CASE REPORT

Postoperative diffuse alveolar haemorrhage: insidious negative pressure or sevoflurane induced?

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SUMMARY

Negative pressure pulmonary oedema is well described in the literature as an uncommon but recognised complication of general anaesthesia; negative pressure diffuse alveolar haemorrhage is a rarer consequence. We report a case of massive haemoptysis following elective general anaesthesia using a laryngeal mask airway device and sevoflurane anaesthetic maintenance. The patient had no obvious signs of laryngospasm or other cause of upper airway obstruction perioperatively. We explore the possibility that the haemoptysis was caused by clinically unapparent negative pressure generation, but also ask whether the anaesthetic agent should be considered as a culprit.

BACKGROUND

Negative pressure pulmonary oedema complicates 0.05% – 0.1 % of general anaesthetics¹; and a much smaller number of cases of negative pressure diffuse alveolar haemorrhage have also been described.^{2–8} There have been surprisingly few previously described occurrences of negative pressure pulmonary oedema following laryngeal mask airway (LMA) rather than endotracheal tube use,⁷ and no reported cases of negative pressure alveolar haemorrhage in these circumstances. There have also been four isolated case reports of haemoptysis following inhalational general anaesthesia, without any clinical indication of negative pressure generation.^{7–10} Only two of these cases^{7,10} directly attributed the haemoptysis to the gas, and peer review in one case questioned whether insidious negative pressure generation may in fact have been a more likely explanation, even in the absence of an obvious airway obstruction or period of paradoxical breathing. However, as further cases such as ours are published showing an increasing number of similar incidences of large-volume haemoptysis with no obvious trigger except for the use of sevoflurane vapour; one must begin to consider the inhaled anaesthetic gas as a potential cause.

CASE PRESENTATION

A healthy 31-year-old muscular Asian male with a medical history significant only for well-controlled type 1 diabetes mellitus, was admitted for an elective haemorrhoidectomy. He had no significant respiratory history, was a non-smoker and denied any illicit drug use. Preoperative examination was unremarkable. Anaesthesia was induced with propofol and fentanyl, and an LMA was

introduced; anaesthetic effect was maintained with sevoflurane gas. The patient was not paralysed, and ventilated spontaneously from early in the operation. Other than some high tidal volume inspirations early in surgery, attributed to painful stimuli and settling with further opioid analgesia, there was nil of note during the intraoperative period. The patient awoke, and the LMA was removed in theatre without any apparent trauma or cause for concern.

While in recovery, the patient acutely desaturated and developed marked respiratory distress. He was immediately commenced on 15 L oxygen via a non-rebreather mask, and oxygen saturations were then recorded at 85%, with a respiratory rate of 8 breaths/min. There was no apparent period of airway obstruction. After supporting respiration with a bag/valve/mask and continuing high-flow oxygen, saturations picked up to 100%. The patient then had a significant episode of haemoptysis (estimated at approximately 200 mL); and then two further episodes of approximately 100 mL each over the next hour.

Examination of the chest revealed right basal coarse inspiratory crepitations, and the patient continued to require high-flow oxygen to maintain oxygen saturations of around 94%. An urgent chest radiograph showed bilateral widespread patchy shadowing, reported as most inkeeping with diffuse alveolar haemorrhage (DAH) or pneumonitis. He was transferred to the high dependency unit (HDU) for monitoring.

INVESTIGATIONS

Blood tests showed a haemoglobin drop from 16.2 g/dL preoperative to 12.7 g/dL, with a haematocrit drop from 47% to 37%, and an unremarkable coagulation screen (fibrinogen 3.36 g/L, prothrombin time 12.1 s, activated partial thromboplastin time 24.7 s) and platelet count ($196 \times 10^9/L$).

DIFFERENTIAL DIAGNOSIS

The patient was transferred to the HDU for monitoring and conservative management. By the next day, there had been no further episodes of haemoptysis, and oxygen saturations were now 96% with 1 L of supplemental oxygen. We considered the possible causes of his presentation; our differential diagnoses included negative pressure-associated DAH, sevoflurane-associated lung injury, airway trauma, an arteriovenous malformation, a connective tissue disease or a vasculitic

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process, such as Wegeners granulomatosis or Goodpasture's syndrome.

A CT scan that day confirmed multifocal air space opacification throughout both lungs, reported as consistent with DAH. A nasal fluoroendoscopy found no upper airway source of bleeding, and a bronchoscopy showed frank blood throughout the small airways but no other abnormalities. A bedside echocardiogram showed normal cardiac valves and left ventricular function. Auto-immune and vasculitis screens were unremarkable (rheumatoid factor <20, antinuclear antibody, antinuclear cytoplasmic antibodies and glomerular basement membrane antibodies were all negative), and HIV and hepatitis tests also showed no infection.

TREATMENT

The patient remained stable and was transferred to a general medical ward the following day. He continued to be managed conservatively and had no further episodes of haemoptysis; by day 2 following the operation, he was able to maintain adequate oxygen saturations on room air. He was discharged home after a further 24 hours of observations, with a low threshold to return if he developed any further symptoms.

OUTCOME AND FOLLOW-UP

Our patient was followed up in clinic 6 weeks later and reported no further episodes of haemoptysis, good resolution of symptoms and a normal chest radiograph appearance.

DISCUSSION

This case interested us as the presentation did not fit clearly with a common diagnosis, and the massive haemoptysis with marked haemoglobin drop seemed to warrant a clear cause. Additionally, with number of cases now in the literature of large-volume haemoptysis where the use of sevoflurane anaesthetic gas seems to be the only common factor or potential cause, we felt it important to describe our patient's experience, as we consider whether this commonly used anaesthetic agent may be a causative factor in these presentations.

Initially, the most likely differential seemed to us to be negative pressure DAH which has been described in a handful of case reports.^{2-4 6-8} It has usually been described in conjunction with the more common phenomenon of negative pressure pulmonary oedema. However, the haemoptysis, in most of these cases, has followed an obvious episode of airway obstruction (laryngospasm^{5 6} or strangulation³), leading to negative pressure generation, and clinical evidence of pulmonary oedema. Additionally, the volumes of haemoptysis described in previous cases have been notably small, with no significant haemoglobin drops recorded. There have also been no previously recorded cases of negative pressure DAH in surgery using an LMA rather than an endotracheal tube.

Our patient did have some classic risk factors for laryngospasm: being a young, muscular male patient undergoing highly stimulating surgery; and negative pressure injury must certainly be considered a likely cause. However, with no evident period of airway obstruction, the mechanism is not clear-cut.

An alternative cause we considered was whether the gaseous agent used for the anaesthetic could have been the culprit. There are four published reports of DAH following anaesthesia with halogenated agents, with no obvious negative pressure event. The first was a large volume—approximately 1000 mL—haemoptysis in a 48-year-old following an uncomplicated anaesthetic for cataract surgery, with sevoflurane gas. The authors attributed the haemoptysis to possible coagulopathy/platelet dysfunction

secondary to the patient's end-stage renal disease, although there was no documented clotting abnormality in the patient's results.⁸ The second was in a 25-year-old following tonsillectomy with desflurane anaesthetic maintenance. The patient had severe chronic snoring, and the writers postulated that this may have weakened the alveolar wall to the degree that the physical pressure from the anaesthetic gases was then sufficient to injure the blood–gas barrier.⁴ In that case, the haemoptysis was large enough to drop the patient's haemoglobin from 13.7 to 6.8 g/dL. The third case was following surgery for a perirectal pilonidal cyst in a 31-year-old man, and the authors suggested the sevoflurane anaesthetic agent as the cause, without any other obvious contributory factors.⁷ Again, there was a large-volume haemoptysis, with a resultant haemoglobin fall from 14.4 to 12.1 g/dL. The fourth case described DAH in a 20-year-old man following an unremarkable anaesthetic (using sevoflurane vapour) for a cystoscopy and urethral stricture dilation, again with no other apparent cause for the haemorrhage, the authors in this case attributing the presentation directly to the use of sevoflurane vapour.¹⁰ The volume of haemorrhage or haemoglobin drop is not described in this case report. In all of the above reports, the patients were managed conservatively and had no further episodes of haemoptysis after the initial event, with good resolution of symptoms occurring without the need for further intervention.

The large-volume haemoptysis described in the first three of the latter cases are quite different from those published relating to an obvious negative pressure event with subsequent pulmonary oedema and associated small-volume haemorrhage. In all the large-volume haemoptysis cases, no mechanical incidents were observed. The mechanism by which inhalational anaesthetic agent may lead to DAH is not yet clear. Mechanisms suggested by previous writers include physical pressure from the anaesthetic gas injuring the very thin blood–gas barrier in the alveoli,⁴ pulmonary endothelial damage from the highly lipid-soluble anaesthetic potentiating the arachidonic cascade in the cell membrane causing increased oxidative stress and inflammatory response¹⁰ or an exothermic reaction (known to occasionally occur) between sevoflurane and the carbon dioxide absorbents in the anaesthetic circuit leading to thermal airway injury.¹⁰

With a number of cases now published in which DAH has occurred without an obvious obstructive precipitant, it would seem prudent to consider whether halogenated anaesthetic agents may also be a rare trigger for large-volume pulmonary haemorrhage. As such, if further anaesthesia is necessary in the future, our patient has been advised to avoid halogenated agents.

Learning points

- ▶ Diffuse alveolar haemorrhage is a rare complication of general anaesthesia, usually associated with an episode of airway obstruction and subsequent negative pressure pulmonary oedema.
- ▶ Presentations usually feature haemoptysis with acute respiratory distress, and widespread infiltrates are seen on chest radiography or CT scan.
- ▶ We must consider whether inhaled anaesthetic agents may rarely trigger diffuse alveolar haemorrhage, as a number of cases have now been reported without an obvious mechanical cause.

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REFERENCES

- 1 Louis PJ, Fernandes R. Negative pressure pulmonary edema. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;93:4–6.
- 2 Schwartz DR, Maroo A, Malhotra A, *et al.* Negative pressure Pulmonary hemorrhage. *Chest* 1999;115:1194–7.
- 3 Diab K, Noor A. Negative pressure pulmonary hemorrhage. *Respir Med CME* 2009;2:170–2.
- 4 Kim JP, Park JJ, Kim NJ, *et al.* A case of diffuse alveolar hemorrhage after tonsillectomy -A case report-. *Korean J Anesthesiol* 2012;63:165–8.
- 5 Mussi RK, Toro IF. Negative-pressure pulmonary edema and hemorrhage associated with upper airway obstruction. *Braslian Chest Journal*;200834.
- 6 Broccard AF, Liaudet L, Aubert JD, *et al.* Negative pressure post-tracheal extubation alveolar hemorrhage. *Anesth Analg* 2001;92:273–5.
- 7 Kim CA, Liu R, Hsia DW. Diffuse alveolar hemorrhage induced by sevoflurane. *Ann Am Thorac Soc* 2014;11:853–5.
- 8 Khanna AK, Kenneth KC. Pulmonary hemorrhage in an outpatient ophthalmic anesthesia setting— it's never "just a cataract". *Journey of Anaesthesiology* 2012;28:520–3.
- 9 Vandse R, Kothari DS, Tripathi RS, *et al.* Negative pressure pulmonary edema with laryngeal mask airway use: Recognition, pathophysiology and treatment modalities. *Int J Crit Illn Inj Sci* 2012;2:98–103.
- 10 Austin A, Modi A, Judson MA, *et al.* Sevoflurane Induced Diffuse Alveolar Hemorrhage in a young patient. *Respir Med Case Rep* 2017;20:14–15.

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