Clinical Reports

Severe bronchospasm during cardiopulmonary bypass

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Purpose: To describe the rare problem of severe bronchospasm occurring during cardiopulmonary bypass in a six-year-old-child.

Clinical features: Severe bronchospasm became apparent on attempting to resume controlled ventilation prior to weaning from cardiopulmonary bypass. The patient had a previous history of asthma but was asymptomatic preoperatively. Aggressive therapy with multiple bronchodilating agents was necessary before cardiopulmonary bypass could be discontinued. The bronchospasm resolved over the first 24 hr after surgery.

Conclusion: Severe bronchospasm during cardiopulmonary bypass is rare. It should only be diagnosed after ruling out other reasons for failure to ventilate. Treatment with intravenous bronchodilators is required. The cause is unknown.

Objectif: Rapporter un cas rare de bronchospasme survenu pendant la circulation extracorporelle (CEC) chez un enfant de six ans.

Éléments cliniques: Le bronchospasme s'est révélé au moment de la remise en marche de la ventilation mécanique précédant le sevrage de la CEC. Le patient avait des antécédents d'asthme mais était asymptomatique avant l'intervention. Un traitement agressif avec plusieurs bronchodilatateurs a été nécessaire avant l'arrêt de la CEC. Le bronchospasme s'est résolu dans les 24 h qui ont suivi la chirurgie.

Key words

BRONCHOSPASM;
CARDIOPULMONARY BYPASS.

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Conclusion: Pendant la CEC, le bronchospasme grave survient rarement. Avant son diagnostic, il faut éliminer toutes les causes possibles d'impuissance à ventiler. Un traitement aux bronchodilatateurs intraveineux est essentiel. La cause en est inconnue.

Severe bronchospasm during cardiopulmonary bypass is infrequent. Since the first report in 1973,¹ only 22 additional cases have been reported, all involving adults, some with a previous history of airway hyper-reactivity.²⁻¹³ We report a case in a child with a known history of atopy and asthma, and present a review of this rare condition.

Case report

A six-year-old boy with recurrent sub-aortic stenosis and aortic valve insufficiency was scheduled for elective resection of a sub-aortic membrane and a pulmonary valve autograft to the aortic position (Ross procedure). His past surgical history was complex; division of a patent ductus arteriosus and repair of coarctation of the aorta had been performed in the neonatal period. A previous operation for subaortic stenosis had been performed at two years of age. The patient had also required numerous surgical procedures to correct anal and renal abnormalities. The proposed operation was necessary to correct a 40–50 mmHg gradient across the left ventricular outflow tract and 2+ aortic regurgitation. Cardiac catheterization data were otherwise normal, demonstrating good left ventricular function, a left ventricular end-diastolic pressure of <10 mmHg and no evidence of pulmonary hypertension. The patient was asymptomatic on the morning of his scheduled surgery and was not taking any medication.

The past medical history included atopic dermatitis and eczema which was treated with cortisone cream. Radioallergoabsorbent testing (RAST) demonstrated high sensitivity to egg white, milk and wheat. The patient also had reactive airways disease which was periodically triggered by over-exertion or upper respira-

tory infections. These episodes usually responded to salbutamol MDI aerosol treatments. An acute episode of asthma at the time of an upper respiratory infection within the past six months required one day admission to the ICU and two subsequent hospital days for treatment with solumedrol, nebulized beta-agonist aerosols and aminophylline. He was discharged taking theophylline ethylene diamine, beclomethasone and salbutamol aerosols, and a five day tapering course of prednisone. Pulmonary function testing following resolution of symptoms was normal without evidence of residual obstructive airways disease. Previous anaesthetic history was unremarkable. There were no drug or food allergies.

On the morning of surgery, physical examination revealed an active, alert boy weighing 19.7 kg. There was no evidence of an upper respiratory infection. Vital signs were within normal limits for his age. The lungs were clear with no evidence of bronchospasm. Laboratory studies and chest radiograph were all normal. The eosinophil count was slightly elevated at 6%.

Midazolam 10 mg *po* was administered for premedication and the patient received two doses of salbutamol aerosol prior to transport to the operating room. Intravenous induction with 5 mg · kg⁻¹ thiopentone, 5 µg · kg⁻¹ fentanyl, 1 mg · kg⁻¹ lidocaine and pre-bypass maintenance of anaesthesia with nitrous oxide and fentanyl (total 50 µg · kg⁻¹) were uneventful. Vecuronium 0.1 mg · kg⁻¹ was used to maintain neuromuscular blockade. An uncuffed 5.5 mm internal diameter oral tracheal tube was inserted, and the lungs were ventilated using a Siemens 900 D series ventilator with a Fisher and Paykel heated humidifier. Initial peak inspiratory pressure was 20 cmH₂O. A trans-oesophageal echocardiogram (TEE) probe was inserted without difficulty. Additional medications administered before CPB included intravenous 25 mg · kg⁻¹ cefazolin, 1.5 mg · kg⁻¹ solumedrol and aprotinin (Test dose 1 ml followed by a loading dose of 240 mg · m⁻² infused over 30 min). Heparin 3 mg · kg⁻¹ was administered and CPB was initiated uneventfully approximately 1.5 hr after induction. The patient was cooled to 28°C before beginning the surgical repair. The surgical procedure consisted of replacing the excised native aortic valve with the pulmonary valve autograft and reconstruction of the right ventricular outflow tract with a pulmonary homograft. Total CPB time was 75 min. Additional medications administered by the perfusionist included calcium chloride, phenylephrine, potassium chloride. Lidocaine 50 mg was administered during rewarming and defibrillation.

In anticipation of discontinuing CPB, dopamine and dobutamine infusions were started at 5 µg · kg⁻¹ · min⁻¹

respectively. The oral endotracheal tube was routinely suctioned of minimal secretions using a 8 Fr catheter. Salbutamol aerosol was administered and manual lung ventilation was attempted. Lung inflation was found to be impossible even with peak inspiratory pressures above 80 cm H₂O. The TEE probe was removed, and the endotracheal tube again suctioned; there were no secretions. Another dose of salbutamol aerosol was administered. As ventilation was impossible CPB was maintained. Suspecting a mechanical problem with the endotracheal tube, this was removed and replaced. Still the lungs, which appeared small and pale, could not be inflated. Fiberoptic bronchoscopy revealed the large airways to be patent and free of secretions, with the endotracheal tube tip 2 cm above the carina. The diagnosis of severe bronchospasm was now established.

Medications were administered via the CPB circuit; Aminophylline 6 mg · kg⁻¹ loading dose and an infusion of 0.6 mg · kg⁻¹ · hr⁻¹, 100 µg epinephrine and infusion of 0.06 µg · kg⁻¹ · min⁻¹ and 125 mg hydrocortisone. The aprotinin infusion was discontinued. Over the next ten minutes ventilation improved slightly. Lung inflation was now possible with peak inspiratory pressures (PIP) of 50–60 cm H₂O but deflation was incomplete. Halothane 1% was administered and the patient was treated with repeated doses of salbutamol aerosols. Ventilation gradually improved with PIPs in the 40–50 cm H₂O range and CPB was discontinued. Haemofiltration of 700 ml took place over 11 min concentrating the pump blood from a haematocrit of 25% to 34%. Protamine 50 mg *iv* was slowly administered without untoward effect.

The first ABG analysis post-bypass revealed a pH 6.96, PCO₂ >99, PO₂ 86, BE -2.1, and a saturation of 92% breathing 100% oxygen. The capnogram demonstrated a severe obstructive pattern with a steep, peaked ascending limb of the tracing. The lungs ventilated equally, but air trapping persisted. Halothane, epinephrine, and aminophylline were continued and a ketamine infusion was started at 2 mg · kg⁻¹ · hr⁻¹. Supplemental fentanyl (100 µg) and vecuronium (2 mg) were also administered. Ventilation slowly but progressively improved. There was no evidence of pulmonary oedema. The PIPs remained between 30 and 40 cm H₂O. Arterial blood gas determination revealed an improving acid base status prior to ICU transfer; pH 7.16, PCO₂ 70, PO₂ 81 BE -1.4, saturation 92% breathing 100% oxygen.

On transfer to the ICU the patient had diffuse inspiratory and expiratory wheezing. Oxygen saturation improved to 98–99% breathing 100% oxygen. The cardiac rhythm and haemodynamic state were stable. There was no evidence of any skin rash or other cutaneous

TABLE Previous case summaries

Author	Year	Pt #	Age/sex	Asthma history	Bronchospasm time	Aetiology	Treatment
Venetti ¹	1973	1	43 F	Cardiac	Pre-separation	?	Hy, D, <i>it</i> E
Shiroka ²	1982	2	51 F	No	Pre-separation	?	A, M, E
		3	50 M	No	Pre-separation	?	A, M
Durant ³	1984	4	64 M	Yes	Post-separation	Lb, Cm, P interaction	A, H, E
Pace ⁴	1984	5	61 M	No	Pre-separation	?	A, T
Hardy ⁵	1985	6	?	No	?	Mech, ac pulm ven congestion	Removal of swab under LA
		7	?	No	?	?	A, E
		8	?	No	?	Protamine	AnH, A, E
Tuman ⁶	1986	9	75 M	No	Pre-separation	?	A, <i>it</i> MplA, M, E, H
		10	40 M	Hayfever	Pre-separation	?	A, H, K, E, M
		11	54 F	No	Pre-separation	?	A, <i>it</i> MplA, M, E, Is
Hentz ⁷	1984	12	49 F	No	Pre-separation	?	B, I
		13	70 F	Yes	Pre-separation	?	B, I
		14	49 M	No	Pre-separation	?	B, I
		15	62 F	No	Pre-separation	?	sc T
		16	67 F	No	Pre-separation	?	B, sc T, E
Hentz ⁸	1986	17	59 M	No	Post-separation	? Protamine	S, Al, <i>it</i> , <i>iv</i> E
Kyösola ⁹	1987	18	53 M	No	Pre-separation	?	H, T, <i>it</i> L
		19	62 F	Possibly	Pre-separation	Ac Pulm oedema	None
Casella ¹⁰	1988	20	22 M	Exercise	Pre-separation	CPB	<i>iv</i> I
Buckingham ¹¹	1989	21	55 M	Hayfever	Pre-separation	?	A, At, M, H, Mp
Neustein ¹²	1992	22	67 F	Yes	Pre-separation	CPB	I, sc T, Hy, E, Alb, A
Inoue ¹³	1994	23	50 M	No	Pre-separation	CPB	A, E, M, Sev, S

A: aminophylline; Al: alupent; Alb: albuterol; At: atropine; B: betamethasone; Cm: cimetidine; D: decadron; E: epinephrine; H: halothane; Hy: hydrocortisone; I: isoproterenol; Is: isoflurane; L: lidocaine; Lb: labetalol; M: methylprednisolone; Mp: metoproteranolol; S: salbutamol; Sev: sevoflurane; T: terbutaline. *iv*: intravenous; *it*: intratracheal; CPB: cardiopulmonary bypass.

changes. Postoperative chest radiograph demonstrated hyperinflation without evidence of foreign body or infiltrates. Shortly thereafter, dopamine and dobutamine were discontinued, and the epinephrine infusion was decreased; this was discontinued 12 hr later. The patient continued to receive 1 mg·kg⁻¹ solumedrol every six hours as well as salbutamol aerosol administration every one to two hours. By the first postoperative day the patient was weaned from epinephrine and ketamine. Breath sounds were dramatically improved with only occasional expiratory wheezing. The trachea was extubated 24 hr postoperatively, and he was discharged from the ICU on the second postop day and home on the fifth postoperative day.

Discussion

Severe acute bronchospasm that became apparent prior to weaning a six-year-old boy from cardiopulmonary bypass is reported. Similar episodes have been described in 23 adult patients;¹⁻¹³ the majority occurring at the time of re-establishing controlled ventilation prior to discontinuing CPB. The clinical features of these cases are outlined in the Table.

In the anaesthetized patient, the diagnosis of bronchospasm should only be accepted once other causes of airway obstruction have been systematically eliminated.

Mechanical factors causing obstruction are common in the paediatric patient; smaller calibre endotracheal tubes are prone to become kinked, obstructed or malpositioned. The intraoperative use of the trans-oesophageal echocardiography probe may also result in airway obstruction.¹⁴ These mechanical causes were all excluded in our patient, and the possible causes for bronchospasm were considered.

Reflex bronchiolar smooth muscle hyper-reactivity is known to occur in association with inadequate anaesthesia and may be triggered by a mechanical stimulus. Though light anaesthesia may occur at the end of CPB, our patient did not exhibit any evidence of this. Intraoperative bronchospasm may also be triggered by an allergic reaction to an anaesthetic or ancillary drug¹⁵ but the time relationship makes this unlikely in this case.¹⁶ Aprotinin may cause allergic reactions, although these are not common. In one study¹⁷ only four allergic reactions were reported among 671 patients (0.6%) in 41 cardiac surgical units. Aprotinin induced IgE-mediated anaphylactic reaction in a sensitized patient presents with symptoms occurring within minutes of the initial dose.¹⁸ Alternatively anaphylactoid reactions may result from histamine liberation through a non-immune mechanism with sudden cardiovascular collapse in a patient without prior sensitization.¹⁹ The described patient had

not been previously exposed to aprotinin, showed no evidence of adverse effects during the hour prior to initiating CPB, and had no cutaneous and cardiovascular changes. Hence, it is unlikely that aprotinin was responsible for the bronchospasm. Other agents which have been implicated in an anaphylactic response during anaesthesia include protamine, blood products and colloidal plasma expanders. Of the various constituents making up the CPB priming solution, type-specific cross matched packed red blood cells, albumin and mannitol could be responsible for the adverse reaction noted in our patient. The only blood product that was administered prior to the appearance of bronchospasm was 150 ml packed red blood cells. These had been correctly cross-matched and there was no evidence of incompatible blood transfusion; the patient's clinical course during CPB was stable and there was no haemoglobinuria. Albumin and mannitol have both been associated with allergic reactions. Although severe reactions occur very rarely, it is possible that one of these agents may have been responsible.^{20,21}

Latex allergy is an important consideration in any patient with specific risk factors and unexplained bronchospasm or cardiovascular collapse during anaesthesia. Though our patient required multiple previous gastrointestinal and urological surgical procedures, no historical or clinical evidence existed for increased sensitivity to latex products.^{22,23} Latex allergy during cardiac surgery has not been previously described, but this possibility must be considered. The lack of any other systemic signs of an allergic reaction or any circulatory instability argues against this diagnosis.

Another possible cause of bronchospasm during CPB, though rare, is an episode of cold urticaria triggered by hypothermia. IgE-dependent mast cell degranulation occurs during cold exposure producing well-circumscribed wheals with raised, erythematous borders. Urticarial eruptions are the hallmark of this disease and the diagnosis of cold urticaria cannot be made on the basis of bronchospasm alone. Isolated bronchospasm during CPB cooling has also been reported²⁴ in a patient with a strong history of cold air induced bronchospasm.

Finally the possibility that biochemical substances released during CPB might trigger bronchospasm in a sensitized patient must be considered. Complement activation by the alternative pathway and the production of anaphylatoxins, C3a and C5a, may be triggered by the extracorporeal membrane oxygenator and its circuit.²⁵ The influence of C5a on neutrophil aggregation and adhesiveness within the pulmonary vasculature results in pulmonary vascular leukosequestration. Theoretically, this may result in pulmonary changes, specifically ventilation/perfusion mismatching and small-airways

obstruction. This has been documented in patients undergoing renal haemodialysis but not in patients subjected to CPB.²⁶ It is our present assumption that substances released during CPB might trigger bronchospasm in a patient with a known history of asthma.

The treatment of bronchospasm in the reported cases (Table) demonstrates a wide variety of pharmacological regimens in varying sequences. Commonly employed were aerosolized beta adrenergic agents in combination with aminophylline, epinephrine and a corticosteroid. Aerosolized agents cannot be effectively administered to a patient with severe bronchospasm, and it is our opinion that intravenous epinephrine played an important role in reversing bronchospasm. Therefore, it should be given priority as a first line of treatment. The relative security of having the patient on continuing CPB lessens the fear of serious arrhythmias while this infusion is being established.

In conclusion, bronchospasm during CPB is very rare but may be extremely severe. All ages may be affected but it would appear to be less common in children as this is the first case report of which we are aware. It most commonly becomes apparent immediately prior to weaning from bypass. In the reported cases it is only rarely associated with a past history of asthma, and there are no other easily identifiable common features in the affected patients. Our patient clearly had a strong history of asthma that had required admission to the ICU and aggressive treatment on one occasion. It is possible that the preoperative administration of salbutamol and the use of lidocaine prior to intubation may have contributed to an uneventful pre-bypass anesthetic course. Whether or not more aggressive preoperative preparation would have prevented the bronchospasm is speculative and the exact precipitating cause of this acute episode is unknown.

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