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Diffuse Alveolar Hemorrhage Induced by Sevoflurane

Sevofluran ile İndüklenen Diffüz Alveolar Hemoraji

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Abstract

We present here a case of diffuse alveolar hemorrhage (DAH) following exposure to inhaled anesthetic sevoflurane. A 29-year-old male was admitted to the plastic surgery department with gynecomastia. Surgery was performed without complication under general anesthesia with intravenously administered midazolam (4mg), fentanyl and inhaled sevoflurane. Immediate hypoxemia and massive hemorrhage was detected at the end of the operation, and a chest radiography revealed bilateral widespread alveolar infiltrates. The serum hemoglobin level dropped by 2.5 g/dl (from 13 to 10.5 gr) in the postoperative setting. The patient was treated with methylprednisolone (1 gr) administered intravenously daily for 3 days. The hypoxemia resolved and alveolar infiltrates on the chest radiograph disappeared on the 4th day. There is limited data in literature reporting on the association between sevoflurane and DAH. None of the predisposing factors or causative reasons for DAH were detected in our case, and so it can be concluded that the use of sevoflurane as an inhaled anesthetic was responsible for the DAH.

Key words: *Alveolar hemorrhage, sevoflurane, anesthesia.*

Öz

İnhale anestezik sevoflurana maruz kaldıktan sonra yaygın alveolar hemoraji (DAH) gelişen bir olguyu sunmayı amaçladık. Burada sunulan hasta, jinekomasti nedeniyle plastik cerrahiye başvuran 29 yaşında bir erkek idi. Genel anestezi altında intravenöz midazolam (4mg), fentanil ve inhale sevofluran ile komplikasyonsuz cerrahi uygulandı. Ameliyat sonunda ani hipoksemi ve masif kanama tespit edildi. Akciğer grafisinde bilateral yaygın alveolar infiltratlar görüldü. Ameliyat sonrası dönemde serum hemoglobin düzeyi 2,5 g/dl (13'ten 10,5 gr'a) düştü. Hastaya 3 gün süreyle intravenöz olarak günlük metilprednizolon (1 gr) tedavisi verildi. Dördüncü günde hipoksemi düzeldi ve akciğer grafisinde alveolar infiltratlar kayboldu. Literatürdeki sınırlı veriler, sevofluran ve DAH arasında bir ilişki olduğunu göstermektedir. Bizim olgumuzda DAH' gelişimine neden olan sebepler ve zemin hazırlayan faktörlerin hiçbiri saptanmadı. Bu nedenle, DAH'dan inhale anestezik olarak sevofluran'ın sorumlu olduğu düşünülmektedir.

Anahtar Sözcükler: *Alveolar hemoraji, sevofloran, anestezi.*

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Diffuse alveolar hemorrhage (DAH) is a rare clinical syndrome that presents in different clinics ranging from a small amount of hemoptysis to life-threatening massive hemoptysis. While connective tissue disorders such as immune-mediated systemic vasculitis, Wegener's granulomatosis and cytotoxic drugs may play a role in its etiology, the exact pathogenesis is not yet known. (1) We reported here a case of DAH attributed to the use of inhaled anesthetic sevoflurane during a gynecomastia operation.

CASE

We present here the case of a 29-year-old male who was admitted to the plastic surgery department due to gynecomastia. His preoperative history, physical examination and laboratory values were unremarkable. The patient was New York Heart Association class I, and was monitored with ECG, pulse oximetry (oxygen saturation) and noninvasive blood pressure. Arterial blood pressure was 130/80 mmHg; Oxygen saturation was 98%, and his heart and respiratory rate at baseline were 90 beats per minute (bpm) and 15 breaths per minute (rpm), respectively. Midazolam 1mg, lidocaine 1 mg/kg, thiopental 7mg/kg, rocuronium 0.6mg/kg and remifentanil 0.5 mg/kg were given to induce anesthesia and intubation was performed. Anesthesia was maintained with 0_2 (%50), air (%50) sevoflurane (%3) and remifentanil 0.125 mg/kg/min. Synchronous Intermittent Mandatory Ventilation was maintained with tidal volume of 500 mL, a respiratory rate of 12 rpm and an inspiration/expiration rate of 1/2. Positive end-expiratory pressure (PEEP) was not applied. Peak inspiratory pressure (P peak) was maintained at 14–16cm H_20. During the intubation and post-intubation, the patient's P peak and Plateau pressure did not reach 30 cm H_20. After 40 minutes from the start of anesthesia, the surgery was completed without complication.

Hemorrhage in the endotracheal tube was detected at the end of the operation, when his vital signs were recorded as blood pressure 110 /70 mmHg, temperature 36.4°C, heart rate 88/min and respiratory rate 32/min. The patient was extubated after the hemorrhage was controlled. Following extubation, the patient experienced a massive hemorrhage and immediate hypoxemia, and was transferred to the intensive care unit (ICU), where he was followed-up extubated. Arterial blood gas tension was measured at pH 7.39, $PaCO_2$ of 40.1 mm Hg and $Pa0_2$ 49.5 mm Hg, with a saturation of 89%. Chest radiography revealed bilateral widespread alveolar infiltrates, and bilateral, centrally located ground-glass opacities were noted on a computed tomographic angiography of the chest, and pulmonary embolism was excluded (Figure 1). The serum hemoglobin level dropped by 2.5 g/dl (from 13 to 10.5 gr) in the postoperative setting. The platelet count was 154,000/μl, prothrombin time/ international normalized ratio was 11.6 seconds/1.0, and partial thromboplastin time was 24.8 seconds.

Serological testing was negative for HIV, viral hepatitis, vasculitis and connective tissue diseases (Antinuclear antibody, Anti glomerular basement membrane antibody, Anti-JO1, Anti- DS DNA, Anti –SSA, Anti-SSB, Anti – SCL70, Anti- SM/RNP, CCP, PANCA, cANCA), and a urinalysis was normal. Daily methylprednisolone (1 gr) treatment was administered intravenously for 3 days, and the hypoxemia resolved and the alveolar infiltrates on chest radiograph disappeared on the 4th day. Flexible bronchoscopy has been evaluated and confirmed that was no abnormality in the bronchial system. A bronchoalveolar lavage cell count revealed polymorphonuclear cells 2.9%; lymphocytes 1.1%; and alveolar macrophages 56%. The patient has no signs or symptoms related to recurrence 4 months after recovery.

DISCUSSION

DAH has a wide clinical spectrum with the potential for massive hemoptysis as well as asymptomatic radiologic abnormalities. The majority of patients have a history of hemoptysis, and decreased hemoglobin should serve as a warning to physicians of the possibility of DAH. Patchy, focal or diffuse alveolar filling processes can be seen on chest radiography and CT. Bronchoscopy should be performed to exclude other causes of hemoptysis and to establish a clinical diagnosis of DAH. Progressive hemorrhagic BAL found in serial samples is diagnostic for DAH. (1) In our case, the serum hemoglobin level dropped by 2.5 g/dl. Clinical, bronchoscopic and radiographic evaluations have been shown to confirm DAH and exclude any other specific causative etiologies.

An inhalational anesthetic agent sevoflurane is used for induction and maintenance of general anesthesia. Given the immediate postoperative onset of alveolar hemorrhage without reason, we can conclude that the causative agent was inhaled sevoflurane. Alveolar hemorrhage occurs in only a small number of cases, although sevoflorane is associated with a number of respiratory side effects, including cough, apnea, laryngeal spasm and respiratory depression.

Lipid soluble volatile gases may increase alveolar permeability by enhancing the arachidonic cascade in the cell membrane, and increased oxidative stress and increased inflammatory response (2,3), and previous studies have suggested that the mechanism of sevoflurane causing DAH may be related to this (4,5). Sevoflurane has also been shown to inhibit platelet function and to reduce platelet aggregation rates (6,7).

There is limited questionable data suggesting that sevoflurane can induce alveolar hemorrhage (4,8,9), and in the three previously-reported cases, the DAH was attributed to the other causes. In the first case the patient had a history of end-stage renal disease and cocaine use; the patient had obstructive sleep apnea in the second case, which can increase airway pressure (4,8); and the third case was reported to show possible relationships between sevoflurane and DAH with concurrent marijuana use (9). The suggestion of this study is controversial, however, as marijuana use has been previously reported as a causative agent for DAH (9,10). In the above reports, the association between drug use and DAH remains speculative. Given the risk of airway obstruction in their patients, Mersh et al. (11) and Hao et al. (12) both suggested that alveolar hemorrhage may be due to negative pressure pulmonary edema together with sevoflurane. In only two cases were none of the predisposing factors or causative reasons for DAH made available, as in our patient. Austin et al. (5) reported on a young male who underwent urethral stricture dilation via cystoscopy, while Cengiz et al. (13) reported on a young male who underwent orthopedic surgery. Interestingly, all of the above patients were young 20–40-year-old males.

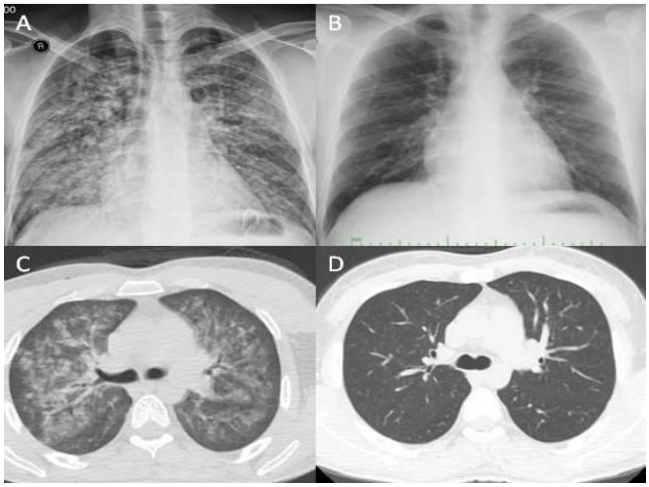

Figure 1: *Chest x-ray and CT showing bilateral infiltrates at initial presentation* ***(a, c)****, Chest x-ray and CT 3 days after pulse steroid* ***(b, d)***

CONCLUSION

It can be concluded that the inhaled anesthetic drug sevoflurane was the responsible agent that induced DAH in our case, given the absence of any other disease or administered agent. Although the mechanism of sevoflurane-causing DAH cannot be fully clarified, it should be kept in mind as the cause of life-threatening DAH.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - B.P.Y., D.G.H., F.O.K.; Planning and Design - B.P.Y., D.G.H., F.O.K.; Supervision - B.P.Y., D.G.H., F.O.K.; Funding - B.P.Y., D.G.H.; Materials – F.O.K., B.P.Y.; Data Collection and/or Processing - F.O.K.; Analysis and/or Interpretation - B.P.Y., D.G.H.; Literature Review - D.G.H., B.P.Y.; Writing - D.G.H., B.P.Y.; Critical Review - B.P.Y.

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