi Y, Hinohara H, Kunimoto F, Saito S, Goto F, Kosaka T, et al. Pilot study of the effects of ONO-5046 in patients with acute respiratory distress syndrome. Anesth Analg. 2004; 99: 872-877, table of contents.

5. Zeiher BG, Artigas A, Vincent JL, Dmitrienko A, Jackson K, Thompson BT, et al. STRIVE Study Group. Neutrophil elastase inhibition in acute lung injury: results of the STRIVE study. Crit Care Med. 2004; 32: 1695-1702.

6. Donnelly SC, MacGregor I, Zamani A, Gordon MW, Robertson CE, Steedman DJ, et al. Plasma elastase levels and the development of the adult respiratory distress syndrome. Am J Respir Crit Care Med. 1995; 151: 1428-1433.

7. Zeiher BG, Matsuoka S, Kawabata K, Repine JE. Neutrophil elastase and acute lung injury: prospects for sivelestat and other neutrophil elastase inhibitors as therapeutics. Crit Care Med. 2002; 30: S281-287.

8. Tamakura S, Shiba T, Hirasawa M, Nakajima M. A phase III clinical study of a neutrophil elastase inhibitor; ONO-5046•Na in SIRS patients. J Clin Ther Med (JPN). 1998; 14: 289-318.

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