incidence of right ventricular catheterization and associated arrhythmias are assessing the location of the J-wire and/or catheter by IVECG and utilizing a pressure transducer to monitor catheter pressure immediately upon removal of the J-wire. The occurrence of arrhythmias during catheter insertion emphasizes the need for continuous ECG monitoring during catheter insertion.

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Bronchospasm after Cardiopulmonary Bypass in a Heart-lung Transplant Recipient

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The development of severe bronchospasm, which delays separation from cardiopulmonary bypass (CPB), has been previously reported in patients undergoing coronary artery bypass grafting.[1–5] These patients responded to conventional treatment for bronchospasm and subsequently did well. We report a case of severe bronchospasm in the denervated lung of a heart-lung transplant recipient, which not only made separation from CPB extremely difficult, but remained a serious clinical problem for the remainder of the patient's hospitalization.

Case Report

A 22-yr-old man with primary pulmonary hypertension was admitted to the coronary care unit in anticipation of heart-lung transplantation. He had developed progressive dyspnea, chest pain, and dependent edema over the previous 18 months, leading to near total exercise intolerance. Even at rest, he required continuous supplemental oxygen and a 75° semi-erect position. He had a long-standing history of exercise-induced asthma (diagnosed by spirometry), which was poorly controlled because of gastric intolerance to the anti-asthmatic medications. Family history was positive for asthma. He was a non-smoker. His weight had been stable around 90 kg. He had undergone general anesthesia for appendectomy 4 yr ago without problems. He denied an allergic history. His current medications were nifedipine 20 mg every 8 h, digoxin 0.125 mg per day, and furosemide 80 mg per day.

At the time of the preoperative physical examination, the patient was dyspneic sitting upright in bed. He was afebrile, arterial blood pressure 138/80 mmHg, heart rate 90 bpm, and respiratory rate 22 breaths/min. There was no cyanosis and trace pedal edema. Breath sounds were clear but distant. Cardiac examination revealed a 2/6 systolic murmur at the left lower sternal border on inspiration, normal S_1, loud P_2, no S_3, and no right ventricular heave. There were occasional ectopic beats. Chest radiograph showed cardiomegaly with enlargement of the right ventricle and both pulmonary arteries. Electrocardiogram showed right ventricular hypertrophy with a strain pattern

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and bi-atrial enlargement. Chemistry values were: sodium 141 meq/l, potassium 4.0 meq/l, chloride 106 meq/l, serum CO_2 23 meq/l, serum urea nitrogen 18 meq/l, creatinine 1.4 meq/l, glucose 83 meq/l, total bilirubin 0.5 mg/dl, direct bilirubin 0.1 mg/dl, calcium 9.7 mg/dl, phosphate 4.3 mg/dl, uric acid 10.6 mg/dl, total protein 6.8 g/dl, albumin 4.4 g/dl, aspartate aminotransferase 18 *iu*/l, alanine aminotransferase 26 *iu*/l, and lactic dehydrogenase 227 *iu*/l. His complete blood count showed white blood cells 16,200/cu mm (79% polymorphonuclear, 15% lymphocytes, 6% monocytes), hemoglobin 15.6 g/dl, packed red cell volume 45.5%, and platelets 249,000/cu mm.

The donor was a 16-yr-old man who had been hospitalized for a gunshot wound to the head 4 days prior to the transplant. He had no history of medical problems. Prior to transplantation, the donor was receiving cephamandol 1 g every 4 h, dexamethasone 6 mg every 4 h, and pitressin. His blood and urine cultures were negative 2 days prior to transplantation, and sputum culture from admission was negative. There was no history of aspiration by the donor. With a FI_{O_2} of 0.4, the donor's pa_{O_2} was 99 mmHg, pa_{CO_2} 31 mmHg, and pH_a 7.55. With a FI_{O_2} of 1.0, pa_{O_2} increased to 418 mmHg.

The recipient was transported to the operating room following administration of cyclosporine 10 mg/kg. No anesthetic premedication was given. Intravenous catheters, a radial arterial catheter, and a left internal jugular double lumen catheter were placed with local anesthesia and sterile technique. Prior to induction of anesthesia, the arterial blood pressure was 140/80 mmHg, heart rate 88 bpm, respirations 22 breaths/min, and right atrial pressure 27 mmHg. Anesthesia was induced with fentanyl 25 μg/kg, diazepam 0.16 mg/kg, and pancuronium 0.1 mg/kg iv. Using sterile conditions, an endotracheal tube was inserted without difficulty on the first attempt. Breath sounds were equal with scattered wheezes. Initial peak inspiratory pressure (PIP) was 50 cm H_2O, but this decreased to 30 cm H_2O over the ensuing 15 min. Arterial blood pressure declined to 122/70 mmHg, heart rate remained at 88 bpm, and right atrial pressure remained at 27 mmHg. Anesthesia was maintained with iv fentanyl, diazepam, and pancuronium while breathing 100% oxygen. The donor heart and lungs were harvested *en bloc* and placed in a basin of Collin's solution (a balanced electrolyte solution) during transport between operating rooms. Implantation of the donor organs was performed without incident. The donor to recipient ischemic time was 85 min.

Attempts were made to ventilate the newly implanted lungs after 2 h of CPB. Initially, we were unable to inflate either lung with PIP 50 cm H_2O. When a PIP of 100 cm H_2O was used, the left lung quickly expanded, protruded into the surgical field, and would not deflate, even when the breathing circuit was disconnected from the patient. The right lung would not inflate, despite a PIP of 100 cm H_2O. A suction catheter was passed easily through the endotracheal tube, and only minimal secretions were removed, ruling out obstruction due to secretions or kinking of the tube. Fiberoptic bronchoscopy was immediately performed to examine the tracheal anastomosis. This was found to be widely patent and clear of secretions, as were both mainstem bronchi.

A diagnosis of bronchospasm was made, and isoproterenol was administered iv because it was readily available, having been prepared in anticipation of infusion during weaning from CPB. Methylprednisolone, which is usually given after CPB in transplant patients, was administered in two 500-mg iv doses; in this case, during CPB. This treatment produced only minimal improvement in breath sounds or lung movement. A loading dose of aminophylline (5 mg/kg) was then infused over 20 min at the same time 1% halothane was administered. Again, there was no response. Atropine 1 mg was given into the endotracheal tube and furosemide 90 mg was given iv. After 30 min of this treatment, a repeat attempt to inflate the right lung with PIP 70–100 cm H_2O was successful and permitted adequate ventilation to discontinue CPB.

TABLE 1. Blood-gas Data

Sample Time	FI_{O_2}	*p*H	Pa_{CO_2} mmHg	Pa_{O_2} mmHg	Comments
Preoperative	0.3	7.51	41	112	
Pre-induction	0.4	7.50	38	119	
Post-intubation	1.0	7.44	36	449	
During CPB	0.95	7.35	38	312	
45 min post-CPB	1.0	7.32	45	92	
ICU					
3 h post-CPB	0.75	7.34	48	55	
6 h post-CPB	0.75	7.27	54	56	After 1st terbutaline
22 h post-CPB	0.45	7.45	38	81	After 5th terbutaline
48 h post-CPB	0.55	7.48	38	90	After 10th terbutaline

After CPB, PIP was 50 cm H_2O, arterial blood pressure 100/50 mmHg, heart rate 125 bpm, and right atrial pressure 11 mmHg. Arterial blood gases are listed in table 1. Manipulations of the respiratory settings with various combinations of tidal volume, respiratory rate, and inspiratory:expiratory ratio were attempted without improvement in oxygenation.

Upon arrival in the intensive care unit, mechanical ventilation was set at a tidal volume of 950 ml, 17 breaths/min, and positive end-expiratory pressure (PEEP) of 8 cm H_2O. The PIP was 38 cm H_2O. Both inspiratory and expiratory wheezes were present. Attempts at adjusting the tidal volume, respiratory rate, and PEEP were unsuccessful in improving gas exchange. Nebulized terbutaline (1.0 mg in 5 ml normal saline) was administered *via* the endotracheal tube. This was associated with a decrease in wheezing and PIP, but arterial blood gases were unimproved. The terbutaline treatments were repeated every 4 h during the night of surgery. By morning of the first postoperative day, arterial blood gases began to improve. The patient developed fever to 39.7° C during that day, with worsening rales and rhonchi. His condition continued to worsen over the following week with Pseudomonas aeruginosa pneumonia, bronchospasm, sepsis, renal failure, and cerebral edema leading to brain death. He died on the 12th postoperative day. Pathologic examination of the lungs revealed diffuse necrotizing pneumonia with multiple abcesses and hemorrhagic infarcts, as well as multi-organ injury consistent with systemic hypoperfusion.

DISCUSSION

In our case, severe bronchospasm prevented separation from CPB after heart-lung transplantation. Eleven cases of bronchospasm after CPB have been reported previously,[1–6] including an episode similar to our patient's following the first implantation of the artificial heart.[6] Bronchospasm has not been reported after heart-lung transplantation. We have performed ten heart-lung transplantations at our institution; bronchospasm did not occur in the other nine patients.

Hyperinflation and inability to deflate the lung were evidence of air-trapping, a characteristic sign of airway obstruction. Fiberoptic bronchoscopy ruled out mechanical causes of obstruction shortly after the problem developed, making bronchospasm the most probable etiology.

There are two unique aspects of this case. One is the fact that the transplanted lungs are denervated, which clearly demonstrates that neural (parasympathetic) mechanisms are not involved in this patient's bronchoconstriction. Second, the lung recipient had pre-existing asthma, while the lung donor did not. The history of asthma in the recipient may or may not be related to the development of the bronchospasm, but, if it is related, it suggests that asthma is a systemic disease.

The fact that the beta-adrenergic drug, isoproterenol, had no effect could mean that smooth muscle constriction was not the primary problem, but that edema or small airway secretions might have incited the bronchospasm. If smooth muscle constriction was the primary event, the patient may have had little or no response to isoproterenol if he had decreased responsiveness of beta-adrenergic receptors or a depressed cAMP response to the drug. There is evidence that there may be a defect in the beta-adrenergic mechanism in cells of asthmatic patients.[7] The fact that the recipient had a history of asthma, while the donor did not, would make this mechanism improbable, unless one contends that the receptors are not in the lung.

It is possible that the donor may have had an infectious process ongoing at the time of transplantation, which eventually led to the diffuse, necrotizing pneumonia the recipient subsequently developed. This is hard to prove, since the preoperative sputum cultures were negative and there was no evidence of a pulmonary infection in the immediate perioperative period. It has been shown that pulmonary infections increase the airway reactivity of both normal subjects and those with asthma.[8-10] The mechanism by which infection is postulated to increase airway reactivity is sensitization of irritant receptors and enhancement of vagal reflexes.[8-10] Since denervation abolishes irritant receptor and vagal reflexes,[11] bronchoconstriction would more likely be due to bronchial edema and release of humoral factors. An infection could have increased the reactivity of the donor's lungs prior to transplantation, contributing to the bronchospasm during surgery. However, there was no evidence of bronchospasm in the donor prior to transplantation.

Additional factors that might have had a role in bronchoconstriction were the combination of pulmonary atelectasis during CPB, removal of the lungs from the donor, placement of the lungs into Collins's solution (which contains potassium chloride, a smooth muscle constrictor), and surgical manipulation during implantation into the recipient. Although there is no longer any vagal input, the human lung has parasympathetic ganglia that could possibly exert some cholinergic action on the bronchial smooth muscle. This may explain why atropine administered directly into the lung *via* the endotracheal tube seemed to have an effect. Studies have shown inhaled atropine to be an effective bronchodilator.[12]

As noted by Hirshman,[7] numerous factors are responsible for bronchospasm during anesthesia. Any of the anesthetic drugs given could possibly induce an allergic reaction leading to bronchospasm. However, no signs of a reaction were noted earlier in the case when the drugs were given, nor did the patient develop any skin erythema, urticaria, or hypotension.

Biochemical mediators known to initiate bronchoconstriction include histamine, leukotrienes, and Prostaglandins $F_{2\alpha}$ and D_2. CPB is associated with increases in the amounts of both prostaglandins E_1 and $F_{2\alpha}$,[13,14] presumably due to decreased pulmonary clearance of these substances, although others suggest that they result from disrupted white blood cells in the lung during CPB.[15] While prostaglandin E_1 is a bronchodilator, prostaglandin $F_{2\alpha}$ is thought to induce bronchoconstriction.[7] Other circulating factors that can produce bronchospasm include the C3a and C5a anaphylatoxins, which are produced by complement activators during CPB.[16] Platelets and white blood cells contain many bronchoactive substances, including serotonin and kinins, which may be released during CPB. Mast cells and basophils, which may be activated during CPB, have been shown to have an increased ability to release mediators when taken from allergic patients. Although our patient did not have an allergic history, his exercise-induced asthma may involve some of the same mechanisms. Therefore, our patient's bronchoconstriction could solely be the result of CPB. It is also possible that the process of heart-lung transplantation decreases pulmonary clearance of these mediators, exacerbating their effects.

In conclusion, we present a case of severe bronchospasm after CPB in an asthmatic patient who has been transplanted with denervated, "normal" lungs. That the underlying asthma in this patient remained a factor even after being transplanted with non-asthmatic lungs suggests that asthma might be a systemic disease, rather than a phenomenon restricted to the lungs.

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