CASE REPORT

An adolescent with severe neurogenic pulmonary oedema after spontaneous cerebellar haemorrhage

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Abstract - This report presents a patient who developed fulminant pulmonary oedema as a complication of spontaneous cerebellar haemorrhage. In spite of persisting hypoxaemia under ventilation with high levels of FiO2 and PEEP, it was decided to proceed with a surgical evacuation of the haematoma. Fortunately, after the patient was turned to the prone position, oxygenation improved rapidly. This observation suggests that prone ventilation can be a valuable tool in the treatment of neurogenic pulmonary oedema (NPE). This report also comprises an overview of pathophysiology, diagnostic measures, monitoring and treatment of NPE. Although the exact mechanism remains unclear, there is growing evidence that NPE is caused by a pressure overload mechanism, which is supported by this case.

Keywords - Neurogenic pulmonary edema, spontaneous cerebellar hemorrhage, adolescent, prone ventilation, severe central nervous system (CNS) injury, pathophysiology, diagnosis, monitoring, therapy, hydrostatic pulmonary edema, increased lung vascular permeability, pressure overload mechanism, catecholamine storm.

Introduction

Neurogenic pulmonary oedema (NPE) is a potentially life-threatening complication of severe central nervous system (CNS) injury. It has been frequently reported in cases of subarachnoid haemorrhage and traumatic brain injury, but can be observed after any form of cerebral or even cervical spinal cord injury [1]. We report a case of severe early pulmonary oedema following spontaneous intracerebellar haemorrhage in an adolescent.

Case Report

A previously healthy, 18-year-old man was at home when he suddenly became nauseous and complained of a severe headache. His parents noticed a progressive loss of consciousness. On arrival at the emergency room, he was comatose with a Glasgow Coma Scale of E1M4V1. Pupils were isocoric with normal reaction on light, the corneal reflexes were positive and there were no focal deficits. Further examination showed a blood pressure of 190/110 mmHg, a heart rate 120 of bpm, and oxygen saturation (SpO2) of 98% with 2L oxygen supplementation. He was coughing up profuse pinkish foamy sputum and bilateral crackles were noted. A severe central nervous system (CNS) injury complicated by NPE was suspected. Prompt endotracheal intubation was performed and mechanical ventilation was started. During transport to the radiology unit, the patient became haemodynamically unstable with hypotension and alternating tachycardia and bradycardia, which was treated with colloids, atropine and norepinephrine. Brain computed tomography (CT) scan (Figure 1) revealed a large cerebellar haematoma with blood in the ventricular system resulting in a hydrocephalus and signs of brainstem compression. During transport to the ICU he developed progressive hypoxaemia, despite mechanical ventilation with an inspired oxygen concentration (FiO2) of 100% and positive end-expiratory pressure (PEEP) of 15 cm H2O. Arterial blood gas (ABG) analysis showed pH 7.27, PaCO2 6.2 kPa, PaO2 8.9 kPa, HCO3 20.8 mmol/L and O2 saturation 92%. Chest X-ray (Figure 2) revealed diffuse bilateral pulmonary infiltrates. ECG showed a sinusbradycardia of 50 bpm with ST segment depression in II, III, AVF, V5 and V6 with inverted T-waves in I, aVL, V5 and V6 and frequent ventricular extrasystoles. Dobutamine was started to treat a possible cardiogenic component of the pulmonary oedema. In consultation with the neurosurgeon, it was decided to surgically evacuate the haematoma.

On arrival in the operating room, oxygen saturation was 80%. Fortunately, after the patient was turned to the prone position, his oxygen saturation rose to 100%. The procedure consisted of acute release of the cerebellar haematoma and placement of an external ventricular drain which went uneventfully. After readmission to the ICU, the patient was respiratorily stable and PEEP and FiO2 were scaled down to 5 cm H2O and 25% respectively over the following days. However, vasomotor instability with hypotension and sinusbradycardia persisted for 2 days. This was treated with vasopressors and inotropics. Echocardiography demonstrated a globally reduced left ventricular function without regional wall motion abnormalities. Heart enzymes were slightly elevated with a CK-MB of 21.5 ng/L and TroponineT of 1.52 ng/L. After two days, the patient became also haemodynamically stable and inotropic support was stopped. His neurological condition also improved. An angiography was performed but revealed no evidence of arterio-venous malformation (AVM) or aneurysm as a cause of bleeding. After four days, an attempt to detubate was made but failed because of excessive sputum production and inadequate coughing. A tracheotomy was performed and the patient was discharged to the neurological medium care unit. After two months of hospitalization, he was discharged to...
a rehabilitation centre. His gait was ataxic and he could already communicate by shaking his head for “yes” and nod for “no”.

Discussion
Pathophysiology
Exactly 100 years ago, the first case report of NPE in a human being was described by Shahanan [2]. However, the exact pathophysiological mechanism still remains unclear. Some data suggest a pressure overload mechanism with formation of hydrostatic oedema: increased intracranial pressure (elicited by the central nervous system injury) will alter the function of the neurons in the so-called NPE trigger zones [3]. These centres are located in the hypothalamic, brainstem and cervical spinal cord nuclei and are responsible for a massive sympathetic discharge, resulting in systemic and pulmonary vasoconstriction with redistribution of blood to the pulmonary circulation and an increase in pulmonary capillary hydrostatic pressure. This will lead to formation of hydrostatic pulmonary oedema. Subsequently, the catecholamine storm can result in reversible cardiac injury, myocardial depression and worsening of the hydrostatic pulmonary oedema [4].

Another theory states that NPE is caused by increased lung vascular permeability. Indeed, several case reports have pointed out that the oedema of patients, who have developed NPE, may have a protein concentration similar to that of plasma [5]. This can be explained by the activation of a systemic inflammatory response with extravasation of intravascular fluid [1]. Both a central and a peripheral origin of cytokines and chemotactic factors produced following a severe CNS injury, have been suggested. Indeed, a severe CNS injury causes a local inflammatory reaction. Cytokines produced by this reaction can gain access to the systemic circulation after disruption of the blood-brain barrier and cause the stimulation of target cells in the peripheral organs. Severe biological insults may also directly result in a peripheral inflammatory response in the lung and other organs. The catecholamine storm elicited by a severe CNS injury may be responsible for the stimulation of cytokine expression and an inflammatory process in the lungs [1]. However, the formation of protein-rich oedema can also be explained by increases in hydrostatic forces and subsequent barotrauma to the basement membrane of the alveolar capillaries and alveolar epithelium. Our case-report also provides support for a hydrostatic mechanism since the formation of NPE was within one hour after the injury whilst the cascade of an inflammatory response would take a longer time to cause such extravasation of intravascular fluid [3].

In the literature, NPE after spontaneous cerebellar haemorrhage has already been described [6,7]. This is not surprising considering the anatomical proximity of the NPE trigger zones. Moreover, animal studies have pointed out that the cerebellum also takes part in cardiovascular and respiratory control, particularly through the IX-b vermian sublobule. Goncalves et al even state that isolated IX-b sublobule dysfunction without compression of the underlying brainstem, can elicit NPE [7]. This hypothesis may explain why our patient was already coughing up pinkish foamy sputum before the brainstem reflexes were affected.

Diagnosis and monitoring
The clinical features of NPE are non-specific. A decreased Glasgow Coma Scale or other signs of CNS injury (headache, nausea and vomiting) combined with signs of acute pulmonary oedema (dyspnoea, tachypnoea, pink frothy sputum, cyanosis, basal bilateral pulmonary crackles) must raise suspicion of the presence of NPE. Other causes of acute respiratory failure include aspiration pneumonia and acute heart failure, which can resemble the clinical signs of NPE [8]. Moreover, ECG abnormalities and increased levels of CK-MB and TnT are observed in more than 50% of patients with NPE, including in our case [9]. Bilateral diffuse pulmonary infiltrates seen on chest X-ray, are also not specific for NPE. A brain CT scan is an important diagnostic tool.
to clarify the cause of NPE. Extended haemodynamic monitoring may facilitate treatment of patients with NPE, without improving mortality. The transient increase in the pulmonary artery occlusion pressure (PAOP), elicited by ‘the catecholamine storm’, is usually not found in clinical practice because of its short duration and the delay in measurement [3]. A decreased cardiac output, due to reversible cardiac injury, is seen in one third of the patients [9].

**Treatment**

The primary goal in the management of NPE is to treat the underlying CNS injury as soon as possible [1]. The neurological outcome would probably have been more favourable in this case if neurosurgery had been started immediately after imaging. Further therapeutic options are primarily supportive but are extremely important since the hypoxia that results from NPE may worsen the neurological injury. These options include mechanical ventilation with high levels of Fio2 and PEEP. However, high levels of PEEP can theoretically increase ICP by increasing intrathoracic pressure and subsequently impeding venous cerebral drainage. Furthermore, PEEP may decrease cardiac output, with a consequent decrease in cerebral perfusion pressure (CPP). Nevertheless, PEEP values lower than 15 cmH2O have been shown not to influence cerebral perfusion pressure [1]. This case report also demonstrates the beneficial effect of the use of prone ventilation on arterial oxygenation in patients with NPE. A tremendous increase in oxygen saturation was noted after the patient was turned to the prone position. This can be explained by alveolar recruitment in dorsal lung regions combined with minor derecruitment in ventral regions when PEEP is applied [10]. Reduced lung compression by the heart in the prone position has also been proposed as a mechanism for improved ventilation-perfusion matching [11]. In addition, lung perfusion in the prone position is more homogeneous. Shunt conditions are therefore reduced [12]. Mechanical ventilation in the prone position is a worldwide accepted alternative in the treatment of patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). On the other hand, the application of prone ventilation in the setting of NPE has been described only once [13]. In this case report, Fletcher et al postulate that prone ventilation should only be undertaken in conjunction with measurement of ICP because of the risk of increases in ICP during prone position. In our case, prone ventilation was also not applied until the operation for lack of measurement of ICP. Last but not least, if there are signs of myocardial impairment, efforts should be made to improve myocardial contractility and to decrease preload and afterload in an attempt to minimize the cardiogenic component of NPE. In practice, beta-stimulating catecholamines, such as dobutamine, are the drugs of choice [14]. Therapy with diuretics is justifiable if the circulating blood volume and CPP can be maintained.

**Conclusion**

This case illustrates that a dramatically evolving case of NPE can have a moderate and even favourable outcome if the diagnosis is made in time and if treatment of the CNS injury is not delayed. Thus, it is important to consider the development of this clinical entity in patients with respiratory failure and conceivable CNS injury. Application of prone ventilation can be valuable if hypoxaemia is refractory to conventional mechanical ventilation in the setting of NPE. Although the exact mechanism still remains unclear, there is growing evidence that NPE is caused by a pressure overload mechanism, which is supported by this case.

**The work was performed at the Academic Hospital Maastricht The Netherlands**

**Support was provided solely from institutional and/or departmental sources.**

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