

Neurogenic Cardiopulmonary Instability with Pulmonary Edema after a Traumatic Head Injury

– A case report –

Department of Anesthesiology and Pain Medicine, Konkuk University Hospital, Konkuk University School of Medicine, Seoul, Korea

Duk-Kyung Kim, M.D., Kyoung-Min Lee, M.D., Won-Kyoung Kwon, M.D., and Seung-Min Jeong, M.D.

There are substantial clinical and experimental evidences to support the hypothesis that catecholamine surge causes cardiac failure and pulmonary edema after the acute neurological events. A previous healthy 74-year-old man was submitted to an emergency craniotomy for the evacuation of the delayed subdural hemorrhage after a motorcycle accident. After anesthetic induction, profound hypotension and progressive decrease of arterial oxygen tension developed and continued for several hours in spite of fluid loading and inotropic support with dopamine in combination with dobutamine. Electrocardiographic changes and increase of serum cardiac isoenzymes suggesting myocardial infarction were absent. On auscultation, crackles were detected in both lung bases, indicating pulmonary edema. On the basis of the assumption that left ventricular dysfunction was combined with the acute pulmonary edema, with a possible neurogenic component, aggressive management including dobutamine in combination with isosorbide dinitrate was instituted. As a result, these cardio-respiratory complications rapidly resolved without any neurologic sequelae. (**Korean J Anesthesiol 2007; 53: S 52~7**)

Key Words: intracerebral hemorrhage, neurogenic pulmonary edema, ventricular dysfunction.

In the patient with the disease of or the injury to the central nervous system (CNS), sudden onset of pulmonary edema can occur in the absence of cardiovascular and pulmonary risk factors. This is referred to as neurogenic pulmonary edema (NPE).^{1,2)} In some cases, three major categories of cardiac abnormalities are also associated with neurologic injury: cardiac arrhythmia, repolarization abnormalities, and mechanical dysfunction due to reversible and non-ischemic myocardial stunning.³⁾ The left ventricular failure related to CNS lesions, representing the most severe form among them, has been referred to as neurogenic myocardial stunning. In this situation, the deranged myocardium behaves as in a panic due to a sudden burst of catecholamine.⁴⁾

Neurogenic myocardial stunning has been described in the patients with brain tumor,³⁾ seizure,⁵⁾ subdural hemorrhage (SDH),⁶⁾ and aneurysmal subarachnoid hemorrhage (SAH).^{2,7-9)} In the prospective study⁴⁾ that included 715 cases with SAH,

the incidence of transient left ventricular dysfunction was 9.4% (67/715). To the best of our knowledge, severe myocardial dysfunction with the NPE in association with a traumatic head injury has not been reported in Korea yet. Therefore, we report a case of profound myocardial dysfunction with the pulmonary edema, successfully reversed after the prompt treatment with dobutamine and nitrate.

CASE REPORT

A 74-year-old man (169 cm, 62 kg) was visited the Emergency Department after a motorcycle accident. He complained of headache with blood pressures of 140-150/70-80 mmHg, pulse rates of 70-80 beats/min, and respirations of 16-18 breaths/min. Up to the accident, the patient had been in good health for his age with no history of cardiac or pulmonary disease. Findings of neurologic examination were normal but arterial blood gas analysis showed slightly low partial arterial oxygen pressure (Table 1; ①). Brain computer tomography (CT) showed multifocal hemorrhagic contusions in fronto-temporal regions, SDH along the falx cerebri and the right fronto-temporal convexity, and a small traumatic SAH in

Received : March 5, 2007

Corresponding to : Duk-Kyung Kim, Department of Anesthesiology and Pain Medicine, Konkuk University Hospital, 27-2, Hwayang-dong, Gwangjin-gu, Seoul 143-701, Korea. Tel: 82-2-2030-5452, Fax: 82-2-2030-5412, E-mail: dikei@kuh.ac.kr

Table 1. Arterial Blood Gas Results

Time course	ABGA (F ₁ O ₂): pH-PaCO ₂ -PaO ₂ -HCO ₃ ⁻	PaO ₂ /F ₁ O ₂ ratio	Base excess	Lactate
① Preoperative	7.47-27.1-67.6-19.7 (0.2)	338	-2.2	(-)
② 30 min after anesthesia	7.44-25.9-192.0-17.7 (0.5)	384	-4.8	2.9
③ 2 h after anesthesia	7.38-27.2-107.3-16.2 (0.5)	214.6	-7.2	3.4
④ 3 h after anesthesia	7.43-29.7-71.0-19.7 (0.5)	142	-3.3	3.2
⑤ 6 h after anesthesia : PEEP 7 cmH ₂ O	7.40-29.9-139.7-18.8 (0.5)	279.4	-4.4	4.0
⑥ Postoperative 4 h : SIMV mode (Tidal volume = 600 ml, Respiration rate = 10/min, I : E ratio = 1 : 2)	7.53-33.0-99.8-26.6 (0.4)	249.5	3.9	(-)

(-) means unchecked value. PEEP: positive end-expiratory pressure, SIMV: synchronized intermittent mandatory ventilation. The unit of PaCO₂ and PaO₂ is mmHg. The unit of HCO₃⁻ and base excess is mEq/L and the unit of lactate is mmol/L.

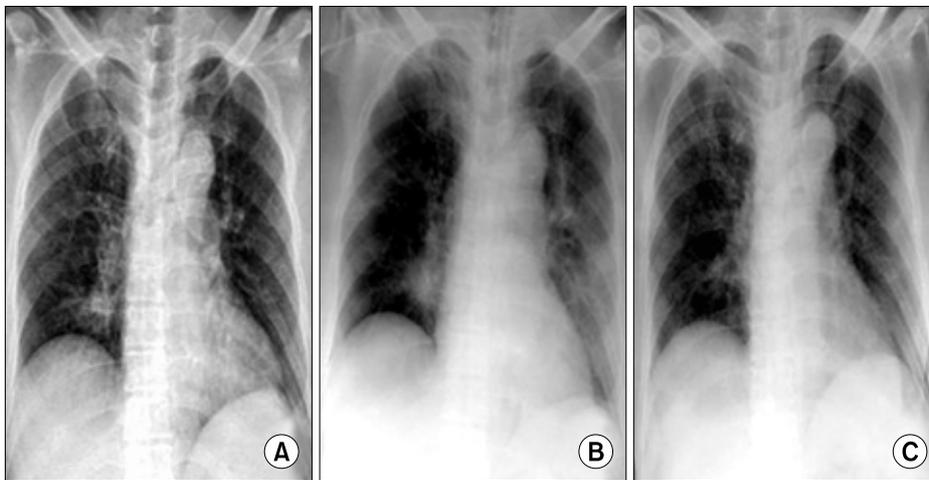


Fig. 1. Chest radiographs in case. (A) Preoperative chest radiograph showing normal. (B) Chest radiograph at the time of transfer to the intensive care unit. Bilateral pulmonary infiltrates compatible with neurogenic pulmonary edema are shown. (C) Chest radiograph on the 3rd postoperative day. Complete radiologic improvement is evident.

the left sylvian fissure. ECG revealed normal sinus rhythm with nonspecific ST-T segment changes and chest radiography were normal (Fig. 1A).

Two days after hospitalization, his mental status declined quickly to drowsiness with a Glasgow Coma Scale of 7/15 and vital sign changed. Brain CT revealed enlarged hematoma in the anterior temporal region, which was extending to inferior parietal region, with mild transtentorial herniation. So, he was scheduled to an emergency craniotomy for the evacuation of the subdural hematoma.

On the arrival of operating room, his consciousness was stuporous and his respiration was rapid and irregular (Table 2; ①). Anesthesia was induced with the intravenous administration of thiopental sodium 150 mg, remifentanyl 50µg, and vecuronium 7 mg. Intubation of the trachea with a wire-spiral 7.5-mm reinforced tracheal tube was performed. Anesthesia was maintained with 1-2% inspired sevoflurane in 50% N₂O and O₂

and continuous infusion of remifentanyl at a rate of 0.1-0.25µg/kg/min by an infusion pump (TE-331 TERUFUSIN SYRINGE PUMP™, Terumo corp., Japan). Monitoring included ECG at lead II, pulse oximetry, invasive artery blood pressure and central venous pressure, esophageal temperature, and quantification of inspired and expired gases by using mass spectrometry.

Thirty minutes after induction, his blood pressures gradually decreased to the range of 65-75/40-50 mmHg and then did not increase despite of two repeated IV administration of phenylephrine 100µg and fluid loading (Table 2; ②). So, inotropic IV therapy was initially instituted with dopamine 5-10µg/kg/min and subsequently in combination with dobutamine (7-10µg/kg/min). However, his blood pressure did not rise and repeat blood gas analysis revealed the metabolic acidosis and the decreased partial arterial pressure of oxygen, despite the condition that he was breathing 50% O₂ (Table 1; ②, ③).

Table 2. Vital Signs and Central Venous Pressure (CVP)

Time course	Blood pressures: SBP/DBP (mmHg)	Heart rate (bpm)	Temp (°C)	CVP (mmHg)
① On the arrival of operating room	105-110/70-75	110	(-)	(-)
② 30 min after anesthesia	65-75/45-50	90-95	35.8	10
③ 3 h after anesthesia : Dopamine (10µg/kg/min) + Dobutamine (7µg/kg/min)	70-80/50-55	90-95	35.7	11
④ 6 h after anesthesia : Dobutamine (7µg/kg/min) + Isoket (1µg/kg/min)	110-120/60-70	75-80	35.5	10
⑤ Postoperative 4 h	120-125/65-75	80-85	(-)	11

(-) means unchecked value. SBP: systolic blood pressure, DBP: diastolic blood pressure, bpm: beats per minute, Temp: temperature. Temperatures were measured by the disposable thermistor placed at mid-esophagus.

After the confirmation of progressive deterioration of arterial blood gas result at postoperative 3 hours (Table 1; ④, Table 2; ③), inspired oxygen concentration was increased to 100%. On auscultation, crackles were detected in both lung bases indicating pulmonary edema. But, pink frothy fluid was not aspirated by repeated endotracheal suction. Even though ischemic ECG changes were not displayed on the monitor, myocardial ischemia was clinically suspected. So, serum cardiac markers were checked, but blood level of creatine kinase, MB fraction (CK-MB) and cardiac troponin I (cTnI) were 7.7 ng/ml (normal range: 0-10.4 ng/ml) and 0.16 ng/ml (normal range: 0-2 ng/ml). On the basis of the assumption that left ventricular failure was combined with the acute pulmonary edema, with a possible neurogenic component, furosemide 10 mg was administered intravenously and isosorbide dinitrate (Isoket 0.1%[®], Schwarz Pharma AG, Germany) was infused at a rate of 1µg/kg/min. Dopamine was discontinued whereas continuous infusion of dobutamine was sustained. Immediately after these pharmacologic interventions, blood pressure eventually improved to 110-120/60-70 mmHg. 7 cmH₂O of positive end expiratory pressure was applied and inspired oxygen concentration was decreased from 100% to 50% (Table 1; ⑤, Table 2; ④). Throughout the remainder of operation, vital signs and blood gas results remained stable, allowing the discontinuation of dobutamine.

At the completion of the operation, prolonged sedation for mechanical ventilation was done with IV administration of midazolam 3 mg and vecuronium 2 mg. During the 7-hour anesthesia, estimated blood loss was approximately 1,200 ml. The patient was given 2,200 ml of acetated Ringer's solution, 1,000 ml of 6% hydroxyl ethyl starch (Voluven[®], Fresenius

Kabi Korea, Korea), and 100 ml of 25% albumin. 2 unit of Packed RBC was transfused and urine output was 690 ml. The patient was transferred to a neurosurgical intensive care unit, where both clinical and radiologic parameters were rapidly improved during the next few hours (Fig. 1B, C, Table 1; ⑥, Table 2; ⑤). 2D-echocardiography at postoperative 1 hour revealed the normal systolic function (a qualitative ejection fraction of 58%) without any wall motion abnormality. A 12-lead ECG at postoperative 1 hour showed the normal sinus rhythm with nonspecific T segment changes. Repeat CK-MB and cTnI levels at postoperative 2 hours were in the normal range (3.9 ng/ml and < 0.02 ng/ml).

With hemoglobin oxygen saturations consistently greater than 96-97%, the trachea was extubated at 6 hours after the initiation of mechanical ventilation in the intensive care unit. On the second day after the operation, the patient's respiratory function was almost normal, although he still required oxygen, 3 L/min through a nasal cannula. Neurologic status remained normal throughout the postoperative period and the patient was transferred to general ward on the fourth day after the operation. He was discharged from the hospital without any respiratory or neurologic complaints on the eleventh postoperative day.

DISCUSSION

Our patient illustrated that a reversible and presumably neurogenic form of cardiac injury might contribute to the profound hypotension and the formation of pulmonary edema related to a traumatic head injury. The reasons why we concluded that the cardio-respiratory symptoms in the patient must

be of a neurogenic origin were as follows: 1) The patient had previously no history of cardiac or pulmonary disease. Especially, he was proven to be in good health from the latest medical check-up in a month before the accident. 2) He presented with signs of acute pulmonary edema and myocardial dysfunction abruptly during the initial 2-3 hours after the intracranial rebleeding. 3) Intraoperative normal range of CVP and urine output suggested that profound hypotension did not result from hypovolemia or congestive heart failure due to a fluid overload. There were no perioperative ECG changes and echocardiographic findings suggesting a myocardial ischemia. Moreover, serial checked cardiac markers such as CK-MB and cTnI were in the normal range. 4) Hypotension developed in the patient did not respond to any therapeutic interventions of increasing the preload, cardiac contractility, and afterload. But, this severe hypotension was transient in nature and thus rapidly improved without any residual deficit on 2D-echocardiography at postoperative 1 hour.

It has been well known that ECG changes commonly occur in the patients with cerebral lesions. This phenomenon occurs in 50-90% of patients with acute intracerebral events.¹⁰⁾ However, the profound left ventricular dysfunction leading to severe hypotension, such as in this case which was shown to be refractory to the simultaneous infusion with dopamine and dobutamine, is a rare event in the patients with an intracranial hemorrhage. As we initially suspected for hypovolemic, drug-induced, or cardiogenic shock, these common conditions must be suspected and corrected. However, profound hypotension was sustained in the neurosurgical patients despite these more common conditions were ruled out, neurogenic myocardial stunning must be considered as one of possible mechanisms. Neurogenic myocardial stunning is presumed to result from an increase in the sympathetic nervous system activity with the exaggerated catecholamine release after brain injuries.^{4,11)} The weight of evidence points to a "catecholamine-mediated injury" hypothesis based on the histological lesions in the myocardium which are similar to those of a catecholamine myocarditis (contraction band necrosis and myocytosis)^{12,13)} and the presence of an elevated level of catecholamine in the serum.¹⁴⁾ It is explained that the high concentrations of catecholamine are suddenly released in a burst immediately after the onset of intracranial hemorrhage, producing circulatory disturbances in the peripheral coronary arteries, which then induced myocardial damages. This catecholamine surge also causes an increase in the systemic vascular resistance, which in turn further reduces

the stroke volume, finally leading to the profound hypotension. Additionally, this sympathetic storm induces a significant damage to the pulmonary vasculature as well as the systemic and the coronary circulations. The resulting increase in the pulmonary vascular hydrostatic pressures, combined with an increased pulmonary capillary permeability, produces NPE. In the retrospective study¹⁵⁾ that included 20 patients with NPE, cardiac index and left ventricular stroke volume index were markedly depressed in 12 of the 20 patients. In other case series of 5 patients with SAH and no history of heart disease, all patients with severe NPE had the profound hypotension requiring inotropic supports.²⁾ The echocardiography of such cases revealed that segmental wall motion abnormalities and reduced ejection fractions could occur concurrently with the signs of NPE during the acute phase and usually returned to normal within 2 to 6 weeks.

Contrast to the typical myocardial infarction, the distribution of neurogenic myocardial injuries is multifocal and unrelated to the coronary vascular distribution.^{4,8)} And neurogenic myocardial stunning is characterized by a transient nature in the majority of patients. From the findings of several studies,^{2,4,11,13)} it is likely that both irreversible myocardial necrosis and reversible and functional myocardial damage may be mixed together in the acute stage of intracranial hemorrhages. Therefore, the relative ratio of functional changes to irreversible necrosis in myocardium seems to determine both the severity and the prognosis of a neurogenic left ventricular dysfunction.

The severity of the neurologic insult is known to determine whether a patient develops myocardial damage. It was found that the more severe the neurologic symptoms, the higher both the central and the peripheral sympathetic nervous activities were.^{4,8)} This was also supported by the finding of Kolin and Norris¹⁶⁾ that the presence of trans-mural damage of heart was related to the size of the intracerebral lesions.

As showed in this case, ECG changes are relatively non-specific markers for the presence of a neurogenic myocardial stunning.^{9,17)} Common ECG abnormalities are QT segment prolongation and T-wave changes, even tachycardia only. One study¹⁸⁾ demonstrated the superiority of the changes of cTnI over the changes of CK-MB in predicting a neurogenic myocardial dysfunction. The major advantage of cTnI is its ability to detect subtle myocardial cell damage that is undetectable by conventional enzyme methods, with high sensitivity and specificity. However, our patient did not show any increase of both cardiac markers perioperatively. Accordingly, the myo-

cardial dysfunction developed in our patient may not be due to the organic change related to a myocardial necrosis but to the functional myocardial disturbance. It was consistent with the relative short duration and the excellent resolution of the myocardial dysfunction in our patient. In the study²⁾ that investigated 5 SAH patients with NPE and cardiac injuries, all patients had upper normal ranges of CK-MB. In the larger study¹⁸⁾ that investigated 39 SAH patients with cardiac injuries, 5.1% (2/39) had normal serum cTnI in spite of the definite clinical evidence of myocardial dysfunction. Macmillan et al¹⁹⁾ also suggested that intraoperative echocardiography would be required to diagnose the neurogenic myocardial stunning because cardiac isoenzyme markers might be inconclusive. However, we did not try it in this case as operative position made its monitoring difficult intraoperatively.

There are two important reasons for requiring the prompt and active treatments to the patients with cardiac and/or respiratory complications of intracranial hemorrhages. Firstly, the impending cerebral ischemia, resulted from an increased intracranial pressure and a decreased mean blood pressure, should be treated immediately. Secondly, the delayed cerebral infarction due to a vasospasm should be prevented. This is especially important during the postoperative courses of subarachnoid hemorrhage, as the delayed ischemic deficits due to a cerebral arterial vasospasm are the major cause of death and disability in the patients who survive the initial hemorrhage.¹⁷⁾ Prophylaxis and treatment of a vasospasm include expanding the intravascular volume, increasing the arterial blood pressure to supra-normal level, and accepting a relatively low hemoglobin concentration. So, persistent hypotension lasting several days can significantly increase the risk of a cerebral vasospasm.

Preload reduction with the use of nitrate or/and diuretics, the inotropic support with dobutamine, and the ventilatory supports were generally used for the treatment of the pulmonary edema. Beltrame et al²⁰⁾ demonstrated that nitrate therapy is as effective a conventional furosemide and morphine therapy in the broader and non-infarct pulmonary edema. Surprisingly, the inotropic support with dobutamine may dramatically improve the condition despite catecholamines cause ventricular asynergy. From the findings of several studies,^{2,15,20)} dobutamine has proven to be especially effective in the patients with the reduced left ventricular work of a neurologic origin. This was also supported by our observation that both hemodynamic and gas exchange parameters significantly improved immediately

after the infusion of dobutamine in combination with isosorbide dinitrate.

In conclusion, the sympathetic surge after intracranial hemorrhages causes significant injuries to the pulmonary, coronary, and systemic circulations, thereby leading to cardio-respiratory manifestations of varying severity, with the neurogenic left ventricular failure related to NPE representing the most severe form. Though we definitely confirmed its presence by intraoperative echocardiography, transient nature (no any residual deficit on 2D-echocardiography at postoperative 1 hour) of the profound hypotension combined with NPE was strongly suggestive for neurogenic myocardial stunning. Therefore, high degree of suspicion for neurogenic myocardial stunning should be devoted to the clinical course when caring for patients with acute cardio-respiratory failure following neurologic events. In such case, the immediate and correct diagnosis of possible neurogenic myocardial stunning followed by the active and aggressive treatment including dobutamine and nitrate may be pivotal to prevent the sequelae of a cerebral ischemia due to the decreased cerebral perfusion pressure.

REFERENCES

1. Bolli R, Marban E: Molecular and cellular mechanisms of myocardial stunning. *Physiol Rev* 1999; 79: 609-34.
2. Mayer SA, Fink ME, Homma S, Sherman D, LiMandri G, Lennihan L, et al: Cardiac injury associated with neurogenic pulmonary edema following subarachnoid hemorrhage. *Neurology* 1994; 44: 815-20.
3. Jarquin-Valdivia AA, Rich AT, Yarbrough JL, Thomson RC: Intraventricular colloid cyst, hydrocephalus and neurogenic stunned myocardium. *Clin Neurol Neurosurg* 2005; 107: 361-5.
4. Sato K, Masuda T, Izumi T: Subarachnoid hemorrhage and myocardial damage clinical and experimental studies. *Jpn Heart J* 1999; 40: 683-701.
5. Chin PS, Branch KR, Becker KJ: Postictal neurogenic stunned myocardium. *Neurology* 2005; 64: 1977-8.
6. Ohtsuka T, Hamada M, Kodama K, Sasaki O, Suzuki M, Hara Y, et al: Images in cardiovascular medicine. Neurogenic stunned myocardium. *Circulation* 2000; 101: 2122-4.
7. Jain R, Deveikis J, Thomson BG: Management of patients with stunned myocardium associated with subarachnoid hemorrhage. *AJNR Am J Neuroradiol* 2004; 25: 126-9.
8. de Chazal I, Parham WM 3rd, Liopyris P, Wijdicks EF: Delayed cardiogenic shock and acute lung injury after aneurysmal subarachnoid hemorrhage. *Anesth Analg* 2005; 100: 1147-9.
9. Raymer K, Choi P: Concurrent subarachnoid haemorrhage and myocardial injury. *Can J Anaesth* 1997; 44: 515-9.
10. Yamour BJ, Sridharan MR, Rice JF, Flowers NC: Electrocar-

- diographic changes in cerebrovascular hemorrhage. *Am Heart J* 1980; 99: 294-300.
11. Connor RC: Myocardial damage secondary to brain lesions. *Am Heart J* 1969; 78: 145-8.
 12. White M, Wiechmann RJ, Roden RL, Hagan MB, Wollmering MM, Port JD, et al: Cardiac beta-adrenergic neuroeffector systems in acute myocardial dysfunction related to brain injury. Evidence for catecholamine-mediated myocardial damage. *Circulation* 1995; 92: 2183-9.
 13. Elrifai AM, Bailes JE, Shih SR, Dianzumba S, Brillman J: Characterization of the cardiac effects of acute subarachnoid hemorrhage in dogs. *Stroke* 1996; 27: 737-41.
 14. Brouwers PJ, Westenberg HG, Van Gijn J: Noradrenaline concentrations and electrocardiographic abnormalities after aneurysmal subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 1995; 58: 614-7.
 15. Bahloul M, Chaari AN, Kallel H, Khabir A, Ayadi A, Charfeddine H, et al: Neurogenic pulmonary edema due to traumatic brain injury: evidence of cardiac dysfunction. *Am J Crit Care* 2006; 15: 462-70.
 16. Kolin A, Norris JW: Myocardial damage from acute cerebral lesions. *Stroke* 1984; 15: 990-3.
 17. Parr MJ, Finfer SR, Morgan MK: Reversible cardiogenic shock complicating subarachnoid haemorrhage. *BMJ* 1996; 313: 681-3.
 18. Parekh N, Venkatesh B, Cross D, Leditschke A, Atherton J, Miles W, et al: Cardiac troponin I predicts myocardial dysfunction in aneurysmal subarachnoid hemorrhage. *J Am Coll Cardiol* 2000; 36: 1328-35.
 19. Macmillan CS, Grant IS, Andrews PJ: Pulmonary and cardiac sequelae of subarachnoid haemorrhage: time for active management? *Intensive Care Med* 2002; 28: 1012-23.
 20. Beltrame JF, Zeitz CJ, Unger SA, Brennan RJ, Hunt A, Moran JL, et al: Nitrate therapy is an alternative to furosemide/morphine therapy in the management of acute cardiogenic pulmonary edema. *J Card Fail* 1998; 4: 271-9.
-