Neurogenic Pulmonary Edema

Edema pulmonary neurogênico

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ABSTRACT

Neurogenic Pulmonary Edema (NPE) is defined as the acute onset of dyspnea or a decrease in PaO2/FiO2 ratio, following an acute central nervous system (CNS) insult, in the absence of other obvious causes of lung injury. The most important cause of NPE is subarachnoid hemorrhage (SAH), followed by cerebral trauma and epilepsy. The incidence of NPE after SAH in the literature may vary from 4 to 23% in greater studies, with SAH accounting for 43-73% of cases of NPE. It is postulated that an excessive adrenergic discharge would lead to pulmonary vasoconstriction and a rapid increase in pulmonary capillary hydrostatic pressure, thus promoting fluid leakage to the alveolar space. NPE is generally treated in a supportive and conservative fashion, and patient management should be focused in the primary insult.

Keywords: Neurogenic Pulmonary Edema, subarachnoid hemorrhage, cerebral hypertension.

INTRODUCTION

Neurogenic Pulmonary Edema (NPE) is classically defined as the acute onset of dyspnea or a decrease in PaO2/FiO2 ratio due to a pulmonary interstitial and alveolar congestion following an acute central nervous system (CNS) insult, in the absence of other obvious causes of lung injury. However, NPE can also be accompanied by neurogenic myocardial failure (tako-tsubo) and has also been reported in the chronic setting of terminal cerebral tumors.

In spite of its high frequency, NPE is an under diagnosed, life-threatening condition. Although it has been recognized for a century, this clinical entity is frequently forgotten in the differential diagnosis of acute pulmonary edema in patients with CNS injury or in the critically ill patient.

EPIDEMIOLOGY

The most important cause of NPE is subarachnoid hemorrhage (SAH), followed by cerebral trauma and epilepsy. Other less common causes may include cervical spine trauma, meningitis, multiple sclerosis, cerebellar hemorrhage, cerebral gas embolism, intracranial tumors and ventricular shunt dysfunction. In the pediatric population, the onset of neurogenic pulmonary edema can occur after encephalitis by enterovirus 71 (Hands, foot, mouth disease), especially reported in Asian countries, and child abuse.
The incidence of NPE after SAH in the literature may vary from 4 to 23% in greater studies\textsuperscript{19,20}, with SAH accounting for 43-73% of cases of NPE\textsuperscript{2,21}. The most important factors for NPE development after SAH are the clinical and radiological severity of bleeding, as well as posterior circulation bleedings\textsuperscript{1}. NPE arises more often between the first and seventh day after SAH, associated with primary or secondary cerebral insults\textsuperscript{1}.

NPE has been reported in up to 20% of cases of severe head injury (Glasgow Coma Scale < 8)\textsuperscript{4}. In an autopsy series, 50% of patients dying from head injury within 96 hours from event presented with NPE, and the incidence of NPE in patients dying at the scene was 32%\textsuperscript{10}.

Status epilepticus is claimed to be the most frequent cause of NPE in some series\textsuperscript{22-26}. NPE generally occurs in the post-ictal period, and may occur repeatedly in a given individual\textsuperscript{2,24,25}. Up to one-third of patients with fatal status epilepticus may have evidence of NPE\textsuperscript{2}.

**PATHOGENESIS**

It is postulated that NPE may be a consequence of two sequential mechanisms: an excessive adrenergic discharge would lead to pulmonary vasoconstriction and a rapid increase in pulmonary capillary hydrostatic pressure, thus promoting fluid leakage to the alveolar space. A hydrostatic edema is seen when transmural pressure exceeds 40mmHg\textsuperscript{23}. Such raise in hydrostatic pressure may damage or induce an inflammatory response to the endothelium and basement membrane, leading to protein leakage and promoting the alveolar exudate typically seen in NPE\textsuperscript{1-3}.

The CNS anatomic sites implicated in the autonomic regulation of pulmonary capillary tonus, thus responsible for NPE when lesioned are the posterior hypothalamus, ventral medulla, including the A1 catecholaminergic neurons, posterior medulla and cervical spinal chord\textsuperscript{1-3}.

It is most likely that any condition leading to an insult to the anatomical areas responsible for pulmonary capillary tonus control may lead to the development of various degrees of NPE. The acute onset of cerebral hypertension and chemical irritation may be important underlying factors, both present in SAH.

Also, the rapidity of increase in intracranial pressure, and not intracranial hypertension alone, seems to be responsible for NPE\textsuperscript{27}. Experimental studies suggest that the level of anesthesia can be a predisposing factor in patients undergoing intracranial surgery\textsuperscript{27-29}, with lower levels being implicated in the development of NPE.

**CLINICAL PRESENTATION AND DIAGNOSIS**

NPE shows a broad clinical spectrum, ranging from the asymptomatic patient to the rapid development of respiratory failure. NPE characteristically presents within minutes to hours from a severe CNS insult, with the acute onset of dyspnea or a decrease in the PaO2/FiO2 ratio\textsuperscript{2}. Mild hemoptysis is estimated to be present in one third of patients\textsuperscript{23}. The physical examination reveals tachycardia, tachypnea and basilar rales.

Chest radiograph typically shows bilateral alveolar infiltrates, but unilateral NPE is possible\textsuperscript{30}. In the pure form of NPE, echocardiography, transesophageal Doppler and central venous pressure values are normal. The electrocardiogram (ECG) is unchanged. However, NPE can be accompanied by neurogenic myocardial failure\textsuperscript{24} or a pre-existing cardiopulmonary disease. Pathologically high cardiac biomarkers without cardiac dysfunction may be present in up to 83% of patients with NPE\textsuperscript{6}.

Pulmonary artery occlusive pressure is characteristically high early in the onset of NPE, but it returns to normal after a short time, making it a poor diagnostic tool in clinical practice\textsuperscript{1}.

Although rarely assessed, estimation of pulmonary capillary pressure may be a better method to assess induced capillary changes in NPE\textsuperscript{31}.

Differential diagnosis with NPE includes aspiration pneumonia, a frequent condition in neurological patients, ventilator-associated pneumonia and ventilation induced lung injury\textsuperscript{1}. The blood level of pro-calcitomin may provide evidence of invasive bacterial infection. The absence of suspicion of aspiration during tracheal intubation and the appearance of tracheal secretions can be helpful clues\textsuperscript{1}. Also, the rapid development of pulmonary edema, absence of fever, and rapid resolution of symptoms are suggestive of NPE. Thus, NPE may be a retrospective diagnosis in many cases.

Definitive diagnosis of NPE is difficult because of the nonspecific nature of clinical signs and routine diagnostic tests. A clinical diagnosis of NPE is based largely upon the occurrence of pulmonary edema in the appropriate setting and in the absence of another obvious cause\textsuperscript{2}.

**TREATMENT**

NPE is generally treated in a supportive and conservative fashion\textsuperscript{2}, and patient management should be focused in the primary insult. Non-invasive ventilation should be preferred if patient level of consciousness allows. Invasive ventilation
should be used cautiously because of the risk of diminished venous return and increase in ICP. Positive-end expiratory pressure (PEEP) values lower than 15 cmH₂O have been shown not to impede the cerebral perfusion pressure. Permissive hypercapnia and prone positioning should be allowed only if ICP monitoring is available. Extracorporeal life support and hypothermia as alternative treatments are reported by some authors.

As NPE may be accompanied by cardiac dysfunction in several cases, care must be taken to reduce pre and after-load and to increase cardiac contractility. Experimental data shows that the use of alpha-adrenergic blockers can hasten the resolution of NPE, but care must be taken to avoid hypotension. Also, the use of epinephrine or norepinephrine does not seem to worsen the pure form of NPE. Some authors report the use of other agents, like Chlorpromazine, beta adrenergic antagonists and Dobutamine.

The pure form of NPE may resolve within 48-72h with adequate treatment. The patient’s prognosis generally depends on the underlying neurological injury. Overall mortality in NPE is estimated in 7-10%.

In a study involving 477 patients with SAH, patients with NPE showed poor neurologic outcome if compared with those without NPE (Glasgow outcome scale 1 to 3 in 77% vs. 25% of patients), and patients with NPE had a high mortality rate most likely due to the severity of their hemorrhage.

An increasing interest in lung harvesting for organ donation demands early recognition and aggressive management of NPE, if progression towards brain death is certain. Graft quality can be affected by even mild forms of NPE. As such, prevention strategies should be initiated early in the beginning of treatment.


References:


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