

Case Report

Neurogenic pulmonary edema caused by spontaneous cerebellar hemorrhage: A fatal case report

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Abstract

Background: Neurogenic pulmonary edema (NPE) is a clinical syndrome characterized by an acute increase of pulmonary interstitial and alveolar fluid. It could result from a significant central nervous system (CNS) insult such as intracranial hemorrhage. However, NPE as a major presenting manifestation of cerebellar hemorrhage was seldom reported.

Case Description: We introduce a rare case of a 34-year-old woman suffering from a fulminant NPE in parallel with a spontaneous cerebellar hemorrhage. Although appropriate supportive measures were taken in the neuroscience care unit, the patient failed to survive hypoxemia within 28 h after hospital admission.

Conclusion: Pathological lesions of the cerebellum may initiate a cascade of reactions including massive sympathetic discharge and catecholamine storm, leading to a dysfunction of both cardiovascular and respiratory systems. By far, no effective therapeutic strategies have been utilized to treat such a situation. Our present report would shed light on the underlying mechanism of NPE.

Key Words: Respiratory dysfunction, neurogenic pulmonary edema, spontaneous cerebellar hemorrhage

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Quick Response Code:**INTRODUCTION**

Neurogenic pulmonary edema (NPE) is a clinical syndrome characterized by acute increase in pulmonary interstitial and alveolar fluid following a significant central nervous system (CNS) insult.^[4] Although NPE was identified over 100 years ago, the pathophysiology is not completely understood. It was putatively associated with an intense activation of the sympathetic nervous system and the release of catecholamines after an abrupt increase in intracranial pressure (ICP).^[5,17] Although intracranial hemorrhage was reported in patients diagnosed with NPE, NPE as a major presenting manifestation of cerebellar

hemorrhage was seldom reported.^[8,24] Herein, we present a case in which a fulminant NPE with fatal consequences that resulted from a spontaneous cerebellar hemorrhage.

CASE REPORT

A previously healthy 34-year-old woman suddenly lost consciousness and collapsed at her home [Figure 1]. On admission to emergency department (ED), she was comatose, with Glasgow Coma Scale (GCS) of 7 (e3v2m2), a little shortness of breath upon exertion, and flaccid in all extremities. Her family denied vomiting prior to the admission, or history of ingestion of other medications,

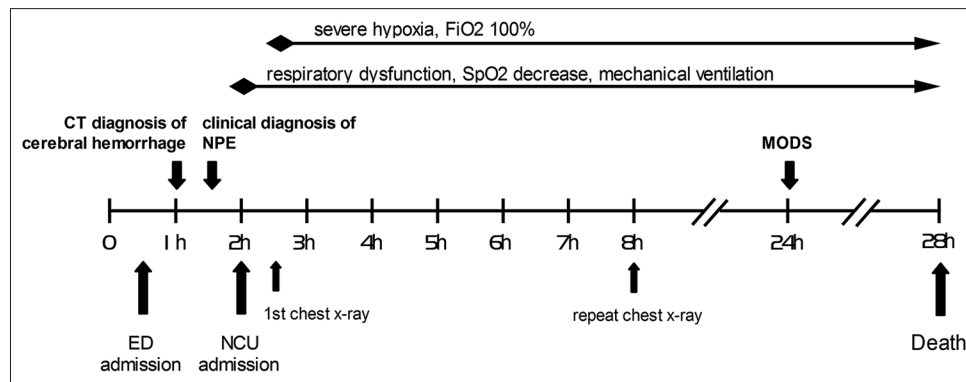


Figure 1: Clinical course and main events of case. ED: Emergency department, NCU: Neuroscience care unit, NPE: Neurogenic pulmonary edema

trauma, neurological disease, and coagulopathy. However, her life signs became unstable, as evidenced by a high fever (39.5°C), a heart rate of 120 beats per minute, a blood pressure of 195/85 mmHg, and a respiratory rate of 22 breaths per minute. Her pulse oximetric saturation (SpO₂) was 98% on 3 L/min oxygen. Laboratory tests did not demonstrate any significant abnormality. The non-contrast brain computed tomography (CT) scan on admission revealed cerebellar vermis and right-sided acute large hematoma in the ventricular system. Also, blood in the ventricular system that resulted in a mild hydrocephalus was observed [Figure 2]. Diagnosis of spontaneous cerebral hemorrhage was made.

An hour later, respiratory dysfunction was observed with shortness of breath, and coughing with pink-tinged, frothy sputum appeared while bilateral crackles were noted. SpO₂ decreased to 70% despite administering continuous supplementary oxygen of 10 L/min. The diagnosis of NPE was made, with a severe CNS injury. The indwelling gastric tube was used for gastrointestinal decompression to avoid the risk of gastric aspiration. Prompt endotracheal intubation was performed and mechanical ventilation was given. In the course of patient's transportation from ED to the Neuroscience Care Unit (NCU), hypotension, tachycardia, and bradycardia occurred. Ringer's lactate, colloids, atropine, and norepinephrine were used to stabilize patient's life signs. When she was in NCU, her GCS deteriorated to e1vTm2. She also developed progressive and severe hypoxia, despite mechanical ventilation with an inspired oxygen concentration (FiO₂) of 100% and a positive end-expiratory pressure (PEEP) of 10 cm H₂O during pressure control ventilation. Arterial blood gas (ABG) analysis showed pH 7.27, PaCO₂ 46.5 mmHg, PaO₂ 66.7 mmHg, HCO₃⁻ 20.8 mmol/L, and O₂ saturation 92%. Chest X-ray was immediately performed, and diffuse bilateral pulmonary infiltrates were observed [Figure 3]. Electrocardiogram showed a sinus bradycardia of 52 beats per minute, but no ischemia. The neurosurgical team was consulted for the cerebellar haemorrhage and agreed that

the best course of management was conservative for her unstable blood pressure and poor hypoxia. Thereafter, she received dobutamine to treat a possible cardiogenic component of the pulmonary edema. Although supportive measures were given including hyperventilation, repeated administration of mannitol and furosemide, and propofol sedation, the patient's condition exacerbated. A repeat chest X-ray exhibited bilateral ground-glass opacities and diffuse interstitial infiltrates [Figure 4]. ABG analysis showed pH 7.40, PaCO₂ 40 mmHg, PaO₂ 70 mmHg, HCO₃⁻ 27 mmol/L, and O₂ saturation 92% on bilevel positive airway pressure (BiPAP) with 100% FiO₂. The patient was in deep coma (GCS 3), and concomitant multiple organ dysfunction syndrome was diagnosed 24 h after hospital admission. The patient died 28 h later, and her family declined an autopsy.

DISCUSSION

Although NPE has been described before, it remains underappreciated. Its sporadic and relatively unpredictable nature and a lack of etiologic-specific diagnostic markers and treatment modalities may, in part, be responsible for its poor recognition at the bedside. It was reported that patients with subarachnoid hemorrhage (SAH) and NPE had a higher mortality rate (10%).^[5] Thirty-one percent of the fatal cerebral hemorrhage patients who died had a clinical diagnosis of pulmonary edema before death.^[23] A review of 686 deaths from head injury or spontaneous CNS hemorrhage demonstrated an incidence of pulmonary edema in approximately 75% of patients with non-traumatic intracranial hemorrhage.^[10] After CNS injury, a prominent hemorrhage can enter into different compartments such as intracerebral, subarachnoid, subdural, or epidural and subsequently cause blood-brain barrier damage. Any intracranial hemorrhage may cause a remarkable increase of ICP owing to a non-expandable bony space, with rather limited mechanisms to decrease it.^[19] Moreover, it was reported that the amount, but not the type of fluid injected intrathecally had a significant impact on hemodynamic and respiratory parameters.^[22]

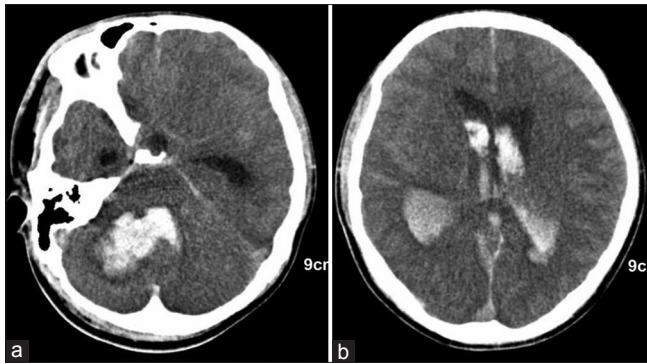


Figure 2: A non-contrast computed tomography scan demonstrates acute large hemorrhage in the cerebellar vermis and right hemispheres (a) with blood in the ventricular system resulting in a mild hydrocephalus (b)

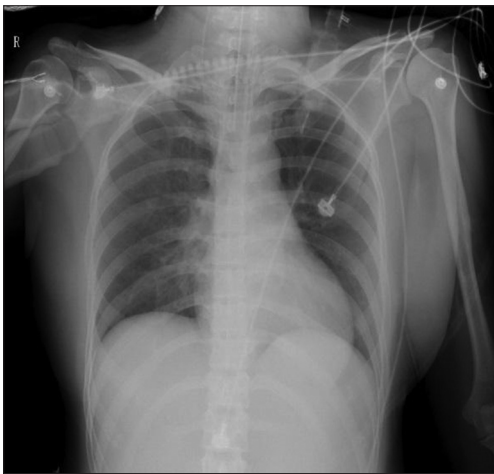


Figure 3: Chest radiograph taken 2 h after admission showed diffuse symmetric alveolar infiltrates, indicating pulmonary edema

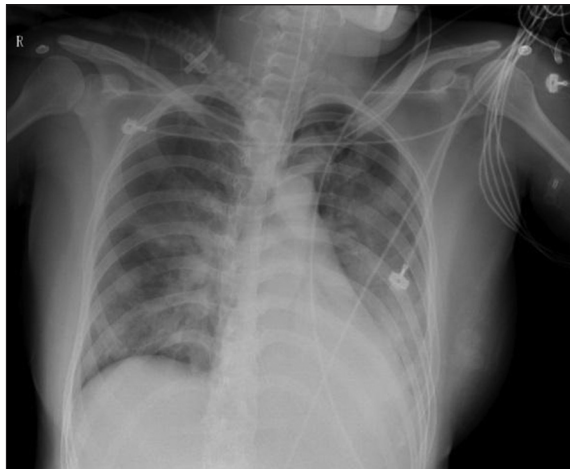


Figure 4: Repeated chest imaging confirmed bilateral ground-glass opacities and diffuse interstitial infiltrates (worse on the left side)

Various CNS disorders related to the intracranial region may result in NPE, but the case of NPE with posterior fossa hemorrhage is not as common as NPE due to cerebral hemorrhage or another cerebral pathology such

as traumatic brain injury, brain tumor, infection, and seizure.^[6,16] Cerebellar hemorrhage accounts for about 10% of all intracranial hemorrhages and about 10% of all cerebellar strokes.^[20] It was considered that lesion sites including the hypothalamus and the ventrolateral medulla were potentially responsible for NPE.^[9] Structural lesions such as sub-lobular IX-b located at the cerebellar uvula, medullary dorsal reticular nucleus located in medulla oblongata, and A1 region and medial reticular nuclei in the medulla may cause massive sympathetic discharge associated with a severe NPE.^[8,9,12,14] These structures are functionally integrated to regulate sympathetic discharge. For instance, electrical and chemical stimulation of the sub-lobule IX-b in cerebellar uvula evoked a characteristic bradycardia and a depressor response, together with a decrease in phrenic nerve activity. Therefore, any lesion or stimulus of this region could cause changes in both cardiovascular and respiratory functions.^[7]

On the other hand, in our case, the immediately mechanical brainstem compression resulted from cerebellar hemorrhage, which is one of the most common clinical complication of this disorder.^[25] Physiologic changes in NPE accompanied with an insult to the brainstem also appear to be a atecholamine surge due to an overwhelming outpouring of massive sympathetic discharge. This produces peripheral vasoconstriction followed by systemic hypertension and a shift of blood from the high-resistance systemic circulation to the relatively low-resistance pulmonary circulation. The elevation in hydrostatic pressure damages the pulmonary capillaries with subsequent pulmonary hemorrhages. Besides, the main variable under the control of the nervous system affecting the pulmonary capillary fluid flux is the pulmonary intravascular pressure. A marked increase in this pressure can force fluid from the vascular compartment, fold the interstitial space, produce pulmonary edema, and impair oxygenation. Experimental catecholamine stimulation in rat model also points toward an increase in pulmonary capillary permeability, enhances fluid filtration into the pulmonary interstitium, and finally induces pulmonary edema after several hours of infusion.^[15] Consequently, catecholamine release results in systemic arterial hypertension, peripheral vasoconstriction, increased pulmonary artery pressure, pulmonary microvascular vasoconstriction, and neurogenic stunned myocardium. There is rapid flooding of the alveoli with protein-rich fluid and is finally converted into pulmonary edema. All clinical NPE cases are characterized by an increase in extravascular lung water following a neurological insult.

Two distinct clinical forms of NPE have been described: an early form that develops within minutes to hours following neurologic injury and a delayed form that develops 12-24 h after the CNS insult.^[3] Symptoms can subside quickly, and therefore, some of the patients do

not display all the expected symptoms such as dyspnea, tachypnea, tachycardia, and respiratory insufficiency after being transported to hospital. Signs and symptoms develop rapidly following the neurological insult, usually within minutes to hours. Patients may also have frothy pink sputum or rales. Chest X-ray reveals the features of pulmonary edema such as bilateral diffuse alveolar infiltrates. Despite the mortality of the fulminant form of NPE being between 60% and 100%,^[12] few studies have identified specific treatment modalities for this condition.

It should be noted that some monitoring method could help improve the outcome. The recently introduced transpulmonary thermodilution indicator (TPID) technique has been diffused in clinical practice and allows an estimation of preload index such as intrathoracic blood volume and “lung edema” index such as extravascular lung water and other derived parameters in critically ill patients.^[18] At the bedside, TPID system can be helpful for distinguishing between hydrostatic and permeability NPE and for guiding appropriate hemodynamic goals by repeat saline injections thereafter.^[13] Lung ultrasound is another relatively new method that has gained a growing acceptance as a bedside diagnostic tool to assess pulmonary interstitial fluid and alveolar edema. Real-time sonography of the lung targeted to detection of B-lines allows accurate noninvasive bedside assessment of respiratory failure as well as quantification and monitoring of pulmonary interstitial fluid, and in guiding the intensivist with fluid management.^[21]

There have been many animal studies (including studies on rats, dogs, sheep, and monkeys) wherein human NPE was successfully simulated to assess the possible therapeutic interventions for NPE.^[4] Cobelens *et al.* reported that interferon-beta (IFN- β) could strongly reduce lung inflammation after experimental SAH and may therefore be an effective drug to prevent SAH-mediated lung injury.^[1] More recently, Chen demonstrated that using brilliant blue G, a selective P2X purinoceptor 7 antagonist, in a rat SAH related NPE model could attenuate lung inflammation and prevent lung–blood barrier disruption and, thus, it may have therapeutic potential for NPE.^[2]

In clinical practice, the goal of therapy of NPE has largely focused on treating the underlying neurologic condition and reducing ICP in order to quell the sympathetic discharge responsible for causing the lung injury. In contrast to the principles of brain resuscitation, where adequate volume is the foundation stone, management of NPE may sometimes require effective volume reduction. In addition, establishment of a therapeutic regimen that allows the combination of protective ventilation with the prevention of hypoxemia and hypercapnia is therefore required for improving oxygenation. Optimal oxygenation may be achieved by using an adequate FiO₂

and by application of appropriate PEEP to avoid the cerebral circulation getting affected by hemodynamic and CO₂-mediated mechanisms.^[11] Furthermore α -adrenergic blockade had shown promise in a patient which was accomplished with concurrent declined catecholamine levels, which may, in part, be because it competitively blocked α -adrenergic receptors and reduced hypertension by brief antagonism of the circulating catecholamines, epinephrine and norepinephrine.^[3]

CONCLUSION

We report a patient with fatal NPE caused by cerebellar hemorrhage around the vermis and right-sided region, with signs of respiratory difficulty and hypertension. This case report highlights the fact that NPE maybe a rare but lethal complication of a variety of CNS lesions, even if the diagnosis is made in time and treatment of the CNS injury is not delayed. Many cases of NPE probably remain unrecognized because of nonspecific clinical signs. Our data showed that acute respiratory failure may be derived from the conceivable CNS injury. Although catecholamine storm mechanism may be one pathogenesis of this condition, more studies and experiences will be needed to understand the roles of NPE.

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