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Challenges Associated with Negative Pressure Pulmonary Oedema: A Case Report and Review

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Abstract: **Negative pressure pulmonary oedema (NPPO) is a rare but serious complication for patients undergoing general anaesthesia. It often presents a diagnostic dilemma, thus posing significant management challenges. Despite the complexity of diagnosis, the pathophysiology and management of NPPO have been extensively studied. We present a case of NPPO in a middle-aged obese patient with high perioperative cardiac risk who underwent an emergency open appendicectomy. This case report details the anaesthetic approach to managing the patient's complex comorbidities, the series of events leading to the diagnosis, and subsequently the management of NPPO. We discuss the challenges encountered in diagnosing and managing NPPO, and review potential preventive measures. Our conclusion underscores that diagnosis of NPPO remains challenging, and early identification of patients at risk with vigilant monitoring is crucial for timely diagnosis and effective management.**

Keywords: **Anaesthetics; Anaesthesia; General; Obesity; Pulmonary Oedema.**

I. INTRODUCTION

Negative pressure pulmonary oedema (NPPO) is a rare but serious complication associated with general anaesthesia, with reported incidence ranging from 0.01% to 1% [1–4]. NPPO is characterised by noncardiogenic pulmonary oedema resulting from a sudden and significant reduction in intrathoracic pressure, and remains a diagnosis of exclusion.

Despite its low incidence, NPPO often leads to life-threatening post-operative pulmonary complications, particularly during the conclusion of anaesthesia [3]. We report a case of NPPO in a 59-year-old obese patient with high perioperative cardiac risk, who underwent an emergency surgical procedure. Knowledge of such cases can increase awareness of the existence of NPPO, allowing for prompt management and avoiding unnecessary treatment.

II. CASE REPORT

A 59-year-old gentleman was admitted to a tertiary centre with an acute abdomen. He presented with multiple comorbidities, including type II diabetes mellitus on insulin treatment, hypertension, obesity with body mass index (BMI) of 35, probable obstructive sleep apnoea (OSA) indicated by a STOP BANG score of 5, and history of ischaemic heart disease (IHD) with two vessels stented nine months ago. He was on dual antiplatelet therapy at the time of presentation. The STOP-BANG score, a widely used screening tool for OSA, is routinely applied in our practice, with a score greater than 4 suggesting a high probability of the condition [5].

A contrast-enhanced computed tomography (CT) scan revealed features indicative of acute appendicitis, leading to the decision for an emergency open appendicectomy. Pre-anaesthetic assessment demonstrated a favourable cardiac status, with more than 4 metabolic equivalents (METS). A point-of-care echocardiogram revealed normal left ventricular (LV) contractility and chamber sizes. Physical examination was largely unremarkable aside from obesity, with no sign of heart failure. Airway assessment indicated a Mallampati score of 1. The patient was stable haemodynamically, with normal saturation and normal chest X-ray (Figure 1). Based on the American Society of Anesthesiologists (ASA) physical status classification, and considering his medical history and comorbidities, he was classified as ASA 3E and scheduled for general anaesthesia with opioid sparing analgesia.

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Modified rapid sequence induction (RSI) was employed to induce anaesthesia. The patient was induced with intravenous (IV) lignocaine 100 mg, IV fentanyl 50 µg, IV propofol 110 mg, and IV rocuronium 100 mg. Intubation was assisted by video laryngoscope, with a percentage of glottis opening (POGO) score of 100%. Following induction, a unilateral right-sided transversus abdominis plane (TAP) block was performed under ultrasound guidance, administering 20 ml levobupivacaine 0.25%. Anaesthesia was maintained with sevoflurane, with O2/N2O titrated to achieve an age-adjusted minimal alveolar concentration (MAC) of 0.8. As part of his analgesic regimen, the patient received IV dexamethasone 8 mg, IV magnesium sulphate 20 mmol, IV oxycodone 2 mg, and IV paracetamol 1 g upon surgical incision. Intraoperatively, he was diagnosed with a perforated appendix without abdominal contamination. The patient received a total of 800 ml crystalloid over the course of the two-hour surgery. Notably, no additional rocuronium top-up was required throughout the procedure.

Upon conclusion of the surgery, the patient was reversed with IV neostigmine 2.5 mg and IV glycopyrrolate 400 µg upon return of spontaneous regular breathing. Prior to extubation, the patient exhibited responsiveness to commands, and maintained adequate saturation with satisfactory spontaneous ventilation. Additionally, there was evidence of robust power recovery clinically, exemplified by sustained head lift and hand grip for longer than 5 seconds. However, upon extubation, he experienced shortness of breath and desaturated to 93%. At that point, his blood pressure (BP) measured 128/72 mmHg, heart rate (HR) was 75 beats per minute (bpm), and auscultation of his lungs revealed bilateral basal coarse crepitations. Immediate intervention included administration of IV frusemide 5 mg and the application of continuous positive pressure (CPAP) at 5 cmH20 with 100% O2. Subsequently, his saturation improved, and he was monitored in the Post Anaesthetic Care Unit (PACU).

In the PACU, while on a face mask at 5 L/min O2, the patient had another episode of desaturation with SPO2 dropping to 92%, with evidence of a shunt. Examination of the lungs revealed coarse crepitations over bilateral lower zones. His BP was 140/85, HR was 82 bpm, and arterial blood gas (ABG) showed type 1 respiratory failure with lactic acidosis. He received another bolus of IV frusemide 10 mg, and non-invasive ventilation (NIV) was initiated. An urgent portable chest X-ray was ordered, revealing features consistent with pulmonary oedema (Figure 2).

Consequently, the patient was admitted to the Intensive Care Unit (ICU) with a working diagnosis of unstable angina complicated with acute pulmonary oedema. In the ICU, his condition gradually improved on NIV, and on the same day of admission, he was successfully weaned to nasal prong O2 supplementation. Repeated chest X-ray revealed a picture of resolving pulmonary oedema (Figure 3). Serial bedside echocardiography and ECG showed no signs of acute myocardial ischaemia, and the patient's serial troponin I level remained static — not suggesting a cardiac aetiology of acute pulmonary oedema.

Ultimately, the patient was discharged from ICU on the second day of admission, and discharged from the hospital in stable condition on the fifth day of hospitalisation.

III. DISCUSSION

NPPO is an acute life-threatening perioperative complication. While establishing a definitive diagnosis may not immediately alter management, it plays a crucial role in avoiding harmful interventions, such as the inappropriate use of antiplatelet therapy in cases misdiagnosed as acute coronary syndrome (ACS). A precise diagnosis also ensures timely and targeted treatment, improving patient outcomes.

The classical description of the pathophysiology of NPPO involves the occurrence of acute pulmonary oedema following excessive negative intrathoracic pressure as a result of deep inspiration over an obstructed upper airway; in most cases, over a closed glottis [3,6]. Although the reported incidence of

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NPPO is low, it is likely underreported due to the difficulty in confirming the diagnosis, and to its typically rapid, self-resolving clinical course [7]. The aetiology of NPPO can be broadly classified into acute and chronic airway obstruction. Conditions leading to acute upper airway obstruction, such as post-extubation laryngospasm, croup, and epiglottitis, can predispose individuals to NPPO. On the other hand, chronic upper airway obstructions resulting from obesity, obstructive sleep apnoea, and any anatomical pathologies, may increase the risk of developing NPPO.

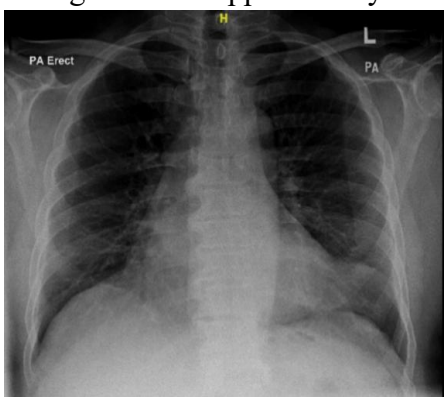

Figure 1. The patient was hemodynamically stable preoperatively, with normal oxygen saturation and a normal chest X-ray.

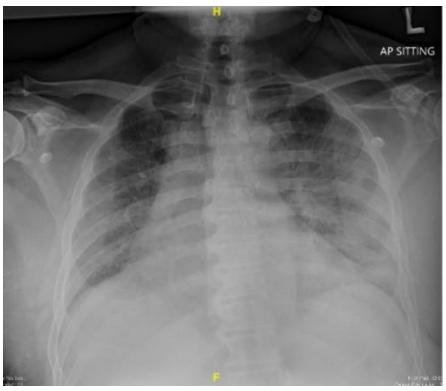

Figure 2. Postoperative portable X-ray of the same patient showing features consistent with pulmonary edema.

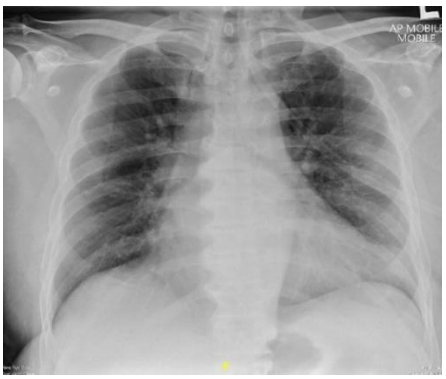

Figure 3. Chest X-ray in the ICU, 4 hours on NIV, showing a picture of resolving pulmonary edema.

Two mechanisms have been proposed to explain the pathogenesis of NPPO [3,7]. Oswalt and colleagues (1977) proposed that the sudden fluctuations in intrathoracic pressure result in significant fluid shifts [8]. This is described as a combination of increased preload and afterload, in addition to a decrease in pulmonary interstitial pressure, ultimately leading to a substantially high hydrostatic pulmonary pressure gradient. According to Starling forces, this results in transudation of fluid into the interstitium from the pulmonary capillary [6]. West and colleagues (1992) described the concept of wall stress failure more than 30 years ago [9]. The increase in transmural pulmonary capillary pressure leads to disruption of the alveolar-capillary membrane, increasing the permeability and resulting in high-protein pulmonary oedema. It is important to understand the possible pathogenesis to ensure a targeted management plan. In this case, a cardiogenic cause of acute pulmonary oedema (APO) was the primary differential diagnosis, in view of the patient's high revised cardiac risk index (RCRI). This was subsequently ruled out, based on serial biochemical markers and ECG findings. Given the risks associated with initiating antiplatelet therapy immediately post-operatively, and observing that the patient's condition improved significantly with NIV support, the decision was made to withhold antiplatelets unless ACS was definitively confirmed. However, statin therapy was promptly resumed in line with standard recommendations.

Another differential considered was inadequate reversal of the neuromuscular blockade. Although the patient demonstrated clinically adequate recovery prior to extubation, perioperative neuromuscular function was not quantitatively monitored, either intraoperatively or during the event. Clinical assessments alone may be inadequate, as evidence suggests that a substantial proportion of patients who seem clinically recovered do not achieve a train-of-four ratio (TOFR) >90%, which poses a significant risk for unsafe extubation [10]. Consequently, we cannot completely exclude residual paralysis or recurarisation in this case. The use of specific reversal agents, such as sugammadex, also warrants discussion, as there have been isolated reports of NPPO following its administration [11]. This underscores the importance of perioperative neuromuscular monitoring, especially in high-risk patients, to minimise avoidable complications.

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Other potential differential diagnoses which were considered include tracheal aspiration and anaphylaxis. In this case, tracheal aspiration was unlikely as the patient was adequately fasted and was extubated awake at the end of anaesthesia. Similarly, the absence of cutaneous allergic rash, mucosal angioedema, rale, or haemodynamic instability excluded the possibility of anaphylaxis [3,4].

In this patient, several clinical findings supported the diagnosis of NPPO, including respiratory distress at extubation, significant hypoxia, coarse crepitations on auscultation, and radiographic evidence of pulmonary oedema on chest X-ray [7]. The patient's underlying obesity and possible history of obstructive sleep apnoea further increased the likelihood of NPPO. Negative findings, such as normal sequential troponin levels and the absence of regional wall motion abnormalities on bedside echocardiography, helped to exclude cardiogenic causes.

Ultimately, NPPO remains a diagnosis of exclusion. It is crucial to systematically rule out other differentials requiring immediate specific management, such as myocardial infarction, while avoiding inappropriate and potentially harmful treatments.

Careful precautions were taken to minimise the perioperative cardiac and pulmonary risk in our patient, who was identified as high risk due to obesity with possible OSA and a high RCRI. Multimodal analgesia including IV lignocaine, IV opioids, IV dexamethasone, IV paracetamol, inhalational nitrous oxide, and regional anaesthesia, was employed to blunt sympathetic reflexes during intubation and surgical stimulation. These measures, alongside careful intraoperative haemodynamic management and a controlled extubation process, aimed to reduce myocardial oxygen demand while maintaining adequate coronary perfusion. Fluid administration was carefully monitored to avoid overload, and multimodal analgesia, supplemented by a regional block technique, ensured optimal pain control. Additionally, muscle relaxant recovery was assessed clinically prior to extubation, although quantitative neuromuscular monitoring was not performed. These strategies were designed to optimise the balance between myocardial oxygen supply and demand.

However, the question remains: could anything have been done differently to prevent this incident? One key area for improvement is the use of neuromuscular monitoring to objectively assess the adequacy of muscle relaxant recovery, especially given the unpredictable pharmacokinetics in obese patients. Quantitative monitoring could have provided a more reliable assessment, reducing the risk of inadequate recovery or residual neuromuscular blockade.

Several authors have suggested techniques to prevent NPPO. The strategies described include use of IV dexamethasone, IV lignocaine, and low-dose IV propofol prior to extubation [1,3,7]. The lesson from this case is early identification of risk factors and vigilant monitoring perioperative to facilitate prompt and effective management.

The use of sugammadex in patients with high RCRI has been advocated as it allows avoidance of anticholinergic agents which would undoubtedly cause tachycardia [12]. However, some case reports have noted NPPO following reversal with sugammadex [11]. It was postulated that there is a difference in the reversal time of upper airway muscles and the diaphragm. Therefore, NPPO develops when there is rapid recovery of respiratory forces in the presence of upper airway collapsibility [11]. This highlights the complexity of managing high-risk patients and the need for tailored approaches to optimise outcomes while mitigating risks.

Management

The general management of NPPO is similar to that of cardiogenic pulmonary oedema, targeted to correct hypoxia, with addition measures to correct upper airway obstruction [1]. The specific management of NPPO includes the application of CPAP by means of NIV or, in rare cases, reintubation [1,6,13,14]. CPAP will reverse the fluid shift by reducing the fluctuation in transmural pulmonary

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capillary pressure.

The use of loop diuretics, specifically frusemide, has been widely reported in case reports and case series on NPPO. Despite its common use, unlike in cardiogenic pulmonary oedema, evidence of its benefit in NPPO is scarce [3,7]. Our argument for its use would be its effect in reducing preload and afterload, which would then reduce the hydrostatic pulmonary pressure gradient [15].

In this case, CPAP was applied via non-invasive ventilation (NIV), and titrated boluses of frusemide were administered. The patient showed rapid clinical improvement while further investigations were carried out to establish a definitive diagnosis. Antiplatelet therapy was deliberately withheld after carefully weighing the benefits against the risks of bleeding, a decision ultimately justified as acute coronary syndrome (ACS) was ruled out. Overall, the management approach was appropriate for immediate intervention and could serve as a reference for developing a structured algorithm for perioperative APO.

IV. CONCLUSION

Diagnosing NPPO remains a challenge clinically, especially in patients with multiple comorbidities. The aetiology and pathophysiology have been well described, allowing for early identification of patients at risk. We advocate vigilant perioperative monitoring in such patients, with mandatory neuromuscular monitoring where available. With early diagnosis, targeted management of airway reestablishment and oxygenation by positive airway pressure are essential to prevent complications while avoiding unnecessary interventions that could potentially cause harm.

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