Pulmonary Edema Occurring Immediately after Surgery

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There have been numerous reports of the occurrence of pulmonary edema in the intraoperative and postoperative period[1-3]. Most occurrences of perioperative pulmonary edema are due to fluid overload, cardiac failure or upper airway obstruction, but pulmonary edema associated with anaphylaxis or anaphylactoid reactions is a rare cause[4]. Furthermore, recently the occurrence of permeability pulmonary edema of unknown cause related to general anesthesia has been reported[5].

This paper presents a report of a case of fulminant permeability type pulmonary edema which developed dramatically immediately following surgery.

Case Report

A 74-year-old Japanese woman, 54 kg in weight and 135 cm in height, was scheduled for subtotal gastrectomy for a gastric cancer. Pertinent family history was negative. Physical examination and her past history revealed blindness in the left eye due to glaucoma beginning at the age of 50, catalact of the right eye and impaired mobility at the right wrist and the left knee joint due to osteoarthritis beginning at the age of 25. Severe hypoproteinemia (plasma total protein 4.9 $g \cdot dl^{-1}$ and plasma albumin 2.8 $g \cdot dl^{-1}$) and a low value of serum cholinesterase (0.45 ΔpH) were noted in preoperative laboratory data while other data examined remained all within normal range. Systolic and diastolic blood pressures, heart rate, ECG, chest x-ray and respiratory function were all within normal limits. Arterial blood gas examination revealed a pH of 7.37, Pa_{O_2} of 73 mmHg, Pa_{CO_2} of 37 mmHg, and a base exess of -3.4 $mmol \cdot l^{-1}$ while breathing room air.

Premedication included 5 mg of diazepam i.m. and 0.4 mg of atropine i.m. Anesthesia was induced by inhalation of a mixture of enflurane, nitrous oxide and oxygen via a face mask. Tracheal intubation was performed facilitating with intravenous administration of vecuronium of 4 mg without difficulty. Then anesthesia was maintained with enflurane and nitrous oxide in oxygen and pulmonary gas exchange was maintained by continuous mandatory ventilation using intravenous pancuronium. Five hundred and sixty ml of fresh frozen plasma for correction of the hypoproteinemia and 1,500 ml of crystalloid solution were given intravenously during the 3 hr operation. Cefazolin 2g i.v. was administered in the mean time. The operative course was uneventful. Estimated blood loss and urinary output were 150 ml and 200 ml, respectively. Residual neuromuscular blockade was reversed by administration of 2 mg of neostigmine and 1 mg of atropine at the end of the operation. The patient soon regained adequate spontaneous respiration and consciousness. At this

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time, hypotension (80/50 mmHg) was noticed and diffuse, coarse, moist rales were audible over both lung fields. Generalized cyanosis became evident and arterial blood gas analysis demonstrated severe hypoxemia (pH 7.33, Pa_{CO_2} 33 mmHg, Pa_{O_2} 43 mmHg at $F_{I_{O_2}} = 1.0$), although neither rash nor urticaria appeared. Hypotension continued in spite of dopamine infusion at a rate greater than 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and bolus administration of ephedrine 20 mg, methylpredonisolone 1,000 mg and urinastatin 150,000 U intravenously. During this time period, a tremendous amount of plasma-like yellowish, clear fluid began to flow out of the endotracheal tube. A chest x-ray revealed pumonary edema without cardiomegaly. There was no abnormality in the ECG and there was normal central venous pressure (7 cm H_2O). Furthermore, the edema fluid obtained by endotracheal suctioning had total protein and albumin concentrations identical with those of the plasma (suction fluid: total protein 3.22 $g \cdot dl^{-1}$, albumin 1.66 $g \cdot dl^{-1}$; plasma: total protein 3.35 $g \cdot dl^{-1}$, albumin 1.75 $g \cdot dl^{-1}$). Four hundred and forty ml of whole blood was then administered rapidly.

The patient was transferred to the intensive care unit (ICU). A Swan-Ganz catheter was inserted via the right internal jugular vein and the following hemodynamic data were obtained: blood pressure 50/39 mmHg, heart rate 119 beats$\cdot min^{-1}$, cardiac index 1.67 $l \cdot min^{-1} \cdot m^{-2}$, mean pulmonary arterial pressure 24 mmHg, central venous pressure 10 mmHg, pulmonary capillary wedge pressure 12 mmHg, systemic vascular resistance index 1629 dynes$\cdot$sec$\cdot cm^{-5} \cdot m^2$, pulmonary vascular resistance index 575 dynes$\cdot$sec$\cdot cm^{-5} \cdot m^2$ during the infusion of dopamine at 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and mechanical ventilation with PEEP 10 cmH_2O. Severe hemoconcentration (Hb 16 $g \cdot dl^{-1}$, Ht 48%), hypoxemia and respiratory and metabolic acidosis (pH 7.093, Pa_{CO_2} 56 mmHg, Pa_{O_2} 43 mmHg, base exess -14.5 $mmol \cdot l^{-1}$ at $F_{I_{O_2}} = 1.0$) were noted. Repeated bolus injections of norepinephrine 100 μg and rapid transfusion of plasma 640 ml followed by infusions of dopamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$, dobutamine 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and norepinephrine 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ were performed. Frequent tracheal suctions were required to eliminate alveolar flooding, which occurred initially at a rate of 200 $ml \cdot hr^{-1}$ and which resulted in over 1,000 ml cumulatively per day. Supplemental intravenous plasma was administered continuously during the pulmonary edema. Urinary output decreased to 18 $ml \cdot hr^{-1}$ after the hypotension episode and poorly responded to plasma transfusion and intravenous administration of furosemide over 100 mg. Continuous arteriovenous hemofiltration (CAVH) through a polymethyl-methacryrate (PMMA) hollow fiber hemofilter with effective surface area 1 m^2 (Toray HF-1.0U filtryzer) by cannulation of the femoral artery and vein was initiated to eliminate excess water. CAVH was continued for about 12 hr with a filtrate volume of 500 $ml \cdot hr^{-1}$ balanced by infusion of crystalloid solution until sufficient diuresis was certificated. Controlled mandatory ventilation was continued with 10–15 cmH_2O of PEEP. The patient retained consciousness in spite of severe hypoxia. Twelve hours after admission to the ICU, her hemodynamics and arterial oxygenation improved as alveolar fluid decreased. Catecholamine infusions were gradually tapered off and stopped on the 5th day in the ICU. Pa_{O_2} returned to a normal level on the 6th day and the patient was extubated and transferred to the surgical ward. Complement fractions C3 and C4 on the second, third and seventh days in the ICU were 42 and 25 $mg \cdot dl^{-1}$, 48 and 37 $mg \cdot dl^{-1}$, and 82 and 81 $mg \cdot dl^{-1}$ (normal values: C3, 60–110 $mg \cdot dl^{-1}$; C4, 20–40 $mg \cdot dl^{-1}$), respectively. The delayed lymphocyte stimulating test (DLST) for cefazolin was made on the second day in the ICU and resulted in a negative response. The patient was discharged from the hospital one month later without sequelae.

Discussion

Perioperative acute pulmonary edema may have various causes, including cardiac failure, fluid overload, hypoproteinemia, air-

way obstruction, acid aspiration, pulmonary embolism, allergy, higher oxides of nitrogen, catecholamine overdose and abnormal reactions to blood products, especially plasma and white blood cells. However, episodes of acute pulmonary edema in the immediate perioperative period are infrequent. In 1970, Cooperman and Price[1] reported that the incidence of acute pulmonary edema in the immediate perioperative period was 1:4500. More recently, Warner et al.[2] reported the incidence was 1:8350.

Permeability type pulmonary edema in the immediate perioperative period is very rare and results from increased permeability secondary to anatomical or functional injury of endothelium. This type of pulmonary edema is associated primarily with endotoxin shock[6-8], upper airway obstruction[3], re-expansion of a collapsed lung[9], hypoxia[10], anaphylaxis or anaphylactoid reaction[4]. Carlson et al.[7] suggested that longer lasting edema fluid production, poorer oxygenation and lower survival rate are typical of permeability pulmonary edema compared with hydrostatic pulmonary edema.

Permeability pulmonary edema may be differentiated from pressure type pulmonary edema by measuring the ratio of protein concentration in the alveolar edema fluid (EP) to that in plasma (PP)[11]. An EP/PP ratio greater than 0.7 is considered typical of permeability pulmonary edema and a ratio less than 0.5 of pressure type[7,8]. Therefore permeability pulmonary edema was suspected most possibly in our case because of her high EP/PP ratio of 0.91. On the other hand, EP obtained by endotracheal suction may be inaccurate because of a possibility of dilution or concentration of alveolar fluid as far as alveolar fluid and airway secreta are concomitantly collected[12,13]. Collection of edema fluid by bronchoalveolar lavage is recommended[12], although this maneuver was impossible in our case because of life-threatening hypoxemia and rapid production of large amount of edema fluid. In the present case, hypoproteinemia, especially hypoalbuminemia and fluid loading during anethesia, may have accelerated her pulmonary edema secondary to decreased plasma colloid osmotic pressure and increased hydrostatic pressure, although hemodynamic data were suggestive of noncardiogenic pulmonary edema.

Pulmonary edema in our case occurred soon after the reversal of muscle relaxant. Neostigmine causes both pulmonary vasoconstriction and bronchoconstriction. The former elevates pulmonary arterial pressure and the latter auguments the intrathoracic negative pressure while restoring the spontaneous breathing[14]. These effects might contribute to manifestation of the pulmonary edema.

In our case anaphylaxis or anaphylactoid reaction might have been also suspected, though rash and edema were both absent and the preoperative intradermal test and the later examined DLST for cefazolin were both negative. Transfusion-related acute lung injury (TRALI) has been reported[15]. TRALI is typically characterized by hypoxemia and pulmonary edema, often developing within two hours after transfusion of whole blood or blood products (especially plasma) that have granulocytic or lymphocytic antibodies. In most cases, there is resolution of the acute lung injury within four days. The severity and time course of the pulmonary edema in our patient seemed similar to those of TRALI, although we did not examine an immunological specificity of the fresh frozen plasma which was transfused during the surgery.

Fisher et al.[5] reported 5 cases of unexplained acute permeability or membrane pulmonary edema related to general anesthesia. No patients received blood transfusion or were subjected to fluid overloading. The pulmonary edemas were noticed 80 to 180 min after induction of anesthesia. The authors suggested as possible causes adverse reactions to thiopental, volatile agents (halothane or enflurane) and nitrous oxide and oxygen.

Treatment of permeability pulmonary edema is rather complicated. Administration of albumin or plasma during permeability pulmonary edema is controversial. Their use may worsen the interstitial edema[16], but it

is necessary to overcome the rapidly developing hypovolemia[4]. In addition to conventional therapies including respiratory care with PEEP, CAVH may be useful for insuring strict regulation of the water balance in a patient with permeability pulmonary edema. Gotloib et al.[17] reported that CAVH may be beneficial because it removes the middle-weight mediators which may play a major role in the pathophysiology of adult respiratory distress syndrome.

In summary, permeability pulmonary edema occurred in the case presented above was posturated to be involved in some immunological reactions, such as drug allergy or transfusion related lung injury. Nevertheless the treatments including frequent tracheal suction, mechanical ventilation with PEEP, supplementation of plasma colloid, inotropic support and CAVH succeeded to recover the patient without sequelae.

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