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Negative-pressure acute tracheobronchial hemorrhage and pulmonary edema

Vasilios Papaioannou, Irene Terzi, Christos Dragoumanis, and Ioannis Pneumatikos

Democritus University of Thrace, Alexandroupolis Medical School, Intensive Care Unit, Dragana 68100, Greece

Abstract
Negative-pressure pulmonary edema is a well-known complication of an acute upper airway obstruction, which may rarely present as acute alveolar hemorrhage in cases of severe capillary stress failure. Hemorrhage from the central airways has also been reported as a rare manifestation of acute tracheobronchial injury, associated with severe disruption of the bronchial vasculature due to highly negative inspiratory pressure. In this clinical report, we describe a case of both acute tracheobronchial and alveolar hemorrhage in a young man, occurring immediately after extubation due to laryngospasm, diagnosed by bronchoscopy with bronchoalveolar lavage (BAL), measurement of the pulmonary edema fluid/plasma protein ratio, and by thoracic computed tomography (CT) scan. We propose that the patient experienced severe postobstructive negative-pressure pulmonary edema, related to increased permeability of the alveolar capillary membrane and a parallel loss of integrity of the bronchial vascular network. Our findings suggest that both changes in the bronchial circulation and mechanical stress failure of the more distal alveolar-capillary system may be induced by severe and acute upper-airway obstruction.

Key words Negative-pressure pulmonary edema · Pulmonary hemorrhage · Bronchoscopy

Introduction

Negative-pressure pulmonary edema (NPPE) has a reported incidence of 0.05% to 0.1% in all anesthetic practices. NPPE associated with post-extubation laryngospasm has been reported in 11% of typically young healthy subjects [1,2]. Furthermore, laryngospasm has been found to be the primary cause of more than 50% of cases of postobstructive pulmonary edema [1]. The course of NPPE is generally uncomplicated, with rapid onset and resolution and a short hospital stay. A review of 146 cases of NPPE found that more than 50% of patients had undergone upper digestive tract surgery [3], although a few cases involving orthopedic, cosmetic, and brain surgery and cases during patients' stay in a medical intensive care unit have also appeared in the literature [4–7]. Alveolar hemorrhage is an extremely rare manifestation of severe NPPE, with only 6 reported cases [8,13], whereas true hemoptysis, resulting from injury to tracheobronchial vessels, has been reported twice and described as negative-pressure injury (NPI) rather than NPPE [14,15]. We present a case of a 20-year-old man who underwent minor orthopedic surgery under general anesthesia and suffered from both acute tracheobronchial and alveolar hemorrhage immediately after extubation, and we suggest that he experienced severe airway and alveolar capillary stress failure.

Address correspondence to: V.E. Papaioannou
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Case report

A 20-year-old, 76-kg man was admitted to our hospital for the operative repair of a traumatic fracture of the neck of the right-thumb metacarpal. He had no previous medical history, and both preoperative electrocardiograph and chest radiograph were normal. General anesthesia was induced with fentanyl 100 μg and propofol 180 mg, and 70 mg of rocuronium was administered for muscle relaxation. Anesthesia was maintained with sevoflurane at 1.5%-2% in 70% nitrous oxide and 30% oxygen. The surgery proceeded uneventfully and the patient received 0.5 l of normal saline during the operation. At the end of the procedure and 40 min after anesthetic induction, the patient was extubated without neuromuscular relaxant reversal, because peripheral twitch monitoring showed 4/4 twitches with a train-of-four. Immediately after extubation, he became agitated and complained of shortness of breath; this was followed by marked respiratory distress with stridor,

cyanosis, and significant arterial oxygen desaturation (70% on a 100% nonrebreather mask), without auscultory evidence of air movement. He also exhibited signs of sympathetic hyperactivity, with heart rate (HR) of 120 beats·min^{-1} and blood pressure (BP) of 180/90 mmHg. We presumed that the patient had experienced an abrupt upper airway obstruction due to laryngospasm; sedation with 200 mg of thiopentone i.v. and muscle relaxation with 80 mg of succinylcholine i.v. were administered within 5 min of the onset of respiratory distress, and an 8.0-mm-internal-diameter tracheal tube was atraumatically inserted. Oxygen saturation increased to 98%; however, a small amount of bright red blood was repeatedly suctioned through the endotracheal tube. A chest radiograph showed bilateral pulmonary infiltrates (Fig. 1) and thoracic CT revealed a bilateral reticular nodular pattern with interseptal perivascular thickening in both dependent (Fig. 2A) and nondependent regions of the lungs (Fig. 2B).

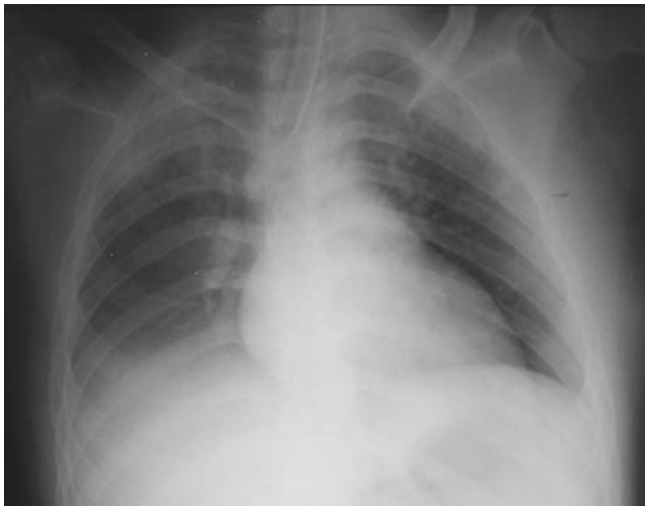

Fig. 1. Chest X-ray after intubation and before admission to the intensive care unit (ICU), showing bilateral mainly mid- and upper-zone interstitial infiltrates, with pleural effusions, mainly at the base of the right lung

The patient was transferred to the intensive care unit (ICU) for further stabilization. Initial arterial blood gas measurement revealed a pH of 7.34, a P_{CO_2} of 44 mmHg, a P_{O_2} of 98 mmHg and an arterial oxygen saturation of 98% on an inspired oxygen fraction of 100%. Hemoglobin concentration was 9.8 g·dl^{-1} compared with 14 g·dl^{-1} before surgery. The endotracheal secretions became increasingly bloody and bilateral inspiratory rales were present up to the apex of the lungs. The patient was hemodynamically stable with a BP of 140/90 mmHg and HR of 90 beats·min^{-1} and neither electrocardiography nor echocardiography revealed any sign of ischemia, systolic or diastolic failure, or regional wall abnormalities. Clinical examination excluded the presence of petechiae and oral or mucosal bleeding, and the complete blood count and coagulation profile were normal.

Bronchoscopy (Olympus, Dallas, TX, USA), performed 1 h after patient's admission to the ICU showed numerous focal punctate hemorrhagic lesions in the central airways. Bronchoalveolar lavage (BAL) of the right middle lobe with six aliquots of 20 ml normal saline each time showed a bloody return whose color was progressively becoming pink, with 95% polymorphonuclear leukocytes and 4.75* $10^3 \cdot ml^{-1}$ white blood cells, but all cultures were negative. Hemosiderophages

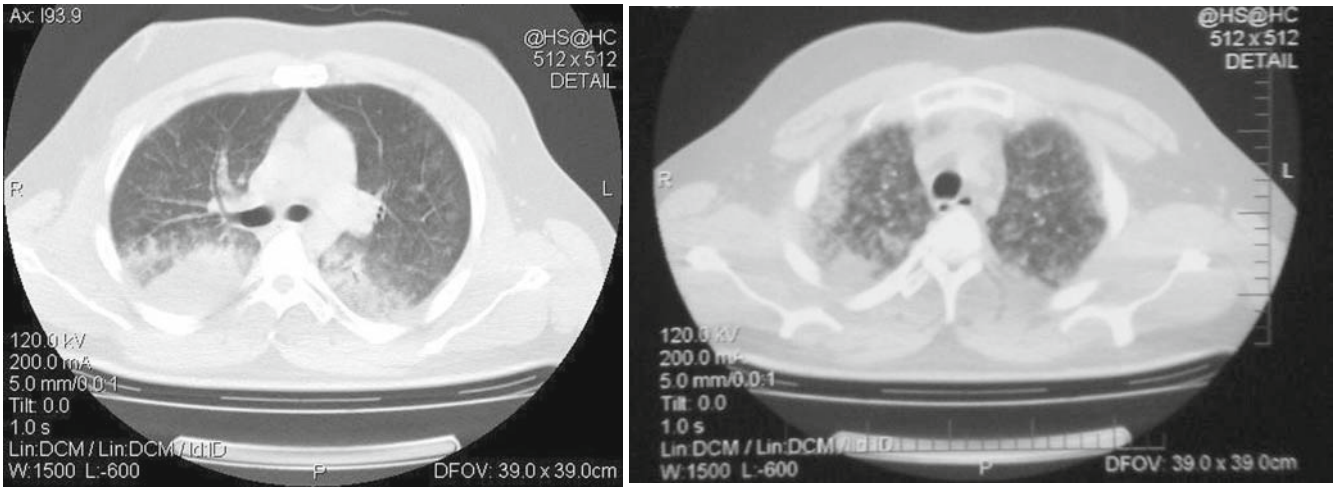

Fig. 2. **A** Emergency chest computed tomography (CT) at the level of the carina, obtained before ICU admission, showing a bilateral reticular nodular pattern with interseptal perivascular thickening and patchy consolidation in the posterior segments of the lungs, indicating edema/hemorrhage in dependent lung regions. **B** Emergency chest CT at a level far above the carina, obtained before ICU admission, showing bilateral reticular nodular pattern with interseptal perivascular thickening in nondependent lung regions. *DFOV*, digital field of view

were absent, excluding chronicity of the bleeding. During bronchoscopy, the pulmonary edema fluid was collected, along with simultaneous plasma samples; the samples were centrifuged and stored at –70°C. The total protein levels in both samples were measured, as previously described [16], and their ratio was found to be 0.85, indicating high-permeability pulmonary edema. A ratio of less than 0.65 is consistent with hydrostatic pulmonary edema, whereas a ratio of more than 0.75 indicates significant capillary wall stress failure with breaks in epithelial barriers and loss of membrane integrity [16,17].

The patient improved progressively over the next 24 h under mechanical ventilation with positive end-expiratory pressure of 10 cmH_2O, tidal volume of 650 ml, and a respiratory rate of 12 breaths·min^{-1}. Supportive treatment included 100 mg of intravenous (IV) furosemide, and a chest radiograph that was performed 24 h after patient's admission to the ICU showed complete resolution of the pulmonary infiltrates. The next day, the patient was successfully extubated and discharged from the ICU.

Discussion

Factors contributing to the pathogenesis of NPPE include: (1) enhanced venous return to the right heart due to the transmission of markedly negative intrathoracic pressure (ITP) to the right atrium (inspiration against a closed airway generates significant negative swings in ITP); and (2) elevation of mean systemic pressure associated with catecholamine-induced venoconstriction due to anxiety and hypoxia that may induce a shift of blood from the systemic to the pulmonary circulation. Both these mechanisms lead to an increase in right ventricular (RV) preload and both right and left ventricular (LV) afterload and the augmented RV volume may reduce LV compliance due to ventricular interdependence. The resulting LV dysfunction further increases pulmonary venous pressure; this may result in fluid filtration into the lungs, according to Starling's equation, and the development of pulmonary edema. In addition, the transmission of negative pleural pressure to the lung interstitium decreases extramural hydrostatic pressure and augments transmural pressure, favoring the formation of transudative edema [18,19].

According to the hypothesis of Pavlin et al. [20], in severe cases of pulmonary capillary wall stress, the development of high-protein edema is possible due to the rupture of the alveolar-capillary membrane. Schwartz DR et al. [8], in the first report of a case of pulmonary hemorrhage due to upper airway obstruction, supported the theory of a spectrum of abnormalities (transudative-exudative-hemorrhagic edema) according to different levels of transmural pressures, whose extreme elevations may contribute to the loss of membrane integrity and lead to alveolar hemorrhage.

The bronchial circulation is a high-pressure system and supplies the main airways and bronchial walls. In cases of significantly negative ITP, increased RV and LV pressures and increased catecholamine-induced systemic vascular resistance may also augment bronchial intravascular pressure, leading to focal hemorrhages throughout the larger airways [14]. Koch et al. [14] and Bhavani-Shankar et al. [15] reported two cases of patients who suffered from airway bleeding after post-extubation upper-airway obstruction, and concluded that hemoptysis was the primary feature of negative-pressure tracheobronchial injury (NPI), and that more distal alveolar-capillary disruption presented as true NPPE.

In our case, the patient experienced post-obstructive pulmonary edema due to laryngospasm. The laryngospasm seemed to be the cause of the upper airway obstruction because it had an abrupt onset, and oxygen saturation was improved by the administration of anesthesia, by muscle relaxation, and by the application of positive-pressure ventilation [21]. Thoracic CT demonstrated a nodular pattern in both dependent and non-dependent regions of the lungs, with patchy consolidation in the posterior segments, indicating a mixed tracheobronchial-alveolar hemorrhage.

Our bronchoscopic findings parallel those of Koch et al. [14] and support the diagnosis of NPI with concomitant alveolar hemorrhage, because BAL revealed a progressively bloody return with a parallel drop in hemoglobin. The edema fluid/plasma protein ratio in our patient was extremely high, indicating severe capillary distress. According to Schwarz MI and Albert [22], NPPE may rarely fall into the category of imitators of acute respiratory distress syndrome (ARDS). In addition, both the theory of Pavlin et al. [20] and Marland and Glauser's [23] report of a case with re-expansion pulmonary edema and increased protein ratio support the hypothesis that our patient experienced acute high-permeability NPPE, whose rapid and favorable outcome excluded other possible immunological causes.

However, there are some limitations to our findings, because we did not calculate the rate of alveolar fluid clearance, which remains intact in cases of absence of severe epithelial injury [16,17]. In cases of normal clearance mechanisms, protein concentration in the edema fluid will rise over time because progressive absorption of lung water may increase protein levels [24]. Thus, it is necessary to collect fluid as soon as possible. In our patient, edema fluid collection was performed 2 h after intubation, limiting the accuracy of this measurement [17]. Also, the possibility of massive blood aspiration from central to peripheral airways inducing an

inflammatory response cannot be excluded; however, the rapid amelioration of our patient's condition under positive ventilation does not support this hypothesis.

Conclusion

In conclusion, significantly negative ITP after post-extubation upper airway obstruction may lead to the development of either hydrostatic or high-permeability pulmonary edema, depending on capillary stress, with or without tracheobronchial hemorrhage.

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