Neurogenic pulmonary edema

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Neurogenic pulmonary edema is a potential complication of severe central nervous system insult. In the patient described, neurogenic pulmonary edema resulted from gunshot injuries to the head. Aggressive supportive care and intravenous administration of dopamine successfully resolved this pulmonary complication. Although such treatment is crucial in patients with possibly reversible central nervous system injury, the patient described had irreversible brain injury. The authors discuss current theories of the pathogenesis as well as diagnosis and treatment options.

(Key words: Pulmonary edema, head injury, central nervous system insult)

Neurogenic pulmonary edema is a recognized phenomenon associated with severe acute central nervous system (CNS) injury, most commonly severe head trauma. This complication has also been described in patients with intracranial hemorrhage,[1,2] tonoclonic seizures,[3] and tumor,[4] as well as in association with anesthesia induction.[5] Although the complete pathogenesis of neurogenic pulmonary edema remains unclear, it is believed to result from massive sympathetic discharge following acute CNS insult[6] or acute elevation in intracranial pressure (or both).[4] Although some studies point to increased capillary pressure as the cause for lung fluid shifts,[1] others suggest changes in pulmonary capillary permeability as a primary mechanism.[7] We describe neurogenic pulmonary edema following severe penetrating head trauma and review the medical literature.

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Report of case

A 20-year-old man who had two gunshot wounds to the head was brought to the trauma bay of the emergency department. The patient had had an uncomplicated endotracheal intubation at the scene by Fire/Rescue technicians. On arrival at the emergency department, the primary survey revealed that the patient had a patent airway with clear bilateral breath sounds, peripheral pulses with a labile heart rate ranging from 100 to 170 beats per minute. The patient was unresponsive with nonpurposeful movement of all extremities and fixed pupils dilated to 6 mm. The patient was fully exposed, and two gunshot wounds were seen in the left parieto-occipital region of the scalp with herniation of gray matter.

The secondary survey revealed no other injuries. A nasogastric tube and Foley catheter were placed. A roentgenogram of the chest revealed no fractures or active disease. The initial blood gas analysis, with the patient receiving 100% oxygen and manual ventilation, showed the following values: PaO_2, 456 mm Hg; $PaCO_2$, 16 mm Hg; pH, 7.57; and bicarbonate, 15 mmol/L.

The head roentgenogram demonstrated multiple intracranial bullet fragments. Vital signs remained stable, and the patient was transported to the computed tomography (CT) scanner. After the patient's placement on the CT scanner guerny, copious pink, frothy secretions were seen in the endotracheal tube. The secretions required frequent suctioning. Pulmonary auscultation at this time was significant for wheezing and diffuse rales. During the CT scanning of the patient's head, systolic blood pressure dropped to 70 mm Hg while the patient remained in sinus tachycardia (110 to 120 beats per minute).

Initial resuscitation was begun with a bolus infusion of 500 mL of lactated Ringer's solution. Fluid resuscitation was restricted to avoid worsening cerebral edema. In the absence of injuries to the trunk or extremities, the hypotension was thought to be strictly in response to the neurologic insult. Therefore, epinephrine was administered intravenously

in 0.2-mg increments (total, 1 mg administered over approximately 3 minutes) until the systolic blood pressure reached 90 mm Hg. A dopamine drip infusion was started at 4 μg/kg per minute. Approximately 20 minutes after the initial infusion of dopamine, the amount of pulmonary secretion decreased, with only occasional suctioning required. Findings on lung examination improved dramatically.

The CT scan of the head revealed complete obliteration of the paramesencephalic cisterns, ventricles, and sulcal pattern; bullet fragments in the right parietal and occipital lobes; and right-sided epidural hematoma.

The patient was transported to the surgical intensive care unit. A second chest x-ray series demonstrated a diffuse alveolar infiltrate without pulmonary vascular congestion or cardiomegaly. Four hours after the initiation of the dopamine drip infusion, findings on a third chest x-ray returned to almost normal. No evidence of neurologic function was ever obtained, consistent with a mortal wound with deteriorating neurologic function until brain death. The patient met the criteria for brain death the following day. Organ donor status was obtained from the family.

Discussion

This report describes an example of neurogenic pulmonary edema as a result of severe penetrating head trauma. The outpouring of frothy secretions from the patient's endotracheal tube dramatically illustrates the speed and extent to which neurogenic pulmonary edema can appear following acute CNS insult. Simmons and associates[8] provided the first detailed accounts of pulmonary edema after severe head trauma during the Vietnam war. They described a series of combat casualties in which pulmonary edema was found at autopsy of 17 of 20 patients who died within minutes of intracranial trauma. These cases included young men who had suffered mortal missile injuries to the head, many without further injuries similar to the patient we describe here.

In contrast to other forms of pulmonary edema, neurogenic pulmonary edema occurs in the absence of underlying heart or lung dysfunction or disease. Research by Mackersie and colleagues[7] suggests that a change in the pulmonary capillary permeability plays a primary role in the pathogenesis of neurogenic pulmonary edema. By measuring extravascular water in a group of patients with neurogenic pulmonary edema versus a control group, they found pulmonary edema present with *normal* pulmonary vascular pressure and *normal* plasma protein content. They concluded that an increase in pulmonary microvascular permeability appears to be a major factor in the pathogenesis of neurogenic pulmonary edema.

It is generally agreed that the underlying mechanism of neurogenic pulmonary edema is associated with the well-documented massive sympathetic discharge following severe CNS injury.[6] Some researchers[6,9] have proposed that this sympathetic discharge results from disturbed hypothalamic function and is primarily α-adrenergic in nature. Theodore and Robin[9] believe this sympathetic discharge results in systemic vasoconstriction, causing a net shift in blood from the systemic to the pulmonary circulation and transiently increasing pulmonary blood volume. They hypothesize that the effect of increased pulmonary blood volume on pulmonary venous pressure is exacerbated by the concomitant pulmonary vasoconstriction that also occurs in response to the sympathetic discharge. The resulting drastic increase in pulmonary venous pressure causes a severe, transient rise in pulmonary capillary pressure. This sudden rise in capillary pressure results in unbalanced Starling forces and an acute transudative pulmonary edema. Subsequently, this acute rise in capillary pressure causes secondary structural pulmonary vascular damage resulting in hemorrhage, altered capillary permeability, and persistent protein-rich (exudative) pulmonary edema.

Because of the many, incompletely understood factors that produce neurogenic pulmonary edema, diagnosis can be difficult and is essentially one of circumstance.[10] In the case described here, the diagnosis was based on the presentation of fulminant pulmonary edema in a young man with severe penetrating head trauma and no likely underlying heart or lung disease. In less clear circumstances, the diagnosis of neurogenic pulmonary edema cannot be predicted, and one should not, for example,

regard the appearance of noncardiogenic pulmonary edema as a result of neurologic insult until other causes have been excluded.[10]

Although treatment of neurogenic pulmonary edema was not critical in the outcome of the case presented because of the irreversible nature of the brain injury, therapy of neurogenic pulmonary edema is crucial in those patients with reversible CNS injury, as lung function ultimately contributes to systemic oxygen transport. The treatment of neurogenic pulmonary edema is largely supportive and includes positive-pressure ventilation with positive end-expiratory pressure (PEEP).[6,11] Associated increases in intracranial pressure can be treated concomitantly with hyperosmolar agents, diuretics, and hypocarbia. Because of the association of PEEP with increased intracranial pressure, the intracranial pressure should be monitored closely and, if neurologic deterioration occurs, PEEP should be reduced. Medical therapy has been reported to successfully treat neurogenic pulmonary edema in isolated cases. The α-adrenergic blocker chlorpromazine is one such agent, and its success in treatment of neurogenic pulmonary edema follows the theory that neurogenic pulmonary edema is mediated by a massive α-adrenergic discharge.[12] This treatment modality is limited, however, in that it needs to be initiated before pulmonary damage has occurred, that is, during or shortly after neurologic insult.

In 1991, Knudsen and coworkers[11] reported that neurogenic pulmonary edema secondary to subarachnoid hemorrhage in a 58-year-old woman was successfully treated with dobutamine. They hypothesized that the resolution of neurogenic pulmonary edema in their patient can be related to the positive inotropic effect of dobutamine, resulting in an increase in cardiac output and subsequent reflex withdrawal of sympathetic tone and decrease in total peripheral vascular resistance. Continuing with this hypothesis as to the beneficial effects of dobutamine, Knudsen and colleagues propose amrinone and milrinone, inhibitors of phosphodiesterase-III, as possible treatment for neurogenic pulmonary edema. These drugs are so-called inodilators in that they increase cardiac output and lower pulmonary vascular resistance.

Comment

Neurogenic pulmonary edema is a significant complicating sequela of severe CNS injury and must be recognized and treated in patients who have had potentially reversible neurologic insult. Further human studies are needed to fully elucidate the roles of elevated pulmonary capillary pressure and increased pulmonary capillary permeability in the pathogenesis of neurogenic pulmonary edema and to determine the effectiveness of different modes of drug therapy, such as phosphodiesterase inhibitors, in its treatment.

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