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Case Report

Diffuse Alveolar Hemorrhage from Sevoflurane Toxicity

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Abstract

A twenty-year-old male was admitted with hemoptysis and respiratory failure after orthopedic surgery. Based on imaging and bronchoscopy, he was diagnosed to have diffused alveolar hemorrhage. After complete evaluation it was determined to be caused by sevoflurane, an inhaled volatile halogenated gas. He was managed conservatively and recovered well.

Keywords: Diffuse alveolar hemorrhage; Drug toxicity; Thoracic imaging; Hemoptysis; Respiratory failure

Background

Diffuse Alveolar Hemorrhage (DAH) is a serious pulmonary syndrome characterized by hypoxemia, pulmonary infiltrates, anemia and often hemoptysis. DAH can be caused by an immune-mediated or nonimmune-mediated process [1]. We describe a case of DAH caused by sevoflurane, an inhaled volatile halogenated gas.

Case

A twenty-year-old male without any past medical history presented to the emergency room for hemoptysis and hypoxemia. He had shoulder tendon repair surgery 4 hours prior. The procedure was performed under general anesthesia, and hemoptysis had started immediately after extubation. It was intermittent, small volume, and persistent at the time of initial evaluation. He also complained of mild dyspnea. He denied wheezing, chest pain, pleuritic symptoms, syncope, leg swelling or pain.

The induction and maintenance of anesthesia were provided with halogenated anesthetic, sevoflurane. Fentanyl and midazolam were also used during endotracheal intubation.

The patient was a college-athlete with no history of smoking, vaping or recreational drug use. There was no history of bleeding diathesis, hematologic disorder or pulmonary disease. He was not on anticoagulation or anti-platelet agents. Family history was limited to a maternal aunt with Systemic Lupus Erythematous (SLE).

Vital signs were a pulse rate of 106 beats/min, respiratory rate 24 breaths/min, pulse oximetry of 96% on 4 liters/min of nasal cannula. Other than a leukocytosis of 13,500 with neutrophilic predominance, renal function and coagulation measures including INR and PTT were within normal limits. Chest radiograph showed bilateral interstitial opacities more prominent centrally with clear costophrenic angles (Figure 1). Computed tomography (CT) chest demonstrated centrilobular ground glass opacities bilaterally with a predominantly central and upper lobe distribution (Figure 2).

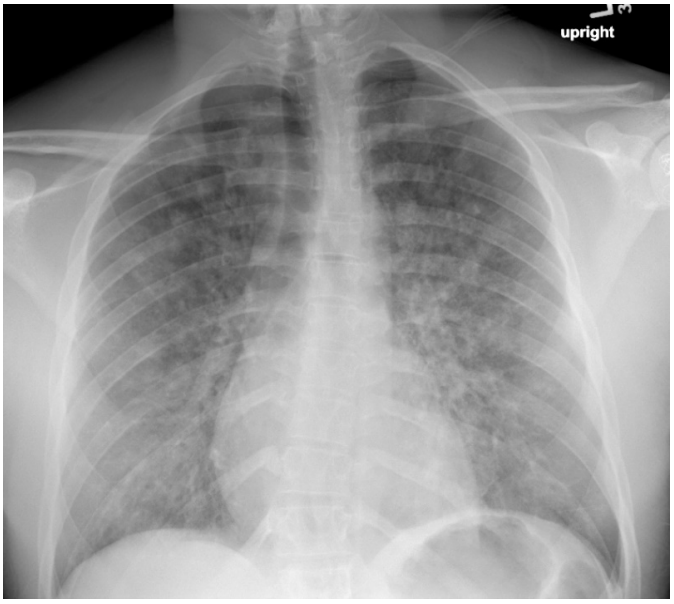

Figure 1: Chest radiograph demonstrating bilateral predominantly central opacities involving upper lobes. No pleural effusion or cardiomegaly noted.

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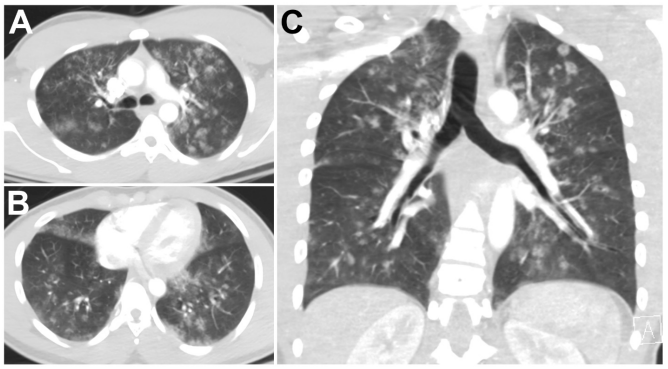

Figure 2: CT chest axial (A,B) and coronal (C) views demonstrating bilateral centrilobular ground glass opacities with central and upper lobe predominance.

Differentials included airway trauma during endotracheal intubation, pulmonary vascular disease including pulmonary embolism and pulmonary parenchymal source such as DAH. Bronchoscopy ruled out airway injury. There was progressive hemorrhagic return on subsequent aliquots on bronchoalveolar lavage confirming the diagnosis of DAH. On cell count, 525 white blood cells (WBC) were noted with 69% neutrophils, 20% lymphocytes, and 10% macrophages. Further workup including ANCA levels and Connective Tissue Disease (CTD) serologies was unrevealing. Moreover, urinalysis did not show protein, blood or active sediment on microscopy. Echocardiogram was unremarkable.

In the absence of an alternative etiology for DAH, the patient was diagnosed with sevoflurane-induced DAH. He was managed conservatively with supplemental oxygen and monitored 24 hours after bronchoscopy. No glucocorticoids were administered. The patient improved with resolution of hemoptysis and hypoxemia at rest and during exercise.

Discussion

Sevoflurane is an inhaled halogenated gas that is utilized for induction and maintenance of anesthesia. It is ideal due to its rapid onset of action and short washout time [2]. Alternate halogenated gases used for this purpose include desflurane which is thought to have a faster recovery time [3].

Sevoflurane induced DAH is extremely rare with only three cases reported in literature [4-6]. Desflurane has also been implicated in one reported case [4]. Patients are usually young in their 20's and 30's and thus far all reported patients have been males. Presentation includes hypoxemia which may be accompanied by hemoptysis as in our case, typically immediately after surgery or extubation. Chest radiograph findings typically demonstrate interstitial opacities centrally distributed, clear costophrenic angles and absence of cardiomegaly. CT chest shows ground-glass opacities and/or patchy areas of consolidation with central and upper lobe predilection [4,5,7]. Bronchoscopy with Bronchoalveolar Lavage (BAL) may be needed to diagnose DAH and rule out other causes.

DAH is thought to occur from capillaritis, bland pulmonary hemorrhage or diffuse alveolar damage [1,8]. Capillaritis is vascular injury to the pulmonary capillary endothelial membrane that leads blood to enter the alveolar spaces. It may be caused by primary and secondary forms of vasculitis. Bland pulmonary hemorrhage is caused by leaking of red blood cells into the alveolar space in the absence of any vascular injury. Causes include mitral stenosis, pulmonary veno-occlusive disease and anticoagulation. Diffuse alveolar damage occurs from direct lung injury in the absence of primary vascular damage. It is often associated with hyaline membranes. Causes of diffuse alveolar damage include acute respiratory distress syndrome and inhalational injury [8].

We suspect that bland pulmonary hemorrhage is the likely mechanism of injury in sevoflurane-induced DAH. This is supported by the rapid onset and the quick clinical and radiographic resolution typically seen even without pharmacologic therapy. In our case, other inflammatory processes such as vasculitis were excluded.

It is reported that a sevoflurane metabolite, fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether may cause renal toxicity [9] although there is no direct evidence that this can also cause pulmonary endothelial injury. Volatile gases are also lipophilic and can trigger the arachidonic cascade that may cause alveolar permeability and increased oxidative stress leading to DAH [10]. CRP was elevated in our patient as was reported by Kim JP et al., although the pro-inflammatory state secondary to recent surgery makes interpretation difficult [7].

Our patient was managed conservatively with supportive management and supplemental oxygenation. In the three previously described cases, two were managed with systemic steroid therapy. The patient who required endotracheal intubation did not receive systemic steroids although was liberated from mechanical ventilation in three days [4-6]. Kim et al. utilized methylprednisolone 1 gram daily for 3 days while Cengiz et al. used methylprednisolone 500 mg on day #1 and 80 mg daily on day #2-3 [4,5]. Rapid radiographic resolution was seen in all previously reported cases.

Conclusion

We describe a case of sevoflurane induced DAH, a recently described disease affecting young males, leading to DAH and hypoxemic respiratory failure. While more cases need to be described in literature, this entity appears to be self-limiting although systemic glucocorticoids have been used.

Conflict of Interest

The authors have no conflict of interest, Informed consent was obtained from the patient.

Author Contributions

All authors meet ICJME authorship criteria.

Contributor NAK was responsible for gathering data, organization and coordination of the manuscript. Authors NAK, KD and IMA were all involved in the writing of the manuscript including reviewing and editing the manuscript.

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