Case Report

Negative pressure pulmonary edema after craniotomy through the endonasal transsphenoidal approach

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Abstract: We describe a case of negative pressure pulmonary edema that occurred in the post-anesthesia care unit in a patient who had undergone transsphenoidal resection of a pituitary adenoma. Negative pressure pulmonary edema is an uncommon complication of general anesthesia. In this case, the patient’s nasal cavity had been filled with surgical packs and she had not become accustomed to breathing through her mouth, in addition to her large tongue and small oropharyngeal cavity, residual effect of anesthetic may resulting in tongue falling which caused airway obstruction. The main causative factor is excessive negative intrathoracic pressure generated by the patient’s spontaneous forced inspiration in an effort to overcome the airway obstruction. It typically developed rapidly, and may be life threatening if not diagnosed promptly. After re-intubation for a short period of mechanical ventilation with positive end expiratory pressure (PEEP 10 cm H₂O) and a bolus of intravenous furosemide, the patient recovered rapidly and discharged 8 days after surgery.

Keywords: Pulmonary edema, airway obstruction, anesthesia, neurosurgery

Introduction

Negative pressure pulmonary edema (NPPE) is the formation of pulmonary edema resulted from acute upper airway obstruction. It appears to be caused by significant negative intrathoracic pressure generated by patient’s forced inspiration against a closed upper airway, resulting in transudation of fluid from the pulmonary capillaries to the interstitium [1]. The incidence of NPPE after general anesthesia is estimated to be 0.05% to 0.1% [2]. It appears that NPPE occurs more commonly than general estimation and is often unrecognized or misdiagnosed, with reported incidence as high as 11% from Tami et al. [3]. It is considered that there be two categories of NPPE: type I includes edema that develops after acute airway obstruction, and type II after the relief of chronic airway obstruction [4]. The following case is an example of type I NPPE, occurred after transsphenoidal resection of a pituitary adenoma.

Case report

A 50-year-old (weight: 55 kg) woman was admitted to West China Hospital to for bitemporal hemianopsia that had developed over 2 years, and 10-day history of headache. Her medical, family and social histories were unremarkable. She had normal body temperature of 36.5°C, heart rate (HR) of 72 beats/min, and blood pressure (BP) of 152/91 mmHg. Magnetic resonance imaging of the brain revealed a 3.5 cm × 3.8 cm × 3.7 cm mass lesion in the sella turcica. The serum levels of prolactin was 53.33 ng/ml (normal level, 6.0~29.9 ng/ml). Other preoperative investigations, including full blood count, serum electrolyte concentrations, electrocardiogram and chest X-ray (Figure 1) revealed no abnormality.

The preoperative diagnosis was pituitary adenoma, and the patient was scheduled for craniotomy through the endonasal transsphenoidal approach under general anesthesia. At intubation it was noted that the patient had a large tongue and a small oropharyngeal cavity, but positive pressure ventilation with a mask as well as intubation were not difficult. Anesthesia induction was performed with sufentanil (20 μg), propofol (100 mg), cisatracurium (10 mg/kg), and midazolam (2 mg). Propofol (4~12 mg/kg/h), remifentanil (0.1~0.2 mg/kg/min) and 1.5 MAC (minimum alveolar concentration) of
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Sevoflurane mixed with oxygen (50%) and air (50%) were used during maintenance of anesthesia and adjusted to maintain the mean artery pressure (MAP) between 60 to 80 mmHg. Ventilation were mechanically controlled to maintain the end-tidal CO\textsubscript{2} between 30-35 mmHg. During surgery the electrocardiogram (ECG), invasive arterial pressure and pulse oxygen saturation (SpO\textsubscript{2}) were continuously monitored and recorded, and maintained the heart rate, blood pressure and SpO\textsubscript{2} at normal levels. Surgery lasted 1 hour. The total volume of intravenous fluid administered was 1000 ml and the urine output was 450 ml.

After surgery, the patient was transferred to the post-anesthesia care unit (PACU) with the endotracheal tube in place. When spontaneous breathing recovered, neostigmine 1 mg, atropine 0.5 mg were administered to eliminate effect of muscle relaxants. The patient was extubated approximately 30 minutes after surgery when she was able to open her eyes, protrude her tongue and make a fist forcefully according to commands. After extubation, the patient breathed spontaneously with supplemental oxygen (3 L/min) by mask while physical condition was observed. Approximately 3 minutes later, the anesthesia nurse found the patients showed body movement, and the SpO\textsubscript{2} waveform was inaccurate. After the SpO\textsubscript{2} probe connected, the patient developed signs of marked upper airway obstruction and the SpO\textsubscript{2} decreased from 100% to 70%. Then she lost conscious and oral lip turned cyanosed. We immediately thrust the lower jaw and performed mask ventilation with positive airway pressure of high-flow supplemental oxygen, assisted by an oropharyngeal airway. This ventilation endeavor was employed until the SpO\textsubscript{2} returned to 100%. Simultaneously, the patient developed arterial hypertension (200/102 mmHg) and the HR increased to 90 beats/min. After timely treated with intravenous nicardipine hydrochloride 0.4 mg, the BP fell to 140/85 mmHg.

The patient recovered rapidly and showed no dysphoria, but suddenly expectorated pink, foamy secretions and the presence of diffuse bilateral rales was noted. We administered furosemide 10 mg intravenously. Analysis of an arterial blood sample taken with the patient breathing supplemental oxygen at a rate of 8 l/min showed: pH 7.288; arterial partial pressures of CO\textsubscript{2} (PaCO\textsubscript{2}) and O\textsubscript{2} (PaO\textsubscript{2}) of 32.6 mmHg and 98.2 mmHg, respectively; base excess -6 mmol/l; lactate concentration 1.9 mmol/l; arterial oxygen saturation (SaO\textsubscript{2}) 98%; and sodium, potassium and hemoglobin concentrations of 145 mmol/l, 3.25 mmol/l and 130 g/l, respectively. The patient’s pulmonary edema improved rapidly and SpO\textsubscript{2} was maintained above 80% with a continuous positive airway pressure (CPAP) mask set at 20 cm H\textsubscript{2}O. Within an hour, the patient showed comfortable but still expectorating a few pink foamy secretions and her SpO\textsubscript{2} failed to recover further. Further arterial blood gases analysis revealed: pH 7.216; PaCO\textsubscript{2} 61.3 mmHg; PaO\textsubscript{2} 79.3 mmHg; base excess -4 mmol/l; lactate concentration 2.9 mmol/l, and SaO\textsubscript{2} 98%. To improve the ventilation and restore the homeostasis, intubation was administered again to facilitate

Figure 1. The patient’s preoperative chest X-ray shows bilateral clear lung fields.

Figure 2. The patient’s postoperative chest X-ray shows diffuse, bilateral opacity throughout both lungs with normal lung volumes, normal heart size, and no pleural effusions.
a short period of mechanical ventilation with a positive end expiratory pressure of 10 cm H$_2$O, and succinylcholine 80 mg and propofol 100 mg intravenously. Endotracheal intubation went smoothly and endotracheal toilet yielded pink frothy fluid. When the patient was stable, she was transferred to the intensive care unit (ICU) with a diagnosis of noncardiogenic pulmonary edema caused by an acute episode of airway obstruction. A follow-up chest radiograph taken in the ICU showed diffused distribution shadow throughout both lungs (Figure 2). The next day the rales was complete disappeared and the trachea was extubated without incident. The patient’s further recovery was uneventful and she was discharged from hospital 8 days after surgery.

Discussion

Diagnosis

The patient was diagnosed with negative pressure pulmonary edema as a result of post-anesthetic upper airway obstruction and was treated with positive pressure ventilation and intravenous furosemide. When the patient’s spontaneous breathing had recovered, we gave neuromuscular blocker antagonist before extubation. 5 minutes after antagonism with neo-stigmine, the patient could open her eyes and protrude her tongue. So the possibility of residual effect of neuromuscular agent was excluded. Although the patient was able to do the actions according to commands, for her large tongue and small oropharyngeal cavity, we still can’t exclude residual effect of anesthetic which might influence the patient consciousness, resulted in tongue falling and caused airway obstruction.

Pituitary adenomas are a diverse group of tumors arising from the pituitary gland. Patients who have pituitary adenoma always complicated with pituitary dysfunction. Patients with non-functioning tumors frequently present symptoms like headache and visual loss whereas the functioning adenomas present with symptoms of hormone excess [5]. It is important to evaluate the patient’s endocrine status preoperatively. Growth hormone secreting lesions result in acromegaly and always developed a hypertrophy of the soft tissues of the mouth, large tongue and a narrowed glottis may complicated with obstructive sleep apnea syndrome which is a challenge for intubation. It was reported in acromegaly, up to 70% of patients with the additional risk of centrally mediated respiratory depression [6]. Above all, for patients with endocrine system abnormalities, we should pay more attention to the risk of upper airway obstruction.

The main differential diagnoses include aspiration of gastric contents, neurogenic pulmonary edema, myocardial ischemia, cardiogenic pulmonary edema and anaphylaxis [7]. In this patient the differential diagnoses could plausibly have been aspiration, fluid overload, a cardiac event, or an allergic or idiosyncratic drug reaction.

Fluid overload was unlikely, as she had received a total volume of 1000 ml, and urine output was 450 ml during anesthesia. In addition, before and after extubation, auscultation of the breath sound revealed no moist crackles or wheezes. A cardiac cause was excluded by a normal ECG, which showed no evidence of ischemic changes. In such cases, an echocardiogram could also be employed to make an assessment of right and left ventricular dimensions and function. An allergic or idiosyncratic reaction was also excluded for there was no evidence of skin rash, erythema or tissue swelling, and no naloxone was administered during the perioperative period. Aspiration pneumonitis caused by application of surgical disinfectant to the mouth during preparation of the surgical field seems unlikely, as the patient’s subsequent clinical and radiographic improvement was so rapid. We cannot completely exclude neurogenic pulmonary edema, although this would be unlikely during surgery for a pituitary tumor [8].

Pathophysiology

Non-cardiogenic pulmonary edema has been observed in a variety of circumstances, including upper airway obstruction (NPPE), acute lung injury, anaphylaxis, fluid maldistribution and severe traumatic brain injury (neurogenic pulmonary edema) [9]. Postoperative NPPE typically occurs from upper airway obstruction, where patients can generate high negative intrathoracic pressures during forced inspiration. Young, healthy, athletic patients seem to be at greatest risk [4].
To prevent bucking response increasing the intracranial pressure (ICP), the extubation for patients with neurological disease is usually done under deep anesthesia. The increased ICP will lead to cerebral ischemia, hypoxia, edema and have a severe impact on patient prognosis. On the other side, the neurological patients are more likely to develop the upper airway obstruction. In this case, the patient’s nasal cavity had been filled with surgical packs and she had not become accustomed to breathing through her mouth. Patients who have undergone transsphenoidal surgery always complicated with pituitary dysfunction and may developed a difficult airway. Therefore, for these patients who underwent extubation should be fully awake, airway reflexes should have recovered completely and the effects of muscle relaxants should have worn off before extubation. To avoid upper airway obstruction and aspiration, complete removal of the secretions and surgical disinfectant in the oral cavity by suction is also necessary, and an oropharyngeal airway should be on hand.

**Epidemiology**

For patients undergoing anesthesia, NPPE is reported to occur after extubation in 74% of cases while during initial airway management were 26%. The most common cause is post-extubation laryngospasm [10]. Other reported causes of NPPE include endotracheal tube obstruction, biting the endotracheal tube and foreign body aspiration [11]. In the remaining 26% of patients, acute upper airway obstruction occurred during management of the airway in patients with head and neck tumors (72%), Ludwig’s angina (14%) and laryngospasm (14%) [12].

**Treatment**

The treatment of NPPE is facilitated by its early recognition, administration of supplemental oxygen and, if necessary, provision of positive pressure to the airway by mask ventilation or mechanical ventilation with intubation. Nonetheless, oxygen supplementation with or without non-invasive positive pressure ventilation remains the most appropriate first line method of preventing or treating NPPE, and intubation may be remedial measures [13, 14]. Avoiding intubation if possible could obviate the need for ICU support, avoids the potential complications of mechanical ventilation and reduces the length of hospital stay. In this case, non-invasive positive pressure mask ventilation facilitated by an oropharyngeal airway and delivery of 100% oxygen was initially applied. However, the patient’s nasal cavity had been filled with surgical packs, in addition her large tongue, small oropharyngeal cavity and possibly developed tongue falling made non-invasive positive pressure ventilation difficult. With positive pressure mask ventilation the symptoms and signs of pulmonary edema progressed rapidly, and it cannot be achieved to maintain her \( \text{SpO}_2 \) above 80% over the next 1 hour. Therefore, the patient was re-intubated with consistent positive pressure ventilation (PEEP 10 cm H\(_2\)O) to improve oxygenation. After ventilation with intubation and PEEP, the condition of the patient improved.

Diuretics are often administered to treat NPPE, but their use is controversial. A case series has been reported in which all patients made complete recoveries from NPPE without the use of diuretics [15]. Other treatments, such as corticosteroids and bronchodilators, have been proposed, but their contribution to the final outcome is also unclear.

**Conclusion**

Typical methods to assess extubation opportunity may not be applicable in all patients especially those undergoing craniotomy through the endonasal transsphenoidal approach for pituitary endocrine lesion, and we should pay much attention to the incidence of upper airway obstruction and NPPE. With appropriate treatment, the prognosis of NPPE is generally good. The patients usually restore completely in 12-48 h. Physicians should be particularly vigilant when treating patients at risk of upper airway obstruction, so that NPPE can be recognized and treated promptly.

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**Disclosure of conflict of interest**

None.
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