A case of life-threatening post-operative diffuse alveolar hemorrhage in patient with recent chemotherapy
-A case report-

Mi-Young Kwon¹, Yoon Kyung Lee², In-Cheol Choi², Eun Ho Lee², Nam-Yun Kim¹, and Young-Jae Chang¹

Department of Anesthesiology and Pain Medicine, ¹National Medical Center, ²Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea

A 53-year-old woman who had undergone total gastrectomy and received adjuvant chemotherapy two months ago underwent adhesiolysis of the small bowel. She presented with sudden desaturation and dyspnea of unknown etiology at postanesthetic care unit. Following ET intubation, the endotracheal tube suction revealed massive hemoptysis. Bilateral lung infiltrated on her chest radiograph and bronchofibroscopic examination disclosed a diffuse hemorrhage on both lung fields without bleeding focus. These findings were consistent with diffuse alveolar hemorrhage (DAH) syndrome. As per our knowledge and search, this is the first reported case of DAH that occurred during the recovery period immediately after general anesthesia. DAH is known to have a high mortality rate and an early detection followed by adequate treatment is essential. (Korean J Anesthesiol 2011; 60: 221-225)

Key Words: Dyspnea, Hemoptysis, Hemorrhage.
Case Report

A 53-year-old female patient, 161 cm and 46 kg was diagnosed with mechanical ileus and admitted for adhesiolysis. She underwent total gastrectomy for cancer of stomach 2 months ago and had received adjuvant chemotherapy three weeks ago; 2nd time with S-1 (TS-1®, Jeil Pharmaceutical Co., Ltd, Seoul, Korea) 60 mg bid, for 14 days plus cisplatin (Cispuran®, Dong-A Pharmaceutical Co., Ltd, Seoul, Korea) 60 mg/m² on day 1. There was no previous history of cardiopulmonary disease, allergies, tuberculosis exposure, or smoking.

On her visit to emergency room, vital signs of the patient were as follows: body temperature, 37.2°C; heart rate, 106 beats/minute with a regular rhythm; SpO₂, 100% (on room air); and blood pressure, 116/86 mmHg. Physical examination revealed distended and diminished bowel sounds. Laboratory findings on ER were: white blood cell (WBC) count, 3.3 × 10³/mm³; hemoglobin (Hb), 12.8 g/dl; platelet count, 184 × 10³/mm³; C-reactive proteins (CRP), 0.56 mg/dl; PT (INR), 1.05 (normal, 0.8-1.3); and activated PTT, 20.9 sec (normal, 25.0-35.0). A preoperative chest X-ray, pulmonary function test and electrocardiogram were within the normal range. She was premedicated by oral midazolam (3.75 mg).

After the patient was taken to the operating room, she was on ECG standard leads II, noninvasive monitors for blood pressure, heart rate, arterial oxygen saturation, capnogram, and bispectral index. The patient underwent 3 minutes of denitrogenation with 100% oxygen through a facemask following which 2% propofol and remifentanil with the Master target controlled infusion was given (Orchestra® Base Primea; Fresenius-MCM GmbH, Germany) after administration of lidocaine (40 mg). After confirming loss of consciousness, rocuronium (0.5 mg/kg) was administered. Endotracheal intubation was then performed without any complications. After verifying that patient continued to have clear breath sounds in both lung fields, the tube was fixed at a depth of 20 cm at the level of incisor teeth. The ETCO₂ was monitored by capnogram and maintained at 35-40 mmHg.

During the operation, 700 ml of Hartmann solution was administered. After discontinuing the anesthetics, she began to respire spontaneously. A mixture of glycopyrrolate (0.4 mg) and pyridostigmine (15 mg) were administered for muscle recovery and the endotracheal tube was carefully extubated. She was awake fully and had no complaints of any discomfort or respiratory disturbance except for the surgical site pain, and she was therefore transported to the post anesthetic care unit. Oxygen at 5 L/min was administered through a Venturi mask when the pulse oximetry indicated a SpO₂ of 97%.

Fifteen minutes after extubation, the pulse oximeter indicated SpO₂ of 70%. A sudden onset of dyspnea and hemoptysis developed. The patient was promptly intubated and approximately 50 ml of fresh blood was suctioned through the endotracheal tube. A bronchoscopy was immediately performed to determine the cause of hemoptysis and hypoxia. The apparent bleeding was localized to originate from right upper lobe in the beginning, but the bleeding continued to become bilaterally with no identifiable bleeding focus (Fig. 1). The chest radiograph revealed bilateral diffuse alveolar infiltrates (Fig. 2). Arterial blood gas analysis after endotracheal intubation and mechanical ventilator applied were: arterial oxygen tension (PaO₂), 55 mmHg; arterial carbon dioxide tension (PaCO₂), 47 mmHg; pH, 7.31; Hb, 10.5 g/dl.

The patient was transferred to the intensive care unit (ICU) due to her unstable vital signs. The vital signs measured upon arrival showed a blood pressure of 80/50 mmHg, heart rate of 162/min and SpO₂ of 90% and Swan-Ganz catheter was inserted. The blood test results revealed the following: Hb, 8.7 g/dl; hematocrit, 26%; platelet count, 57,000/mm³; WBC count,

![Image](image1.png)

**Fig. 1.** Fiberoptic bronchoscope showed the generally diffuse fresh blood at bronchial trees.
900/mm³; absolute neutrophil, 640/mm³. The PT was 19.8 sec and the activated PTT was 37.1 sec. The vasopressor drugs such as dopamine, norepinephrine and vasopressin were infused to stabilize the blood pressure and hydrocortisone (300 mg) was injected. Five units of packed RBCs, 6 units of fresh frozen plasmas and 10 units of platelets were transfused for 7 hours. A bronchoscope was performed again at the ICU by pulmonologist after the vital signs were stable. The bronchoscopy revealed presence of alveolar hemorrhage in both lungs and no focal bleeding sources again. Urinary analysis with microscope and serologic laboratory were checked.

Five days after the intubation, the patient sufficiently recovered and subsequently mechanical ventilation was discontinued. On the postoperative day 6, there was no evidence of alveolar hemorrhage by bronchoalveolar lavage (BAL). Bilateral infiltration resolved and confirmed by high resolution computed tomography (HRCT) scan images (Fig. 3). The patient became symptom-free and was discharged from the hospital 20 days after the surgery. S-1 was excluded from the chemotherapy regimen in this patient and no recurrences of symptoms were observed after discharge.

**Discussion**

The term ‘diffuse alveolar hemorrhage’ refers to a distinct form of pulmonary hemorrhage that originates from the pulmonary microcirculation including alveolar capillaries, arterioles, and venules [1]. It is also known by names such as intrapulmonary hemorrhage, diffuse pulmonary hemorrhage, pulmonary alveolar hemorrhage, pulmonary capillary hemorrhage, alveolar bleeding, or microvascular pulmonary hemorrhage [2]. Dyspnea, cough, hemoptysis, and new alveolar infiltrates in conjunction with bloody BAL establish the diagnosis of DAH.

DAH can occur in association with various drugs and a wide variety of clinical disorders, many of which have overlapping features of glomerulonephritis, immune complex, and antiglomerular basement membrane disease [1]. Since the serological investigations and renal ultrasound were unremarkable for immune or renal disease in our case, together with the careful exclusion of these causes, several elements led to the suspicion that her lung damage was an expression of drug-induced adverse reaction.

Drug-induced lung injury may represent three mechanisms such as an immune or hypersensitivity reaction, an injury to the alveolar capillary basement membrane, or a coagulation defect [3]. In this case, there was no clinical or laboratory evidence of vasculitis and preoperative thrombocytopenia. We suspect that the drug may have a role to play in causing DAH [3] in this case.
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References

1. Collard HR, Schwarz MI. Diffuse alveolar hemorrhage. Clin Chest Med 2004; 25: 583-92, vii.
2. Fontenot AP, Schwarz MI. Diffuse alveolar hemorrhage. In: Interstitial Lung Disease. 4th ed. Edited by Schwartz MI, King TE Jr: Hamilton, B.C. Decker, Inc. 2003, pp 632-56.
3. Schwarz MI, Fontenot AP. Drug-induced diffuse alveolar hemorrhage syndromes and vasculitis. Clin Chest Med 2004; 25: 133-40.
4. Dimopoulou I, Bamias A, Lyberopoulos P, Dimopoulos MA. Pulmonary toxicity from novel antineoplastic agents. Ann Oncol 2006; 17: 372-9.
5. Takiuchi H, Ajani JA. Uracil-tegafur in gastric carcinoma: a comprehensive review. J Clin Oncol 1998; 16: 2877-85.
6. Tada Y, Takiguchi Y, Fujikawa A, Kitamura A, Kurosu K, Hiroshima K, et al. Pulmonary toxicity by a cytotoxic agent, S-1. Intern Med 2007; 46: 1243-6.
7. Ohara G, Satoh H, Hizawa N. Pulmonary toxicity by an oral antineoplastic agent, S-1. Intern Med 2008; 47: 187.
8. Trisolini R, Lazzari Agli L, Tassinari D, Rondelli D, Cancelleri A, Patelli M, et al. Acute lung injury associated with 5-fluorouracil and oxaliplatin combined chemotherapy. Eur Respir J 2001; 18: 243-5.
9. Izumikawa K, Nakano K, Kurihara S, Imamura Y, Yamamoto K, Miyazaki T, et al. Diffuse alveolar hemorrhage following itracona-
zole injection. Intern Med 2010; 49: 497-500.
10. Lesesne JB, Rothschild N, Erickson B, Korec S, Sisk R, Keller J, et al. Cancer-associated hemolytic-uremic syndrome: analysis of 85 cases from a national registry. J Clin Oncol 1989; 7: 781-9.
11. Nalos PC, Kass RM, Gang ES, Fishbein MC, Mandel WJ, Peter T. Life-threatening postoperative pulmonary complications in patients with previous amiodarone pulmonary toxicity undergoing cardiothoracic operations. J Thorac Cardiovasc Surg 1987; 93: 904-12.
12. Ingrassia TS 3rd, Ryu JH, Trastek VF, Rosenow EC 3rd. Oxygen-exacerbated bleomycin pulmonary toxicity. Mayo Clin Proc 1991; 66: 173-8.
13. Gao J, Zhao WX, Xue FS, Zhou LJ, Xu SQ, Ding N. Early administration of propofol protects against endotoxin-induced acute lung injury in rats by inhibiting the TGF-beta1-Smad2 dependent pathway. Inflamm Res 2010; 59: 491-500.
14. Travis WD, Colby TV, Lombard C, Carpenter HA. A clinicopathologic study of 34 cases of diffuse pulmonary hemorrhage with lung biopsy confirmation. Am J Surg Pathol 1990; 14: 1112-25.