Review Research Paper

Acute Neurogenic Pulmonary Edema: The Unaddressed Mechanism of Death

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Abstract

Impaired pulmonary function is a frequent but poorly understood complication of acute head injury. A potential early contributor to the pulmonary dysfunction seen in Head injury patients is neurogenic pulmonary edema (NPE). Neurogenic Pulmonary Edema is pulmonary edema that is associated with neurological diseases in patients in whom no other cardiac or pulmonary cause for the edema is apparent. It is associated with several acute neurological catastrophes; including spontaneous intracranial haemorrhage in general and Sub-arachnoid haemorrhage secondary to aneurysmal rupture in particular, sudden unexpected death in epilepsy, and traumatic brain injuries of various types. Often, very less described in the literature, this can be an immediate cause of death in patients with head injuries. Its pathophysiology is multifactorial but largely unknown. It's not only for the clinician to be aware of this clinical entity but it's also important for the Forensic Medicine expert to know about the pathophysiology, clinical presentation and autopsy findings of NPE. This paper aims to review the current concepts on pathophysiologic mechanisms involved in the development of NPE and discuss the facts which are relevant for a Forensic expert.

Key Words: Neurogenic pulmonary edema, Head injury, Haemorrhage, Sudden death

Introduction:

Neurogenic pulmonary edema is related to conditions associated with severe brain injury, such as head trauma [1, 2], subarachnoid haemorrhage, intraparenchymal haemorrhage [3], cerebellar haemorrhage [4], status epileptics [5] and acute hydrocephalus. [6] Additionally, there are single case reports of electroconvulsive therapy [7, 8], hanging [9] and primary spinal cord haemorrhage. [10]

Meningeal haemorrhage is the most common cause of neurogenic pulmonary edema. Although NPE was identified over 100 years ago, it is still underappreciated in the clinical arena. The unawareness of this clinical condition for the person conducting the autopsy can often lead to misinterpretation of the autopsy findings.

Background:

NPE found its mention in the medical literature more than a century.

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It was in 1903 that Harvey Williams Cushing first described the connection between CNS injury and hemodynamic dysfunction. [11]

Later, in 1908 findings of pulmonary edema were reported by W. T. Shanahan in 11 cases of epileptic seizure. With the progress of science the clinicians gained more interest in pulmonary complications secondary to head injuries. In 1969, Capt. Simmons reported findings of alveolar edema and haemorrhage in the lungs of 17 soldiers dying after isolated bullet head wounds in the Vietnam War. [12]

Epidemiology:

Most of the information about NPE has originated from individual case reports and therefore it is very difficult to give an idea about the overall incidence of NPE in cases of Head Injury. From the epidemiological literature available it can be said that overall 7% of the patients with NPE die. [13, 14]

In patients with SAH, reports of NPE incidence range from 2% to 42.9%. [14. 16] It is further reported that patients with SAH who develop NPE have higher mortality rates. [14]

This can be speculated that reason for less number of epidemiological studies is probably the poor condition of the patient secondary to Head Injury and hence more attention of the clinician on the urgent treatment when pulmonary edema develops.

Further, unawareness of the entity by the Forensic Expert is expected to lead to low documentation.

Pathophysiology:

The pathophysiology linking the neurologic, cardiac, and pulmonary conditions in NPE has been subject to debate and controversy since the recognition of NPE as a clinical entity. NPE has been often described as an unusual complication of sudden increase in Intracranial Pressure (ICP). [17]

It is believed that this abrupt increase in ICP gives rise to an intense activation of sympathetic nervous system and release of catecholamines. How this autonomic nervous system activation affects the pulmonary capillary permeability remains dubious and enigmatic.

To explain this, many theories like neuro-cardiac theory and neuro-hemodynamic theories have been described till date, but the 'blast theory' remains central to discussion. This theory proposes a mechanism both for hydrostatic pressure and vascular leak.

It says that following the release of catecholamine there is a sudden increase in systemic and pulmonary pressures and there is a 'net' shift of blood volume from the systemic circulation to the pulmonary one.

This pressure difference further causes barotrauma to the endothelium which is responsible for the transudative vascular leaks and protein rich edema. [18]

Clinical Presentation:

NPE characteristically presents within minutes to hours of a severe central nervous system insult such as subarachnoid haemorrhage or traumatic brain injury.

However, more rapid onset (immediate) and delayed onset (hours to days) have been described. [2-4] Resolution usually occurs within several days. [5]

Dyspnoea is the most common symptom, although mild haemoptysis is present in many patients. The physical examination generally reveals tachypnoea, tachycardia, and basilar rales. Chest radiographs typically show a normal size heart with bilateral alveolar opacities, although unilateral opacities have also been described. [6-8]

Hemodynamic measurements are usually normal by the time NPE is diagnosed, including the blood pressure, cardiac output, and pulmonary capillary wedge pressure.

There is a broad range of severities of NPE and mild cases may never be detected. While NPE can be fulminant and contribute to death, mortality is more commonly due to the neurologic insult that precipitated the onset of NPE.

Post-mortem Findings:

The autopsy findings of NPE are often non-specific and are not described much in the available literature. It becomes indispensible to take a review of the clinical notes of the deceased before coming to a diagnosis of NPE.

The diagnosis of 'pure' NPE is a diagnosis of exclusion and, by traditional definition, requires documentation of non-cardiogenic pulmonary edema in the setting of neurological injury.

It should be kept in mind that large volume fluid resuscitation is often employed for patients of head injury and this may obviously lead to pulmonary overload. [18] It is also important to differentiate the findings of aspiration pneumonia from that of NPE.

Aspiration pneumonia is a very common instance in patients of head injury. NPE is characterised by presence of frothy, often blood tinged sputum and a more central distribution of the alveolar disease. On a contrary in case of aspiration pneumonia there is often a history of vomiting, witnessed aspiration.

In such cases gastric contents can be found in the oropharynx and the distribution of alveolar disease is more in the dependent parts of the lungs. These findings should be correlated with the pre-mortem x-rays of the patients.

A study conducted on18 comatose patients with severe acute intracranial injuries resulting from trauma or spontaneous subarachnoid haemorrhage determined the pulmonary findings by using thermal green dye technique to objectively determine extravascular lung water. Extravascular lung water was determined post mortem in five patients using the gravimetric method of Pearce.

The results suggest that pulmonary edema is a distinct clinical event occurring frequently after acute intracranial injury. [19]

One single case study describes hypoxic brain damage, cerebral edema and pyknosis of nerve cells in the medulla oblongata, along with the presence of pulmonary edema as diagnostic finding of NPE. [13]

Conclusion:

NPE is a distinct clinical entity which is seen in cases of head injury. Its occurrence is grossly understated due to the severe nature of the concomitant disease with which it is associated. It is recommended that in every case of head injury, both the clinician and the Forensic Medicine expert should be vigilant in diagnosing NPE so that it can be both diagnosed

and treated properly and also that its presence in cause of death can be more appropriately noted and documented.

References:

1. **Rogers FB, Shackford SR, Trevisani GT, Davis JW, Mackersie RC, Hoyt DB.** Neurogenic pulmonary edema in fatal and nonfatal head injuries. The J of trauma. 1995;39(5):860-6; discussion 6-8.
2. **Bratton SL, Davis RL.** Acute lung injury in isolated traumatic brain injury. Neurosurgery. 1997;40(4):707-12.
3. **Muroi C, Keller M, Pangalu A, Fortunati M, Yonekawa Y, Keller E.** Neurogenic pulmonary edema in patients with subarachnoid hemorrhage. J of neurosurgical anesthesiology. 2008;20(3):188-92.
4. **Young Y-R, Lee C-C, Sheu B-F, Chang S-S.** Neurogenic cardiopulmonary complications associated with spontaneous cerebellar hemorrhage. Neurocritical care. 2007;7(3):238-40.
5. **Wąsowska-Królikowska K, Krogulska A, Modzelewska-Hołyńska M.** Neurogenic pulmonary oedema in a 13-year-old boy in the course of symptomatic epilepsy–case report. Med Sci Monit. 2000;6(5):1003-7.
6. **Aslam AF, Aslam AK, Vasavada BC, Khan IA.** Cardiac effects of acute myelitis. International journal of cardiology. 2006;111(1):166-8.
7. **Tsutsumi N, Tohdoh Y, Kawana S, Kozuka Y, Namiki A.** A case of pulmonary edema after electroconvulsive therapy under propofol anesthesia. Masui The Japanese journal of anesthesiology. 2001;50(5):525-7.
8. **Nelson AM, McMorrow ME.** Neurogenic Pulmonary Edema: A common complication of central nervous system injury. AJN The American Journal of Nursing. 2002;102:44-8.
9. **Watanabe M, Higashimoto I, Niina K, Kawabata M, Osame M.** An autopsy case of neurogenic pulmonary edema due to suicide by hanging. Nihon Kokyuki Gakkai zasshi= the journal of the Japanese Respiratory Society. 2000;38(10):797-800.
10. **Inobe J-i, Mori T, Ueyama H, Kumamoto T, Tsuda T.** Neurogenic pulmonary edema induced by primary medullary hemorrhage: a case report. Journal of the neurological sciences. 2000;172(1):73-6.
11. **Cushing H. I.** On the Avoidance of Shock in Major Amputations by Cocainization of Large Nerve-Trunks Preliminary to their Division. With Observations on Blood-Pressure Changes in Surgical Cases. Annals of Surgery. 1902;36(3):321-45.
12. **Simmons RL, Heisterkamp CA, Collins JA, Genslar S, Martin AM.** Respiratory insufficiency in combat casualties. 3. Arterial hypoxemia after wounding. Annals of Surgery. 1969;170(1):45-52.
13. **Antoniuk SA, Oliva LV, Bruck I, Malucelli M, Yabumoto S, Castellano JL.** Sudden unexpected, unexplained death in epilepsy autopsied patients. Arquivos de neuro-psiquiatria. 2001;59(1):40-5.
14. **Fontes RB, Aguiar PH, Zanetti MV, Andrade F, Mandel M, Teixeira MJ.** Acute neurogenic pulmonary edema: case reports and literature review. Journal of neurosurgical anesthesiology. 2003;15(2):144-50.
15. **Friedman JA, Pichelmann MA, Piepgras DG, McIver JI, Toussaint LG, 3rd, McClelland RL, et al.** Pulmonary complications of aneurysmal subarachnoid hemorrhage. Neurosurgery. 2003;52(5):1025-31; discussion 31-2.
16. **Solenski NJ, Haley EC, Jr., Kassell NF, Kongable G, Germanson T, Truskowski L, et al.** Medical complications of aneurysmal subarachnoid hemorrhage: a report of the multicenter, cooperative aneurysm study. Participants of the Multicenter Cooperative Aneurysm Study. Critical care medicine. 1995;23(6):1007-17.
17. **Kosnik EJ, Paul SE, Rossel CW, Sayers MP.** Central neurogenic pulmonary edema: with a review of its pathogenesis and treatment. Child's brain. 1977;3(1):37-47.
18. **Lee K, Rincon F.** Pulmonary complications in patients with severe brain injury. Critical care research and practice. 2012;2012:207247.
19. **Mackersie RC, Christensen JM, Pitts LH, Lewis FR.** Pulmonary extravascular fluid accumulation following intracranial injury. The Journal of trauma. 1983;23(11):968-75.