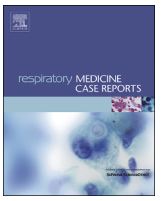
Respiratory Medicine Case Reports 45 (2023) 101906

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr



Case Report

Diffuse alveolar hemorrhage induced by inhaled Sevoflurane. Case report and literature review

Jaime H. Jordan [a], Santiago Pedroza [b], Einar S. Billefals [a], Gustavo Cruz [a, *]

[a] Fundación Valle del Lili, Departamento de anestesiología, Cra 98 No. 18 - 49, Cali, 760032, Colombia
[b] Fundación Valle del Lili, Centro de Investigaciones Clínicas, Cra 98 No. 18 - 49, Cali, 760032, Colombia

ARTICLE INFO

Handling Editor: DR AC Amit Chopra

Keywords:
Alveolar hemorrhage
Sevoflurane
Inhaled anesthetics
Anesthesia

ABSTRACT

Diffuse alveolar hemorrhage secondary to sevoflurane inhalation is a rare condition. It should be considered in postoperative patients presenting symptoms of hemoptysis, hypoxemia, or radiographic alveolar infiltrates. We present the case of a 42-year-old man who experienced a diffuse alveolar hemorrhage following sedation with sevoflurane during a low-risk orthopedic procedure. Initially, the patient presented hemoptysis, hypoxemia, and dyspnea. X-ray findings suggested alveolar hemorrhage and the diagnosis was confirmed with fiberoptic bronchoscopy. The patient improved under the care of the pulmonary service and was discharged. Early identification and management of this respiratory complication were crucial for a successful recovery.

1. Introduction

Diffuse alveolar hemorrhage (DAH) is a condition characterized by the accumulation of intra-alveolar red blood cells resulting from the rupture of the alveolar-capillary membrane [1]. The diagnosis of DAH is suspected in the presence of any of the classic triad findings, including hemoptysis, hypoxemia, and bilateral alveolar infiltrates on chest radiography [2]. This condition can impair gas exchange and lead to respiratory failure, which may be fatal [1]. While DAH is commonly associated with systemic vasculitis or connective tissue diseases, it can also occur as a result of isolated inflammation of the alveolar vasculature [3]. Therefore, it is important to investigate potential factors such as drug exposure or toxic inhalation [4].

We present a case of a 42-year-old man who developed spontaneous DAH following Sevoflurane inhalation during a low-risk orthopedic surgery.

2. Case report

A 42-year-old male patient with no significant medical history, ASA I, was scheduled for endoscopic decompression of the left carpal tunnel. Anesthetics used for the procedure included 1% propofol at a dose of 2 mg/kg, remifentanil using target-controlled infusion at a concentration of 3 ng/ml, fentanyl at 1 mcg/kg, and 2% sevoflurane with a gas flow rate of 1 L/min and a 50% oxygen-air mixture for maintenance, without any invasive airway devices. There were no signs of airway obstruction during the procedure, with assisted ventilation at a tidal volume of 6–8 ml/kg. Airway pressures were maintained between 18 and 22 cmH2O, and the respiratory rate was 12–16 cycles per minute.

The surgical procedure was successfully completed within a total duration of 20 minutes. In the recovery room, the patient experienced an episode of hemoptysis (approximately 100 ml of fresh blood) accompanied by mild desaturation (89%) and dyspnea. On

* Corresponding author.
E-mail address: gustavo.cruz@fvl.org.co (G. Cruz).

https://doi.org/10.1016/j.rmcr.2023.101906
Received 22 June 2023; Accepted 4 August 2023
Available online 6 August 2023

physical examination, the only positive finding was a bilateral inspiratory crackle detected upon chest auscultation. The patient denied any recent close contact with individuals exhibiting respiratory symptoms or any pertinent medical history. As an initial measure, a complete blood count (CBC) and a chest X-ray were requested, and oxygen therapy was initiated via nasal cannula (2 L/minute) to achieve oxygen saturation above 90%.

The CBC revealed severe lymphopenia (Table 1), and the chest X-ray showed bilateral perihilar alveolar infiltrates (Fig. 1). A chest CT angiogram was requested, revealing nodular opacities with a "ground-glass" density, suggestive of alveolar hemorrhage. There was no evidence of pulmonary thromboembolism or bronchial artery malformations.

A transthoracic echocardiogram was performed, which showed normal results, ruling out mitral valve pathology. Considering the presence of lymphopenia, HIV testing, and autoimmune diagnostic tests were conducted, all of which yielded negative results (Table 1). Subsequently, the patient was scheduled for a fiberoptic bronchoscopy, which identified findings consistent with acute endobronchitis and evidence of fresh blood within the airway. A bronchoalveolar lavage (BAL) was performed in the anterior basal segment of the lower lobe, resulting in the retrieval of 50 ml of hemorrhagic fluid. The BAL sample was sent for bacterial, mycobacterial, and fungal cultures, PCR for M. tuberculosis, cytology, and iron staining, all of which delivered negative results.

The patient was hospitalized under the care of the pneumology service and showed spontaneous improvement with the resolution of lymphopenia. There were no further episodes of hemoptysis, and the patient no longer required supplementary oxygen. Consequently, he was discharged with a follow-up appointment scheduled in one month.

Table 1
Diagnostic tests.

Test	Result
Red blood cells (x10^6/μL)	4.85
Hematocrit (%)	45%
Hemoglobin (g/dL)	16.2
MCV (fl)	93
Platelets (x10^3/μL)	207
White blood cells (x10^3/μL)	11.52
Neutrophils (x10^3/μL)	11.04
Lymphocytes (x10^3/μL)	0.34
NLR	32
ESR	5
ANAs	Negative
Proteinase 3 antibodies	Negative
Myeloperoxidase antibodies	Negative
HIV antibodies x2	Negative

MCV: Mean Corpuscular Volume**, NLR:** Neutrophil-to-Lymphocyte Ratio**, ESR:** Erythrocyte Sedimentation Rate, **INL:** Immature neutrophil fraction, **ESR:** Erythrocyte sedimentation rate, **ANAs:** Antinuclear antibodies.

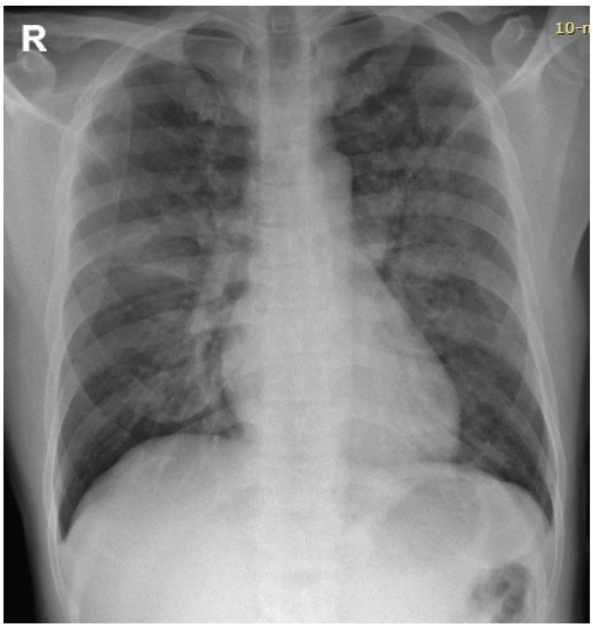


Fig. 1. Anteroposterior chest X-ray.

Table 2
Case reports of diffuse alveolar hemorrhage associated with sevoflurane inhalation.

Case	Sex and Age	Surgery	Presentation	Management	HSL
1 [7]	Male, 21 years	Left hip drainage	Dyspnea, hemoptysis, hypoxemia	NC oxygen, Antibiotics, IV methylprednisolone	3
2 [1]	Male, 31 years	PCE	Hypoxemia, hemoptysis	NC oxygen, IV methylprednisolone	3
3 [8]	Male, 31 years	HRTY	Hypoxemia, hemoptysis	NRM oxygen,	2
4 [9]	Male, 20 years	Cystoscopy + UD	AHRD, Hemoptysis	Reintubation	3
5 [6]	Male, 38 years	Open reduction of TF	AHRD, Anemia	Reintubation, Steroids	3
6 [10]	Male, 48 years	Cataract removal	AHRD	Reintubation	7
7 [2]	Male, 22 years	Mandibular surgery	Hypoxemia, hemoptysis	NC oxygen, IV methylprednisolone	3

HSL: Hospital stay length, **NC:** Nasal cannula, **IV:** Intravenous, **NRM:** Non-rebreather mask, **PCE:** Pilonidal cyst excision, **HRTY:** Hemorrhoidectomy, **UD:** Urethral dilation for stenosis, **TF:** Tibial fracture, **AHRD:** Acute hypoxemic respiratory distress.

3. Discussion

Our patient developed DAH without clinical or serological evidence of an underlying systemic disease. Given the immediate onset of symptoms following surgery, the absence of relevant medical history, and limited exposure to medications, the most likely causative agent was inhaled sevoflurane.

Sevoflurane is an inhalational anesthetic agent used for the induction and maintenance of general anesthesia. When metabolized, sevoflurane primarily produces two compounds: Compound A (fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether) and Compound B (1,1,1,3,3-Penta fluoro-2-(fluoromethoxy)-3-methoxy-propane) [5]. Compound A causes direct renal toxicity, and although the relationship between Compound A and pulmonary toxicity has not been studied, this toxic metabolite may be associated with damage to the alveolar-capillary membrane [6]. Additionally, it is known that other volatile gases can induce pulmonary inflammation and endothelial damage by activating the arachidonic acid cascade. Sevoflurane may have similar mechanisms, potentially increasing alveolar permeability, pulmonary vasoconstriction, and oxidative stress, ultimately triggering an inflammatory response [6].

Including our case, a total of 8 reports of HAD secondary to inhaled sevoflurane were found (Table 2). The clinical presentation in 5 patients consisted of hemoptysis and hypoxemia. Two of these cases (including ours) were managed solely with supplemental oxygen and conservative measures, while corticosteroids were administered in three cases. Three patients experienced acute hypoxemic respiratory distress (AHRD) requiring reintubation, with two of them receiving supplemental oxygen via mechanical ventilation and one patient receiving corticosteroids (Table 2). In all cases, patients were treated with supportive care and did not experience further episodes of hemoptysis after the initial event. They showed good symptom resolution and were discharged from the hospital without complications. Some similarities observed among the documented cases include a comparable age range, onset of respiratory symptoms around one-hour post-surgery, and the presence of male patients in all reported cases, including our own.

The reported cases underscore the clinical variability in sevoflurane-associated DAH, ranging from mild hypoxemia to AHRD. Consequently, prompt diagnosis and treatment are imperative for this condition. Bronchoscopy serves as the pivotal diagnostic tool for HAD, and the persistence of blood in three consecutive lavages from an affected lung area reinforces the diagnosis [3]. This procedure yields optimal results when conducted within the initial 48 hours. BAL samples should be subjected to routine cultures for bacteria, mycobacteria, fungi, and viruses. Initial assessments comprise chest X-ray and high-resolution computed tomography, providing corroborative evidence for the diagnosis and guiding subsequent fiberoptic bronchoscopy. Laboratory investigations encompass CBC, coagulation studies, renal function, and autoimmune testing [3,11].

Supportive measures constitute the cornerstone of HAD treatment, encompassing oxygen supplementation and mechanical ventilation with high positive end-expiratory pressure (PEEP) to attenuate capillary bleeding. High-dose corticosteroids are recommended to control the inflammatory response [11]. Coagulopathy requires vigilant monitoring, with a recommended platelet count exceeding 50,000/μL and an international normalized ratio below 1.5. In cases of persistent bleeding, various prothrombotic treatments, including antifibrinolytics such as tranexamic acid, have been described [3,11].

4. Conclusion

The possibility of sevoflurane-induced DAH should be contemplated in patients who manifest hemoptysis, hypoxemia, dyspnea, or radiological evidence of alveolar infiltrates subsequent to surgery, following the exclusion of other potential causes. Swift identification of the etiology and initiation of supportive treatment is essential for ensuring the patient's survival.

Statements

The study was submitted to the Ethics Committee of the Fundación Valle del Lili as case report No.684 on May 26, 2023 and was approved on June 03, 2023.

Statement of consent

The patient signed a consent form authorizing the publication of his case and the use of clinical pictures.

Funding

The authors declare no external funding for the study.

Declaration of competing interest

None of the authors have personal or financial relationships with organizations that may influence this article.

References

[1] Jean Hsieh, Michelle Gong, Diffuse Alveolar Hemorrhage Induced by Sevoflurane, American Thoracic Society, 2014, pp. 853–855.
[2] S.O. Yasli, F. Dogruel, A.E. Demirbas, D.G. Canpolat, A case of diffuse alveolar hemorrhage after orthognathic surgery: case report with the literature review, Niger. J. Clin. Pract. 25 (2022) 967–970, https://doi.org/10.4103/njcp.njcp_1869_21.
[3] J.A. Park, Treatment of diffuse alveolar hemorrhage: controlling inflammation and obtaining rapid and effective hemostasis, Int. J. Mol. Sci. 22 (2021) 1–18, https://doi.org/10.3390/ijms22020793.
[4] Gámiz Ana, Cabrero Celia, Martín Laura, Diffuse alveolar hemorrhage induced by inhalation of chemicals: a case report and review of the literature, Emerge (2021) 405–408.
[5] Bambarén Carlos, Melind Chu, Impacto ambiental del uso del gas anestésico inhalatorio sevoflurano en un hospital de Perú, Revista Med Herrera (2018) 147–151.
[6] O. Cengiz, A. Kivrak, M. Yegen, M. Demir, Sevoflurane induced diffuse alveolar haemorrhage in a young patient after orthopedic surgery: a case report, Niger. J. Clin. Pract. 23 (2020) 120–122, https://doi.org/10.4103/njcp.njcp_51_19.
[7] M. Ahmed-Khan, K. Moin, C. Funk, Sevoflurane-induced diffuse alveolar hemorrhage, Archive of Clinical Cases 10 (2023) 29–31, https://doi.org/10.22551/2023.38.1001.10235.
[8] R. Mersh, C. Ross, Postoperative diffuse alveolar haemorrhage: insidious negative pressure or sevoflurane induced? BMJ Case Rep. 2018 (2018), https://doi.org/10.1136/bcr-2017-222010.
[9] A. Austin, A. Modi, M.A. Judson, A. Chopra, Sevoflurane induced diffuse alveolar hemorrhage in a young patient, Respir Med Case Rep 20 (2017) 14–15, https://doi.org/10.1016/j.rmcr.2016.11.001.
[10] A.K. Khanna, K.C. Cummings, Pulmonary hemorrhage in an outpatient ophthalmic anesthesia setting it's never "just a cataract.", J. Anaesthesiol. Clin. Pharmacol. 28 (2012) 520–523, https://doi.org/10.4103/0970-9185.101947.
[11] A.R. Lara, M.I. Schwarz, Diffuse alveolar hemorrhage, Chest 137 (2010) 1164–1171, https://doi.org/10.1378/chest.08-2084.