Clinical Case Report

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Negative pressure pulmonary edema after general anesthesia

A case report and literature review

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Abstract

Rationale: Negative pressure pulmonary edema (NPPE) is a dangerous clinical complication and potentially life-threatening emergency without prompt diagnosis and intervention during recovery period after anesthetic extubation.

Patient concerns: A 25-year-old woman has undergone endoscopic thyroidectomy. After extubation, the patient developed acute respiratory distress with high airway resistance accompanied with wheezing, oxyhemoglobin saturation (SpO_2) decreased to 70%. With positive pressure mask ventilation, her condition was stable, SpO_2 99%. However, the patient developed pink frothy sputum with diffuse bilateral rales 30 min later after transported to surgical intensive care unit (SICU).

Diagnoses: Negative pressure pulmonary edema.

Interventions: The patient was undergone assisted ventilation with continuous positive airway pressure (CPAP) and furosemide 20 mg was given intravenously.

Outcomes: Postoperative day (POD) 2 her condition became stable, computed tomography (CT) scan indicated the pulmonary edema disappeared. The patient was discharged 6 days later. No abnormalities were observed during following 4 weeks.

Lessons: Although usually the onset of NPPE is rapid, with individual differences NPPE is still challenging. Increased vigilance in monitoring, diagnosis, and treatment are essential to prevent aggravation and further complication.

Abbreviations: CPAP = continuous positive airway pressure, CT = computed tomography, DAH = diffuse alveolar hemorrhage, HR = heart rate, MAC = minimum alveolar concentration, NBP = noninvasive blood pressure, NIM = network interface module, NPPE = negative pressure pulmonary edema, POD = postoperative day, SICU = surgical intensive care unit, SpO_2 = oxyhemoglobin saturation, TOF = train-of-four.

Keywords: General anesthesia, negative pressure pulmonary edema, perioperative period

1. Introduction

Negative pressure pulmonary edema (NPPE), the noncardiogenic pulmonary edema, is caused by upper airway obstruction and rapid negative intrapleural pressure increasing due to attempts of inspiration against the obstruction. NPPE is a dangerous clinical complication during the recovery period after general anesthesia. NPPE was first reported in 1977. This occurs in 0.05% to 0.1% of cases as a serious complication of general anesthesia with tracheal intubation,[1,2] and more than half of these cases are related to postanesthetic laryngospasm.[3,4] Postanesthetic NPPE is a potentially life-threatening emergency and occurs more frequently than reported in studies, which should cause the attention for anesthesiologists. Here, we presented a rare case of "delayed" NPPE in a young woman after endoscopic thyroidectomy and reviewed the reported cases of NPPE over the past decade.

2. Case report

A 25-year-old woman was admitted to our hospital because of the presence of a left thyroid tumor and was scheduled to undergo standard endoscopic subtotal thyroidectomy under general anesthesia. She was classified with American Society of Anesthesiologists physical status I without a history of cardiorespiratory disease, gastroesophageal reflux, medicine, or surgeries. All preoperative laboratory test results were within normal limits. She had a small jaw with Mallampati grade II intubation. The patient was fasted for 12 h. Vital signs, including noninvasive blood pressure (NBP), electrocardiogram activity, and oxyhemoglobin saturation (SpO_2) were monitored. The patient was premedicated intramuscularly with 1 mg penehyclidine hydrochloride, shortly after which 2 mg midazolam, 80 mg 1% propofol, 15 mg rocuronium, and 25 μg sufentanil were administered. We used a network interface module

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Informed consent: Written informed consent was obtained from the patient for publication of this case report. No additional ethics approval was required, since the study did not comprise a clinical trial, nor use any unapproved medications.

The authors have no conflicts of interest to disclose.

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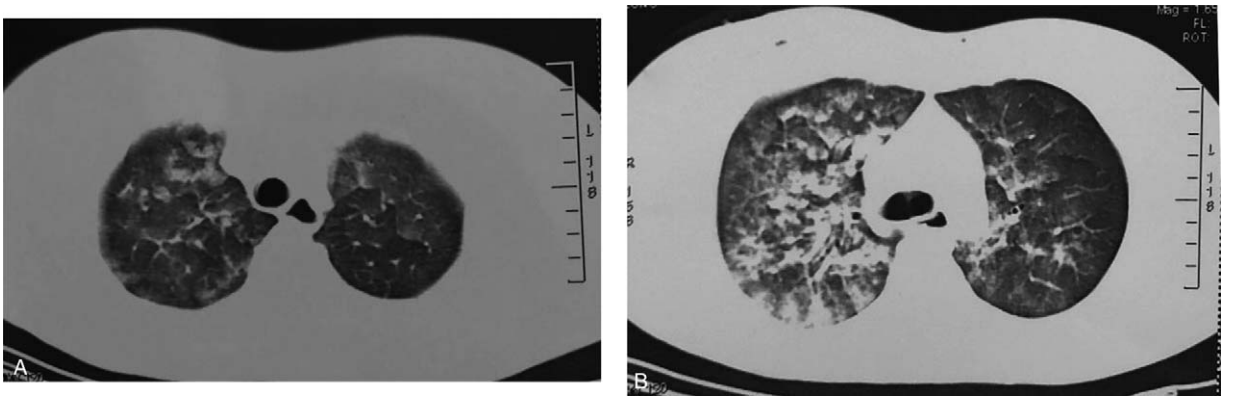

Figure 1. Axial CT scans taken postoperatively showed extensive macular alveolar infiltrations throughout both lungs. (A) Apical infiltrations; (B) basal infiltrations. CT = computed tomography.

(NIM)-response endotracheal tube (7-mm internal diameter, Medtronic, Inc., MN) for visual endotracheal intubation, which helped to monitor the recurrent laryngeal nerve intraoperatively, so no rocuronium was injected after induction. During the operation, the minimum alveolar concentration (MAC) value was maintained within 1.2–1.5 by regulating the inhalation concentration of sevoflurane and nitrous oxide. Tidal volume and rate were adjusted to maintain an end-tidal PCO_2 of 30 to 40 mm Hg. The anesthetic procedure lasted almost 4 h without any complications. A total of 2000 mL of the equilibrium solution was administered during the surgery, the urine output was approximately 500 mL, and blood loss was less than 10 mL. After the patient recovered complete consciousness and breathed spontaneously, she was extubated. Immediately after extubation, the patient developed respiratory distress. We performed mask ventilation with positive airway pressure. There was high airway resistance, and SpO_2 decreased progressively from 100% to 70%, accompanied with wheezing. Injectable propofol (30 mg) was administered intravenously, and positive pressure mask ventilation was continued. Her airway resistance started decreasing, and oxygen saturation gradually improved. Her condition returned normal with SpO_2: 98% to 99%, respiratory rate: 15 to 18/min. The patient was monitored in postanesthesia care unit for 30 min without any further complications. After admission to the surgical intensive care unit (SICU), she expectorated pink frothy sputum and presented diffuse bilateral moist rales. Her respiratory rate increased to 22 to 26/min, and SpO_2 decreased to 60% to 70%. Her heart rate was 95 to 115, and NBP was 90 to 100/50 to 60 mm Hg. An arterial blood sample analysis showed a $PaCO_2$ of 45 mm Hg and PaO_2 of 73 mm Hg. The patient underwent assisted ventilation with 5 cm H_2O continuous positive airway pressure (CPAP) and 100% O_2. Simultaneously, furosemide 20 mg was administered intravenously. The bedside tracheoscope examination showed bloody sputum in the bronchus and congestion in the left and right lung mucosa, mainly in the right lung. Computed tomography (CT) examination revealed multiple patchy densities throughout both the lungs (Fig. 1). Brain natriuretic peptide, D-dimer, and cardiac enzyme levels were within normal limits. Cardiac color ultrasound showed no clinical problems. Two hours later, the pink frothy sputum significantly declined and breathing distress alleviated. The patient underwent associated ventilation for 15 h. The following day, her condition became stable, rales completely disappeared, and a CT scan indicated that most of the pulmonary edema disappeared (Fig. 2). The patient was discharged 6 days later without any complications. No abnormalities were observed during the following 4 weeks.

3. Discussion

NPPE is an acute noncardiogenic pulmonary edema that can be a perioperative life-threatening complication without timely diag-

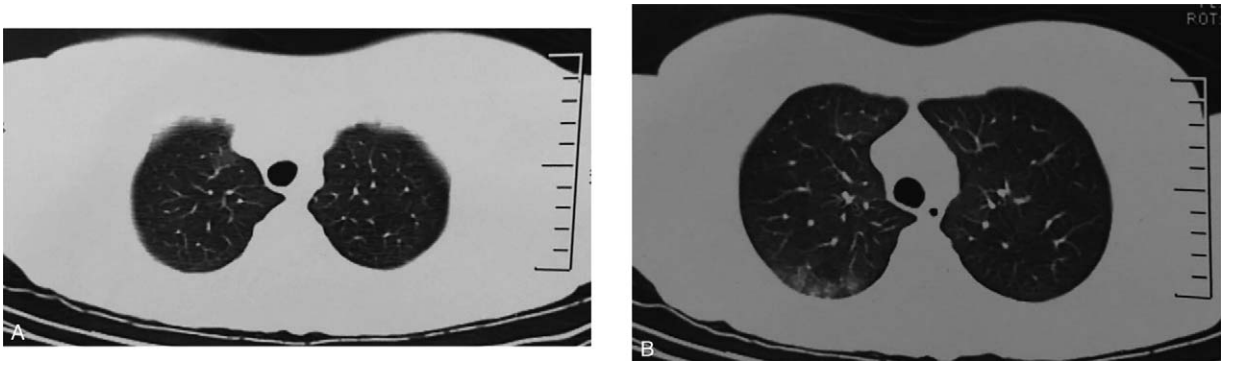

Figure 2. Axial CT scans of recovery phase on postoperative day 2. (A) Apical infiltrations, the same plane with Fig. 1A; (B) basal infiltrations, same plane with Fig. 1. CT = computed tomography.

nosed and treated. It is essential to notice the potential causes, make a rapid differential diagnosis, and determine the effective treatment during the perioperative period before disease aggravation occurs. In this case, pulmonary edema associated with aspiration pneumonia was first excluded. The patient underwent strict fasting with no history of aspiration, and the tracheoscope examination confirmed only bloody sputum in the trachea. A total of 2000 mL of the equilibrium solution was administered at a constant speed and was balanced with preioperative fluid loss. Therefore, pulmonary edema caused by fluid overload was prevented. Our patient was healthy with no history of cardiovascular disease, postoperative cardiac enzyme levels, and ultrasonic cardiogram showed no abnormalities, thus cardiogenic pulmonary edema was also ruled out. In addition, intubation with visual laryngoscope could efficiently prevent inserting the endotracheal tube too deep into the right lung, resulting in re-expansion pulmonary edema. And there was no drug-associated allergy during the entire perioperative period. Considering that the above factors were ruled out, the patient underwent acute airway obstruction after extubation and subsequently developed pulmonary edema. The patient then experienced a rapid recovery after assisted ventilation via CPAP. Therefore, a diagnosis of NPPE was made.

In the past 10 years, 29 reported cases of NPPE related to general anesthesia were shown in Table 1. NPPE usually progresses rapidly. In the most of these reported cases, the time window from the onset of airway obstruction to the development of pulmonary edema symptom was only a few minutes. Krodel et al[5] reported that a 25-year-old man showed the symptoms of pulmonary edema within first hour after surgery without specific time window. Hong et al[6] reported the case that began to present pink frothy sputum soon after clear consciousness. Here, our patients rarely presented pink frothy sputum after reversing the upper airway obstruction-induced dyspnea, she stayed conscious and the time window was over 30 min.

It is widely accepted that the central mechanism of postoperative NPPE is related to rapid negative intrapleural pressure increasing due to forceful inspiration against the obstruction, which can be up to 10 times or more that of normal breathing.[7] A typical event leading to acute airway obstruction associated with postoperative NPPE is laryngospasm. Other procedure that increases the risk of NPPE includes oropharyngeal, head, and neck surgery. Five[8–12] of the reported 29 cases involved upper respiratory tract surgery, and 10[1,3,6,7,13–18] of the cases involved head and neck surgery, which may be related to tissue swelling and the sensitive dilator muscle of the upper airway in head and neck surgeries. Although our patient underwent endoscopic thyroidectomy with no wound in the neck skin, it was inevitable for neck tissue and muscle injury.

Interestingly, 3[15,19,20] of the reported cases suggested that upper airway obstruction was associated with sugammadex, which is a novel selective agent reversing the rocuronium-induced neuromuscular blockade. The authors analyzed that the recovery of train-of-four (TOF) ratio > 0.9 of the upper airway muscle might not be reversed by sugammadex. Thus, the difference in the

Table 1

Reported cases of negative pressure pulmonary edema from 2008 to 2018.

Year	Age (years)	Sex	Type of surgery	Time window	Refs.
2018	22	F	Percutaneous endoscopic interlaminar lumbar discectomy	Rapid	[22]
2018	64	M	Excision of a vocal cord papilloma	Rapid	[12]
2018	84	F	Total hip arthroplasty	Rapid	[23]
2017	28	F	Cholecystectomy	Almost simultaneously	[4]
2017	17	F	Thyroidectomy	Rapid	[15]
2016	25	M	Repair of zygomatic arch and maxillary fractures	Rapid	[7]
2016	15	M	Eye and vitreoretinal exploratory surgery	No mention	[18]
2016	65	F	Thyroidectomy	Immediate after re-intubation	[14]
2015	66	F	Open reduction of orbital wall and nasal bone surgery	Immediate after re-intubation	[10]
2015	28	F	Tonsillectomy	Rapid	[9]
2014	50	F	Transsphenoidal resection of a pituitary adenoma	Rapid	[16]
2014	25	M	Anterior cervical discectomy and fusion	Simultaneously	[17]
2014	26	M	Le Fort I osteotomy and both sagittal split ramal osteotomy	After clear consciousness	[6]
2014	42	M	Laparoscopic appendectomy	Rapid	[20]
2014	76	F	Arthroscopic meniscus repair	Rapid	[19]
2014	37	M	Septoplasty operation	No mention	[11]
2013	22	F	Bilateral mastectomies and one-stage reconstruction	No mention	[24]
2013	77	F	Total gastrectomy	3–4 min after re-tubation	[25]
2013	23	F	Tonsillectomy	Few minutes	[8]
2013	32	F	Laparoscopic cholecystectomy	Rapid	[26]
2012	19	M	Laparoscopic donor nephrectomy	Rapid	[27]
2012	28	F	Thyroidectomy	Immediate after re-tubation	[13]
2011	24	M	Lateral internal sphincterotomy	No mention	[28]
2010	25	M	Excision of back and thigh schwannomas	Within 1 h	[5]
2010	38	F	Radical mastectomy	Few minutes	[29]
2010	34	M	Right wrist laceration repair	Simultaneously	[2]
2009	56	M	Ureteroneocystostomy	Rapid	[30]
2009	27	M	Le Fort I and sagittal split mandibular ramus osteotomy	Rapid	[3]
2008	48	M	Transsphenoidal hypophysectomy	Rapid	[1]

F = female, M = male, Refs. = references.

recovery profile when using sugammadex needs to be further studied. For patients with high-risk upper airway obstruction, sugammadex should be used cautiously in a clinical setting. In our case, the surgeon requested monitoring of the signal of the recurrent laryngeal nerve intraoperatively, so no muscle relaxants were administered after induction. The patient's neuromuscular recovery was already effective and complete postoperatively, which was the basis for increased negative pressure in the lung after upper airway obstruction during the perioperative period. Young, healthy, athletic patients seem to be at risk for NPPE.[4] However, one quarter of these reported cases are the patients over 55 years old. Thus, crucial attention should be given to NPPE discovered in old patients.

It is believed that decreased intrathoracic pressure leads to an increased venous return, increased pulmonary venous pressure, and increased vascular permeability contributes to transudation of fluid from the pulmonary capillaries into the alveolar space. Additionally, insufficient ventilation induced hypoxia and acidosis, which further increase the pulmonary vascular resistance and associated with alveolar membrane-capillary injuries. Our patient underwent a bronchoscopy examination and bloody sputum and congestive plaque in the mucosa were found, which indicated severe damage. Contou et al[21] performed a retrospective analysis in which 15 of 149 patients with diffuse alveolar hemorrhage (DAH) underwent NPPE episodes. Moreover, there is one case showed secondary T wave and ST segment dynamic changes,[12] and two cases of secondary acute subendocardial myocardial infarction[11,14] following NPPE, which might also be associated with acidosis and hyperadrenergic response induced by dyspnea. It is implied increasing attention should be paid on the complications secondary to NPPE.

With proper treatment, NPPE could rapidly dissipate, and its clinical symptoms and auxiliary features can be improved within 12 to 48 h.[5,7] Relieving airway obstruction is a primary step, and the treatment for NPPE mainly focuses on improving respiratory function and supportive care. There is consensus that CPAP or mechanical ventilation with a certain level of positive end-expiratory pressure is often needed. Two cases of 29 reported cases had no sign of airway obstruction and treated without assistant ventilation.[2,22] All patients recovered and discharged within 10 days. In recent years, some authors have strengthened the efficacy of bronchodilators. Although the obstruction may not be caused by bronchospasm, studies showed that β agonists might increase alveolar fluid clearance to alleviate the symptoms of pulmonary edema.[5] Other medicine, including diuretic and steroids, are still heavily debated because of their controversial role, and there is still no explicit decision regarding their use.

In view of reported NPPE cases in the decade plus our case, three tips were summarized as following to update the understanding of NPPE for effectively prevention, diagnosis, and treatment:

1. there are individual differences of time window from the relief of airway obstruction to the development of pulmonary edema. Anesthesiologists should carefully monitor the patients with high-risk factor of NPPE, drawing enough attention for the patients with any condition of postanesthetic upper airway obstruction, even if obstruction symptoms are relieved,
2. NPPE is rare but fatal complication, which could induced further sever complication. Symptoms of pulmonary edema occurs after upper airway obstruction with other factors ruled out, NPPE should be considered,
3. treatment of NPPE includes careful monitoring, reliving airway obstruction, oxygen supplementation, and assistant ventilation. There is heavy debate for drug treatment and doctors should avoid overmedication.

4. Conclusion

With individual differences, NPPE is still challenging although the etiology and pathophysiological process has been well debated. We have reported a case of delay-NPPE in young woman, and reviewed the reported cases of NPPE over past decade to update the knowledge of NPPE. Increased vigilance in timely monitoring, diagnosis and treatment are essential to prevent aggravation and further complication.

Author contributions

Conceptualization: Guoqing Zhao.
Data curation: Ruizhu Liu, Jian Wang.
Writing – original draft: Ruizhu Liu.
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