Recurrence of Asthma after Removal of Adrenaline Secreting Pheochromocytoma

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Only four cases of asthma attack after adrenalectomy in pheochromocytoma have been reported[1-4]. The combination of pheochromocytoma and asthma troubles anesthesiologists, since therapy for either disease can have a detrimental effect on the other. We report our experience of an asthmatic patient with adrenaline secreting pheochoromocytoma and discuss the choice of drug in such cases.

Case Report

A 55-year-old, 60 kg man was scheduled for removal of adrenaline secreting pheochromocytoma. Abdominal echography revealed a mass lesion in the right adrenal gland. Plasma epinephrine and norepinephrine concentration were 3,320 pg·ml^{-1} and 2,670 pg·ml^{-1}, respectively. Urinary total metanephrine was 17.56 mg·day^{-1} (normal range: 0.05 ~ 0.23) and normetanephrine was 72.48 mg·day^{-1} (normal range: 0.07 ~ 0.26). The patient had a history of marked hypertension and diabetes mellitus. On admission, blood pressure was 230/120 mmHg and heart rate 110 beats·min^{-1}. His cardiac and thyroid functions were within normal limits. Though he had developed frequent asthma attacks until he was 18 years old, his symptoms regressed spontaneously and he has experienced no severe attacks since then. Oral amosulalol[5-7], the latest investigational agent, was administered at the daily dose of 40 mg 10 days before surgery. Amosulalol is an α, β-adrenergic blocker that has relatively greater affinity for α-adrenergic receptors than for β-adrenergic receptors. Its affinity for α-adrenergic receptors is twice that of phentolamine, while its affinity for β-adrenergic receptors is one quarter that of propranolol. Despite this therapy, a systolic blood pressure exceeded 230 mmHg early in the morning twice in that week. After the dose of amosulalol was increased to 60 mg, hypertension was successfully controlled. Methylprednisolone (500 mg, iv) was administered the night before surgery to prevent bronchospasm. The patient was premedicated with oral diazepam (15 mg) two hours before surgery and with scopolamine (0.5 mg, im) one hour before surgery. On arrival in the operating room, blood pressure was 198/120 mmHg and heart rate 82 beats·min^{-1}. Peripheral venous and left radial artery catheters were inserted. Anesthesia induction consisted of midazolam (20 mg, iv) and vecuronium (12 mg, iv). The trachea was intubated uneventfully after the administration of lidocaine (60 mg, iv).

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Breath sounds were clear and bilaterally equal. A pulmonary artery catheter was inserted through the right antecubital vein after tracheal intubation. The ECG, blood pressure, pulmonary arterial pressure, central venous pressure, oxygen hemoglobin saturation (Sa_{O_2}), end-tidal CO_2 tension (Et_{CO_2}), and mixed venous oxygen saturation ($S\bar{v}_{O_2}$) were monitored continuously. Anesthesia was maintained with nitrous oxide (67%), enflurane (1.5 ~ 4%), and oxygen. Both plasma epinephrine and norepinephrine concentrations increased to over 10,000 $pg \cdot ml^{-1}$ during tumor manipulation. Intraoperative hypertensive crises were successfully treated with phentolamine (1.5 ~ 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$). However, the administration of verapamil (10 mg, iv) was ineffective against tachycardia during tumor manipulation. We decided to avoid the administration of β-adrenergic blockers because we considered that they might cause severe bronchospasm in this case. After adrenalectomy, blood pressure decreased to 64/45 mmHg and $S\bar{v}_{O_2}$ decreased to 54%. Blood pressure was successfully restored within a few minutes with epinephrine (0.6 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and norepinephrine (0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$). No signs of asthma were noted during the surgery. At the end of the surgery, plasma catecholamine level was still ten times as high as the normal level (6,100 $pg \cdot ml^{-1}$). He remained intubated and was transferred to the intensive care unit, where he was noted to have bronchospasm. An arterial blood gas analysis at that time, with an FI_{O_2} of 0.4, revealed a pH of 7.24, Pa_{O_2} 117 mmHg, Pa_{CO_2} 54 mmHg, and a base excess of -3.6 $mEq \cdot l^{-1}$. Infusion of aminophylline was started at a rate of 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Piping rales diminished the next day. As piping rales was noted again after tracheal extubation, the rate of infusion of aminophylline was increased to 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$. This treatment improved asthma attack. An arterial blood gas analysis with an FI_{O_2} of 0.4, revealed a pH of 7.46, Pa_{O_2} 134 mmHg, Pa_{CO_2} 42 mmHg, and a base excess of -0.4 $mEq \cdot l^{-1}$. The postoperative course in the intensive care unit was otherwise uneventful, and he was discharged from the intensive care unit two days after surgery.

Discussion

The recurrence of this patient's asthma after adrenalectomy suggests that the rapid decline in the level of serum catecholamine led to bronchoconstriction. Adrenalectomy in dogs reduces sympathetic relaxation of airways to 75%[8]. This finding indicates that the level of serum catecholamine contributes predominantly to sympathetic relaxation of airways. His plasma epinephrine concentration decreased markedly after removal of pheochromocytoma. This rapid reduction might have provoked asthma attack, as β-adrenergic receptors of pheochromocytoma patients are desensitized due to the chronic excess of catecholamines[9,10].

β-adrenergic blockers such as propranolol may cause severe bronchospasm in an asthmatic, and their use to control tachycardia should be avoided in such cases. In the management of this case, we used α-adrenergic blockers to control hypertension and Ca-antagonists to control tachycardia instead of β-adrenergic blockers during the operation. Ca-antagonists have direct action on tracheobronchial smooth muscle and inhibit the release of mediators from activated mast cells[11]. Not only decreases the responsiveness of β_2-adrenergic receptors decreases, but also both the number and the responsiveness of bronchial α-adrenergic receptors increase in asthmatic individuals[12,13]. α-adrenergic

blockers can cause bronchodilatation under these circumstances. Furthermore, α-adrenergic blockers increase cyclic AMP in asthmatic patients[14].

If Ca-antagonists do not relieve tachycardia or arrhythmia, we consider choosing selective β_1-adrenergic blockers or pindolol which has the lowest bronchoconstricting effect of all β-adrenergic blockers[15]. However, the administration of β-adrenergic blockers requires careful consideration, because atenolol, one of the selective β_1-adrenergic blockers, has been reported to cause bronchospasm in an asthmatic[4].

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