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Cold-induced Bronchospasm during Coronary Artery Bypass Surgery

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SEVERE bronchospasm during anesthesia and surgery can be life-threatening, and, fortunately, the incidence is low.[1] The few reported cases of bronchospasm during cardiac surgery have been noted to occur at termination of cardiopulmonary bypass (CPB), after patient rewarming. We report the case of a patient with asthma who developed severe bronchospasm associated with patient cooling during CPB, and we suggest an additional therapeutic modality in the treatment of intraoperative bronchospasm.

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Case Report

A 64-yr-old, 82-kg woman presented with a 6-month history of worsening exertional angina and dyspnea on exertion. There was no history of orthopnea, paroxysmal nocturnal dyspnea, ankle edema, or myocardial infarction. Other medical history was significant for well controlled hypertension, noninsulin-dependent diabetes, retinal hemorrhage, and a 30-yr history of asthma. Because her asthma was worsened by cold weather, she regularly spent the winter in the warmer climates. She had been treated with β-agonist inhalers for many years and had received an aminophylline preparation, but not for the last year. Her last asthma attack was 8 months before admission and was relieved by the use of a β-agonist inhaler. She never required tracheal intubation to treat her asthma and did not report recent upper or lower respiratory infections. She was allergic to penicillin and iodine, with an allergic manifestation to both of a rash, and not bronchospasm. Her preoperative medication included albuterol and beclomethasone inhalers, glipizide, diltiazem, enalapril and a nitroglycerin patch. Although she had never received systemic steroids

previously, prednisone (30 mg/day) was started by her pulmonologist prophylactically 1 week before surgery. Her surgical history included a hysterectomy and tonsillectomy under general endotracheal anesthesia without difficulty. She was now admitted for coronary artery bypass graft surgery.

Physical examination revealed a moderately obese woman in no distress. Her blood pressure was 160/100 mmHg, heart rate 76 beats/min, and respiratory rate 16 breaths/min, and she was afebrile. Her lungs were clear except for a mild expiratory wheeze in the mid right lung field that cleared with coughing. The cardiovascular examination results were within normal limits.

Preoperative laboratory study results, including chest x-ray and electrocardiogram, were normal. Pulmonary function tests revealed moderate obstructive airway disease with a forced vital capacity of 2.24 L (73% predicted) and a forced expiratory volume in 1s of 1.20 L (60% predicted) without significant improvement with bronchodilators. Cardiac catheterization revealed a left ventricular ejection fraction of 70%, with lesions in the left anterior descending, right, obtuse marginal 1, obtuse marginal 2, and diagonal coronary arteries.

In addition to her usual medications (except Glipizide), the patient was premedicated with 7 mg morphine sulfate intramuscularly; and 2 mg lorazepam, 150 mg ranitidine, and 10 mg metoclopramide orally. At arrival to the operating room, the chest was clear to auscultation. A 14-G peripheral venous catheter, right internal jugular oximetrix pulmonary artery catheter, and a 18-G right radial arterial catheter were inserted preinduction. She then received 1 g cefazolin by slow intravenous injection (the cefazolin infusion was completed at least 2 h before the development of any bronchospasm). She demonstrated no reaction to the cefazolin, and her lungs remained clear to auscultation. Vital signs preinduction were blood pressure 170/90 mmHg, heart rate 75 beats/min, pulmonary artery pressure 30/10 mmHg.

Anesthesia was induced with 35 μg/kg fentanyl, 3 mg midazolam, 1% enflurane, and 20 mg vecuronium. After tracheal intubation, the lungs were mechanically ventilated with tidal volume 800 ml, respiratory rate 10 breaths/min, inspiratory:expiratory ratio 1:2.5, and inspired oxygen concentration 100%. Her lungs were clear to auscultation, and peak inspiratory pressure was 25 cmH_2O. Arterial blood gas analysis revealed *p*H 7.50, arterial carbon dioxide tension 36 mmHg, and arterial oxygen tension 507 mmHg. An esophageal stethoscope/temperature probe, Foley catheter with temperature probe, and a transesophageal echocardiogram probe were placed after induction. Echocardiographic examination revealed 1+ mitral regurgitation and normal left and right ventricular function. Hydrocortisone (100 mg) was given after induction. Before bypass, anesthesia was maintained with additional fentanyl (4.5 mg) to a total of 92 μg/kg, enflurane (0.5–1%), vecuronium (20 mg), and midazolam (additional 2 mg). The patient remained hemodynamically stable before CPB without wheezing. The peak inspiratory pressures remained at 25 cmH_2O. The patient received 35,000 U heparin, and CPB was begun using a membrane oxygenator. The patient was not initially cooled, and normothermic CPB was maintained while the surgeon placed a retrograde cardioplegia cannula and identified and exposed the coronary arteries. Since the aortic cross-clamp was not yet applied and small amounts of blood were ejected from the heart, ventilation was continued with a respiratory rate of 4 breaths/min. There was no hemodynamic evidence of light anesthesia. After approximately 30 min, patient cooling was initiated with the arterial blood rapidly cooled to 30° C (body temperature eventually decreased to 30° C as well). Within 1–2 min after cooling had begun, airway pressures increased rapidly to a peak pressure of greater than 70 cmH_2O. The entire breathing circuit was checked and found to be clear, and all valves were in working order. Ventilation was stopped, the aortic cross-clamp placed, and cardioplegia given. The lungs were then noted to remain maximally inflated, crowding the mediastinum, despite the endotracheal tube (ETT) being disconnected from the circuit and left open to room air. Hand ventilation was attempted, and the reservoir bag was found to be noncompliant, with no ability to ventilate. Auscultation *via* the esophageal stethoscope revealed no breath sounds. The ETT was suctioned, lavaged, and found to be clear. A 4.5-mm fiberoptic bronchoscope was passed down the ETT, no mucus plug or other abnormalities were seen, and the ETT was noted to be in the trachea, 2 cm above the carina. Albuterol inhaler (multiple doses *via* the ETT), aminophylline (675 mg, intravenous), diphenhydramine (75 mg, intravenous), methyl prednisolone (1 g, intravenous), and ranitidine (75 mg, intravenous), were given with no response. Enflurane was administered *via* the CPB pump oxygenator, with no improvement in the bronchospasm. Additional fentanyl (4.5 mg, for a total of 145 μg/kg), midazolam (14 mg), and vecuronium were given, again with no improvement in lung compliance. Intravenous epinephrine and aminophylline infusions were started, and multiple doses of isoproterenol lavage were given down the ETT. There was no improvement in lung compliance. Twenty minutes after all of these drugs were given, the surgeon completed the distal anastomosis and rewarming was begun. When the bladder temperature reached 34° C, the ventilation began to improve rapidly, and peak pressures decreased to 30–35 cmH_2O. Auscultation revealed diffuse wheezing. Over the next 30 min, as the bladder temperature increased to 37° C, wheezing resolved and peak inspiratory pressure decreased to 28–30 cmH_2O. The patient then was separated from CPB without difficulty, and received 290 mg protamine intravenously. There was no recurrence of the bronchospasm.

The post-CPB course was uneventful. β-Agonist inhalers and intravenous steroid therapy were continued in the intensive care unit, and the trachea was extubated on the 2nd postoperative day. Postoperative chest x-ray results were normal. The patient continued to recover, and was discharged home on the 8th postoperative day.

Discussion

Several reports have described bronchospasm during CPB.[2–5] In all of the previous reports, the bronchospasm was first noted to appear at the end of CPB, after patient rewarming, when ventilation was reinstituted in preparation for separation from CPB. In our case, the bronchospasm was noted to be temporally related to cooling of the patient early in the course of CPB and, despite maximal treatment, did not abate until rewarming was instituted.

Several causes are possible, other than bronchospasm, for high airway pressures and decreased ability to ventilate the lungs during anesthesia and surgery. These include airway obstruction due to a kinked ETT, mucus or blood plugging within the ETT (or below the ETT within the tracheobronchial tree), faulty inhalation or exhalation valves, mainstem intubation, and a herniated ETT cuff. These were ruled out by the easy passage of

a suction catheter down the ETT and by a fiberoptic bronchoscopy performed through the ETT. Additionally, a thorough check of the breathing circuit and valves showed no abnormalities. Pneumothorax is another possible cause, but is unlikely to have caused the inability to deflate the lungs with lung hyperexpansion into the mediastinum.

Bronchospasm may result from irritation of the carina by the ETT; this was ruled out by fiberoptic bronchoscopy. Bronchospasm can be caused by an allergic reaction to antibiotics, anesthetics, and blood products or secondarily by histamine release caused by anesthetics or other drugs. Protamine in particular has been known to cause bronchospasm. This patient had a known allergy to penicillin. There is a known cross-sensitivity of 5–10% between the penicillins and the cephalosporins, and this patient received cefazolin preinduction. Nevertheless, this appears to have been an unlikely cause of the bronchospasm in our patient. The premedicants, antibiotics, and anesthetic agents were given at least 2 h before the onset of the bronchospasm. Additionally, the bronchospasm occurred before any blood product or protamine administration.

Inadequate anesthesia is a known cause of bronchospasm in asthmatic patients,[1] but was not likely in our patient. In addition to the morphine/lorazepam premedication, this patient received greater than 90 μg/kg fentanyl, 5 mg midazolam, and enflurane all before the development of bronchospasm. Although the enflurane was discontinued on initiation of CPB, the fentanyl and midazolam should have been enough to ensure adequate anesthesia, and the bronchospasm did not develop until 30 min after the enflurane was stopped. Additionally, the bronchospasm was not diminished with the reintroduction of enflurane and the addition of more fentanyl (to a total of 145 μg/kg).

The lack of response to the bronchodilating effects of the enflurane may be a result of the continued presence of a potent bronchospastic trigger in this patient (cold). Additionally, Pasch *et al.* have reported no improvement in airway resistance in patients with asthma or chronic obstructive pulmonary disease following the use of halothane or enflurane anesthesia.[6] Although, in high concentrations, enflurane is commonly thought to cause bronchial smooth muscle relaxation, the effects are variable and may depend on the concentration of enflurane[6] and the continuing presence or absence of the bronchospastic trigger. Korenaga *et al.*[7] have shown that the bronchodilating effects of the potent inhalational agents may due to effects on vagal tone and that direct bronchial muscle relaxation is only seen in very high concentrations (above those clinically used).

Cardiopulmonary bypass is known to cause increased levels of C3a and C5a complement anaphylatoxins.[8] The magnitude of these elevations have been shown to be directly related to the length of CPB and to occur more with bubble oxygenators as opposed to membrane oxygenators. While C3a and C5a have been shown to cause histamine release and possibly bronchospasm, the bronchospasm occurred early in the course of CPB, using a membrane oxygenator, and improved after patient warming and during CPB.

Our patient developed severe bronchospasm shortly after the initiation of cooling on CPB. Patient cooling has not been reported previously as a cause of bronchospasm. While there is no direct proof that cooling caused the bronchospasm, it is suggested strongly by two facts. First there is the temporal relationship between the onset of the bronchospasm and the active lowering of the patient's blood temperature. Second is the fact that, despite aggressive and maximal bronchodilator therapy, the bronchospasm did not at all improve until after the patient was rewarmed. All of the bronchodilator agents were in place at least 1 h before rewarming and were without effect. The initiation of rewarming resulted in a rapid and dramatic improvement.

Cold air is a known cause of bronchospasm in asthmatic patients.[9–11] The mechanisms of cold air-induced bronchospasm are not clear. Although histamine may be involved in cold cholinergic urticaria[12] and exercise-induced bronchospasm, it is probably not involved in cold air-induced bronchospasm.[13] The activation of leukotriene D_4 may play a role in mediating cold air-induced bronchospasm, which can be blocked by a specific antagonist to leukotriene D_4.[10] Breakdown products of arachidonic acid also have been implicated in cold air-induced bronchospasm, which can be prevented by a specific antagonist to 5-lipoxygenase, the enzyme that catalyzes the breakdown of arachidonic acid.[11]

Preoperatively, this patient gave a strong history of cold air-induced bronchospasm. While this is not an uncommon complaint in asthmatic patients, it was severe enough in this patient for her to move to a warmer climate during the winter months. Cooling of the tracheobronchial tree from the blood side may cause the release of some of the same humoral and local factors. We propose that the same mechanisms that contribute

to cold air-induced bronchospasm may have played a role in the bronchospasm induced by cooling of the blood in this asthmatic patient.

We suggest that some of the newer techniques of warm cardioplegia and warm CPB should be considered in a patient with a strong history of cold air-induced bronchospasm. Additionally, while a full discussion of the management of intraoperative bronchospasm has been presented elsewhere,[1,14,15] perhaps patient warming should be considered as a therapeutic option when the patient is cold as a result of CPB in the setting of cardiac surgery or as a result of other, common causes of hypothermia in the setting of noncardiac surgery.

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