The Clinical Characteristics of Negative Pressure Pulmonary Edema

Ren-Guang Wu

Department of Internal Medicine, Chung-Kang Branch, Cheng Ching General Hospital

Abstract

Negative pressure pulmonary edema (NPPE) or postobstructive pulmonary edema (POPE) is a form of noncardiogenic pulmonary edema that results from the generation of high negative intrathoracic pressure needed to overcome upper airway obstruction [1]. It typically develops rapidly and can be life-threatening if not diagnosed promptly. Following an episode of acute airway obstruction or the relief of chronic upper airway obstruction, patients with NPPE develop sudden, unexpected and often severe pulmonary edema. Awareness of this uncommon condition is crucial if the physician is to make an early diagnosis and initiate successful treatment. NPPV may develop in several clinical situations follows a sudden, severe episode of upper airway obstruction, such as postanesthetic laryngospasm, postextubation laryngospasm, epiglottitis, croup, choking and strangulation. It also develops after surgical relief of chronic upper airway obstruction. (J Intern Med Taiwan 2015; 26: 63-68)

Key Words: Negative pressure pulmonary edema, Postobstructive pulmonary edema

Introduction

Negative pressure pulmonary edema (NPPE) is a form of noncardiogenic pulmonary edema that results from the generation of high negative intrathoracic pressure needed to overcome upper airway obstruction. NPPE is a clinical entity of great relevance in anesthesiology and intensive care. It typically develops rapidly and in relative healthy persons who are capable of producing large negative intrathoracic pressure (NIP), and can be life-threatening if not diagnosed promptly. NPPE is also an uncommon complication of anesthesia usually resulting from laryngospasm during extubation (approximately 0.1%). The most common risk factors are young age, male sex, and head or neck surgery. NPPE is an example of a pulmonary edema develops despite the fact that the heart and lungs are working well.

Many causes of upper airway obstruction leading to NPPE have been mentioned. Two distinct subclasses of NPPE have been described in the literature: type I is associated with forceful inspiratory effort in face of an acute airway obstruction, whereas type II occurs after relief of a critical airway obstruction[2]. Common etiologies for type I NPPE include laryngospasm, epiglottitis, croup, choking, foreign body, strangulation, hanging, endotracheal tube obstruction, laryngeal tumor, goiter, postoperative vocal cord paralysis, and near drowning. Type

Reprint requests and correspondence：Dr. Ren-Guang Wu
Address：Department of Internal Medicine, Chung-Kang Branch Cheng Ching General Hospital, No.118, Sec. 3, Chung-Kang Rd., Xitun Dist., Taichung City 407, Taiwan

II is more common after relief of a chronic partial upper airway obstruction, as may be expected after adenoidectomy or large tonsillectomy[3].

Incidence

Pulmonary edema in association with upper airway obstruction was first described in 1927, when it was witnessed in an experimental dog model. NPPE was first described in human in the 1960s as an autopsy finding in victims of suicidal hanging[4]. Since then, a variety of causes have been reported, with postanesthetic laryngospasm being the most common, about 50% in adults[5]. The incidence of laryngospasm with general anesthesia is estimated to be 9 in 1,000 patients. In patients with laryngospasm, it is believed about 10% develop subsequent pulmonary edema[6,7]. The true incidence might be underestimated because of many cases may be misdiagnosed or undiagnosed. The overall incidence of NPPE is less than 0.1% in all surgeries performed under general anesthesia while the incidence of development of pulmonary edema in acute upper airway obstruction (type I NPPE) ranges from 9.6-12% and that in chronic airway obstruction (type II NPPE) is 44%[8]. In postextubation subglottic edema, studies have reported an incidence of NPPE of up to 9.6 percent. It is estimated that 11% of all patients requiring active intervention for acute upper airway obstruction develop NPPV. Among pediatric patients, acute epiglottitis and croup leading to upper airway obstruction comprise greater than 75% of NPPE[9].

Etiology

The most common cause of NPPE in adults remains postextubation laryngospasm. Other causes of obstruction of upper airway leading to NPPE include the following[10,11]:

- Endotracheal tube obstruction (biting, displacement, secretions)
- Croup and epiglottitis especially in children
- Upper airway tumors, foreign bodies, goiter
- Hanging and strangulation
- Obstructive sleep apnea
- Chocking, near drowning
- Vocal cord palsy, difficult intubation, or inspissated tracheal secretions

Pathogenesis

NPPE is a potentially fatal condition with a multifactorial pathogenesis. There are at least two theories exploring the development of NPPE (table 1), and the hydrostatic mechanism accounts for the most instances.

The normal NIP during inspiration ranges from -2 to -8 cmH2O, yet it could increase upwards of -140 cmH2O in young healthy people. NPPE is a manifestation of upper airway obstruction, the large NIP generated by forced inspiration against an obstructed airway leads to an increase in pulmonary vascular volume and pulmonary capillary transmural pressure, creating a risk of disruption of the alveolar–capillary membrane. The hypoxia increases pulmonary vascular resistance (hypoxic pulmonary venous constriction, as opposed to systemic venous circulation in the body). The result is right ventricle dilation, interventricular septum shift to the left, and left ventricular diastolic dysfunction. All of these conditions result in increased left heart pressure load, and thereby enhance intramural hydrostatic pressure of pulmonary microvasculature. The increase in transmural pressure and fluid transudation out of the capillaries and into the lung interstitium and alveoli, leads to the formation of pulmonary edema.

Although NIP is the primary pathophysiology of NPPE, hypoxemia, hypercarbia, acidosis, and hyperadrenergic state all contribute to its development[10]. Hypoxemia increase pulmonary vascular resistance resulting in a rise in pulmonary capillary pressure. Hypercarbia redistributes blood from the systemic circulation to the pulmonary vasculature.

Table 1. Two common theories exploring the development of NPPE[12,13]

Hydrostatic mechanism	Mechanical stress mechanism
* High NIP augments venous return to the right heart -> increased pulmonary venous pressures, while NIP also decreasing perivascular interstitial hydrostatic pressure -> movement of fluid from the pulmonary capillaries into the interstitium and alveolar spaces -> transudate pulmonary edema	* Respiration against an obstructed upper airway -> increased transmural pulmonary capillary pressures -> disruption of the alveolar epithelial and pulmonary microvascular membranes -> increased pulmonary capillary permeability and protein-rich pulmonary edema

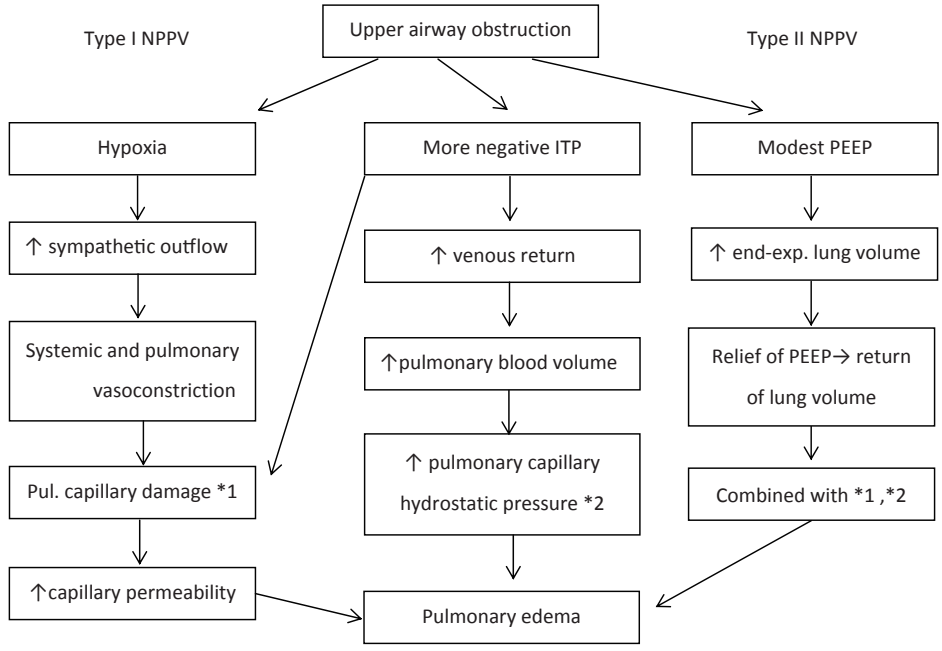

Figure 1. Postulated mechanisms of pulmonary edema secondary to upper airway obstruction (type I and type II NPPV).

Hypoxemia and acidemia have myocardial depressant effects, which all contributes to pulmonary edema formation[14]. The Sympathetic outflow increased venous return from venoconstriction, and increased afterload due to increased systemic vascular resistance[10].

Cause of NPPE II

The cause of NPPE II is less clear than that of NPPE I. It has been postulated to explain why some pulmonary edema often occurs after relief of the airway obstruction. The expiratory efforts against a closed airway create an auto-PEEP leading to increased intrathoracic pressure, and prevents venous return[15]. It may actually protect against the formation of lung edema during the obstructing period. After relief of obstruction, there is a subsequent "suction" of fluid to the pulmonary vasculature and combined with a decrease in alveoli pressure, creating a pressure gradient for transudation of fluid leading to pulmonary edema. The different evolving theories of NPPE 1 in comparison with NPPE II are listed in figure 1.

The symptoms of NPPE usually develop immediately after extubation, although sometimes the onset may be delayed up to several hours in the postoperative period. A possible explanation for this delayed manifestation is a positive pressure, created by forceful expiration against a closed glottis, opposing fluid transudation. As airway obstruction relieves, increased venous return causes blood shift from peripheral to central circulation and

hydrostatic transudation[2]. Therefore close postoperative observation must be continued for an extended time in patients experiencing respiratory difficulty.

Nevertheless, NPPE may be more common in ICU patients than is thought; For instance, ventilation with low tidal volume during the acute phase of ARDS in patients with increased respiratory drive can lead to patient–ventilator asynchrony that causes increased breathing effort and the generation of high NIPs that will further worsen pulmonary condition[12]. The strong inspiratory efforts in the presence of increased work of breathing will lead to negative alveolar pressures mimicking the cardiothoracic relationships of NPPE, and may contribute to extubation failure in some patients.

Clinical presentation

The clinical picture is similar irrespective of the cause of pulmonary edema while a history of recent upper airway obstruction usually precedes the development of NPPE. The onset of NPPE may vary from few minutes to several hours (up to 30 hours) following extubation or relief of obstruction. Patient usually presents with acute respiratory distress with signs of tachypnea, tachycardia, pink frothy respiratory secretions, progressive desaturation and crackles on chest auscultation. A review of the literature has revealed a morbidity and mortality rate of 11% to 40% in reported series. There were 189 cases of laryngospasm among the first 4000 incidents[16]. In view of clinical feature, 77% of cases laryngospasm was clinically obvious, but 14% presented as lower airway obstruction, 5% as regurgitation or vomiting, and 4% as desaturation. Most were precipitated by direct airway stimulation (airway manipulation, regurgitation, vomiting, or secretions in the pharynx, but surgical stimulus, irritant volatile agents, and failure to deliver the anaesthetic were also precipitating factors. Desaturation occurred in over 60% of cases, bradycardia in 6% (23% in patients aged <1 year).

Diagnosis

The rapid onset of pulmonary edema following upper airway obstruction should alert physicians to the possible diagnosis of NPPE. NPPE is basically a clinical entity which can be established by diagnosis of exclusion. The main differential diagnosis includes aspiration pneumonitis, cardiogenic lung edema, and anaphylaxis. The findings of normal brain natriuretic peptide (BNP) and troponin levels, preserved systolic function on cardiac ultrasonography, could be differentiated from cardiogenic lung edema. Chest radiograph typically demonstrates bilateral pulmonary opacities consistent with lung edema. Computed tomography of chest shows a preferential central and nondependent distribution of ground glass attenuation[17].

Treatment

Most cases of diagnosed NPPE respond promptly to appropriate therapy which is usually aimed at reversing hypoxia and removal of excess fluid from the lung interstitium[18]. Furosemide is often used to promote diuresis and to remove excess intrapulmonary fluid. Noninvasive ventilatory

Table 2. Different clinical examples of NPPV I, II[11,12]

NPPE I	NPPE II
(1) Upper airway compressive obstruction - hanging, strangulation, upper airway tumors, goiter, endotracheal tube obstruction (biting, displacement, secretions). (2) Inflammatory upper airway narrowing - epiglottitis, croup, laryngospasm. (3) Foreign bodies -chocking, near drowning.	(1) Relief of anatomic obstruction -big tonsils, hypertrophic adenoids, or a redundant uvula (2) Relief of PEEP or positive pressure ventilation - postextubation lung edema, postextubation respiratory failure

support has gained great popularity in recent years and has replaced the traditional invasive ways. The role of noninvasive ventilation (NIV) in treatment of pulmonary edema can be significant as it dramatically reduces the work of breathing and thereby preventing muscle fatigue[19]. Apart from this benefit, NIV may be able to reduce the ventricular afterload, helps in better recruitment of alveoli, minimal disturbances of the hemodynamic parameters, and lesser incidence of ventilator associated pneumonias. The resolution of pulmonary edema usually occurs within 3-12 hours of institution of appropriate therapy[20]. However, in a few cases the complete resolution may take up to 48 hours. The patients have good prognosis if promptly diagnosed and appropriate treatment instituted. However, a significant complication rate does exist and is generally attributed to a delay in diagnosis.

Conclusion

In conclusion, NPPE is a relatively common and often underdiagnosed complication following an episode of upper airway obstruction. Postanesthetic laryngospasm is most common in adults, and acute epiglottitis by far the most common in children. This syndrome should be listed in the important differential diagnosis of perioperative respiratory failure, and also an important clinical entity in post-extubation respiratory distress. NPPE carries a good prognosis if promptly diagnosed and appropriately treated with or without mechanical ventilation.

References

1. Bhaskar B, Fraser JF. Negative pressure pulmonary edema revisited: pathophysiology and review of management. Saudi J Anaesth 2011; 5:308-13.
2. Vandes R, Kothari DS, Tripathi RS, et al. Negative pressure pulmonary edema with laryngeal mask airway use: recognition, pathophysiology and treatment modalities. Int J Crit Ill Inj Sci 2012; 2:98-103.
3. Lang SA, Duncan PG, Shephard DA, et al. Pulmonary edema associated with airway obstruction. Can J Anaesth 1990; 37:210-8.
4. Warren MF, Peterson DK, Drinker CK. The effects of heightened negative pressure in the chest, together with further experiments upon anoxia in increasing the flow of lung lymph. Am J Physiol 1942; 137: 641-8.
5. Louis PJ, Fernandes R. Negative pressure pulmonary edema. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 93: 4-6.
6. Gavel G, Robert WM. Laryngospasm in anaesthesia. Contin Educ Anaesth Crit Care Pain 2014; 14: 47-51.
7. Singh K, Gulia J, Raghove P. Post-operative pulmonary edema after modified radical mastoidectomy. Internet J Otorhinolaryngol 2010; 13: 6-9.
8. Bajwa SJS, Kulshrestha A. Diagnosis, prevention and management of postoperative pulmonary edema. Ann Med Health Sci Res 2012; 2: 180-5.
9. Robert AF, Kristen AB. Emergent management of pediatric epiglottitis. Medscape Infectious diseases CME Update: Nov23, 2014.
10. McConkey PP. Post obstructive pulmonary edema: A case series and review. Anaesth Intensive Care 2000; 28:72–6.
11. Kooy MA, Gargiulo RF. Postobstructive pulmonary edema. Am Fam Physician 2000; 62: 401-4.
12. Malcolm L, Jihad M. Understanding negative pressure pulmonary edema. Intensive Care Med 2014; 40: 1140-3.
13. Fremont RD, Kallet RH, Matthay MA, et al. Postobstructive pulmonary edema: A case for hydrostatic mechanisms. Chest 2007; 131: 1742–6.
14. Kapoor MC. Negative pressure pulmonary edema. Indian J Anaesth 2011; 55: 10-1.
15. Blanch L, Bernabe F, Lucangelo U. Measurement of air-trapping, intrinsic positive end expiratory pressure and dynamic hyperinflation in mechanically ventilated patients. Respir Care 2005; 50: 110-23.
16. Visvanathan T, Kluger MT, Webb RK, et al. Crisis management during anaesthesia: laryngospasm. Qual Saf health Care 2005; 14: e3.
17. Bajwa SJS, Kulshrestha A. Diagnosis, prevention and management of postoperative pulmonary edema. Ann Med Health Sci Res 2012; 2: 180-5.
18. Singh B, Singh I, Sidhu S. Negative pressure pulmonary edema after routine elective surgery. Int I Med and Dent Sci 2014; 3: 501-6.
19. Hoo GW, Byrd RP, Talavera F, et al. Noninvasive ventilation. Medscape CME Update: Apr 4, 2014.
20. Chan SP, Liu HP, Chen CY, et al. An analysis of negative pulmonary edema cases after acute upper airway obstruction. J Emerg Crit Care Med 2012; 23: 131-8.

負壓性肺水腫的臨床特性

吳仁光

澄清綜合醫院中港分院　內科部

摘　要

負壓性肺水腫(NPPE)是一種不常見的臨床症狀，其發生於呼吸道阻塞時，所引起的胸內負壓增加，造成水分移向肺組織間質。負壓性肺水腫可能發生在麻醉合併症，也可能發生在任何原因導致上呼吸道阻塞，或緩解慢性阻塞後的併發症，例如重症患者困難插管或呼吸器使用拔管後出現的呼吸窘迫與低氧血症。早期被診斷出來、呼吸道重新建立、適當的給氧及正壓呼吸器使用，達到有效的治療的目的。負壓性肺水腫常常發生於沒有明顯心臟衰竭危險因子的病患，許多是心肺功能正常或接近正常的病人，因而讓醫護同仁常常忽視了肺水腫的可能性。但如果未被立即辨識、確認，被誤認為其他的肺部急症而進行一系列不必要的檢查與治療，可能導致其他的併發症產生，在某些的文獻報告當中，其死亡率甚至可以高達40%。本篇綜論希望能提醒醫護同仁及早辨識與適當處置負壓性肺水腫，以避免病患不必要的併發症與死亡。