Recurrence of asthma following removal of a noradrenaline-secreting phaeochromocytoma

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Summary

A patient with asthma and a phaeochromocytoma is described. At about the time she was first noted to be hypertensive her asthma resolved spontaneously but bronchospasm returned with some severity when the tumour was removed. The phaeochromocytoma was of the noradrenaline secreting variety. Possible mechanisms through which this catecholamine might have produced the observed alleviation of asthma are considered.

KEY WORDS: hypertension, α -adrenoceptor, noradrenaline.

Introduction

Asthma may improve spontaneously with age particularly as children mature. Complete disappearance for several years followed by severe recurrence is unusual. We report such a relapse of asthma following the removal of a noradrenaline (NA) secreting phaeochromocytoma. The increased plasma level of circulating NA in this patient may have temporarily alleviated the tendency to bronchoconstriction. Such a relationship has not been previously reported.

Case report

A 49-year-old secretary presented in 1982 with a 6-month history of increasing depression. She had felt generally unwell, with a poor appetite, weight loss and occasional nausea but no paroxysmal flushing or palpitation. There had been two episodes of fainting and on the second occasion her blood pressure had been found raised. The patient also described an intermittent pain in the left anterior thigh and groin.

She had first been found to be hypertensive in 1974 and was treated with amiloride and hydrochlorothiazide

although her arterial pressure was never well controlled and in 1977 she was referred to a consultant physician. Although her blood pressure was said to be labile, the highest reading in clinic was 150/95 mmHg and the same treatment was continued. The patient had been asthmatic since the age of 19 years but her symptoms improved spontaneously at about the time she was first found to be hypertensive and she then managed without treatment.

Early in 1982 her arterial pressure was found to be 175/120 mmHg lying, 140/110 mmHg standing and with a regular tachycardia of 140/min which settled to 110/min on resting. Urinary total metanephrines were elevated in two collections at 6.7 and 8.8 μ mol/24 hr (normal range 1.5-4.5) and the estimation of urinary total free catecholamines showed elevated NA levels of 3.3 and >4 mol/day (normal range 0.05-0.5). The plasma catecholamine levels (each figure the mean of three samples) showed gross elevation of the NA concentration at 23.9 nmol/l (normal range 0.87-6.92), adrenaline (A) 0.6 nmol/l (normal <4.24) and dopamine (DA) 0.8 nmol/l (normal <1.54). Arteriography showed a 3 cm diameter tumour in the left para-aortic region at L3/4 level. At operation a 24 g phaeochromocytoma was excised without difficulty. Analysis of the tumour tissue showed NA 0.7 mg/g wet tissue, A not detected, DA 0.002 mg/g. The biochemical results indicated a pure NA secreting tumour.

Postoperatively her blood pressure and NA levels fell to normal such that no further antihypertensive was required. On returning to the ward from the intensive care unit she was noted to be wheezing and it became clear that her asthma had returned after an absence of 8 years. Despite an otherwise good recovery she suffered with almost constant wheezing worse at night and on exercise, and these symptoms persisted when she was followed in the out-patient

clinic. Cromoglycate and isoprenaline (Intal Compound), and salbutamol by inhalation with slow release theophylline were required to bring these symptoms under control.

Discussion

The recurrence of this patient's asthma following removal of the pheochromocytoma suggests that the rapid decline in the level of circulating noradrenaline (NA) led to bronchoconstriction. NA is not usually associated with the production of bronchodilatation but we felt that the time course of her symptoms was such as to suggest that the catecholamine might have caused the disappearance of her asthma. Numerous studies have been performed to investigate the effect of various catecholamines on different preparations of lung tissue. Strip preparations of human peripheral lung contract when NA is applied (Black, Turner and Shaw, 1981) probably due to the vascular element which this preparation contains. When isolated strips of human bronchi (removed at surgery for cancer or immediately post-mortem) have been tested NA has produced a net relaxant effect (Mathe, Astrom and Persson, 1971; Goldie, Paterson and Wale, 1982) presumably due to the ability of NA in high concentration to stimulate the β -mediated effect when the population of α -receptors is sparse. Cabezas, Graf and Nadel (1971) have provided evidence *in vivo* that there are no functionally significant α -adrenergic constrictor mechanisms in the bronchi by stimulating the thoracic sympathetic nerves of dogs and measuring the airways dimensions directly from bronchograms; after pharmacologic β -blockade, sympathetic stimulation did not constrict the airways. There has been considerable debate over the role of α -receptors in airways muscle especially in the smaller airways. Some have argued that they do not exist (Foster, 1966; Guirgis and McNeill, 1969) but it seems more likely that they are present in very sparse numbers (Mathe *et al.*, 1971) and that α -adrenergic constrictor function can only be demonstrated after β -blockade.

An alternative explanation for the disappearance of this patient's asthma rests on the discovery that adrenergic fibres of sympathetic origin enter peripheral parasympathetic ganglia where they inhibit transmission from the cholinergic parasympathetic preganglionic fibres to the neurones of the ganglion (Skok, 1980). This arrangement is best documented in the gut but catecholamine-containing elements have been demonstrated by histofluorescence in the cholinergic ganglia of calf lung (Jacobowitz *et al.*, 1973). The innervation of the bronchi is predominantly parasympathetic constrictor (Mann, 1971) and any reduction in cholinergic traffic would be effectively bronchodilator. High levels of circulating NA

might therefore be expected to mimic the inhibitory effect of the adrenergic neurones reducing acetylcholine secretion at the neuromuscular junction with consequent bronchodilatation.

Some sympathetic fibres terminate on bronchial smooth muscle producing bronchodilatation by stimulation of the β -receptor. It has been suggested (Henderson *et al.*, 1979; Barnes, Dollery and MacDermott, 1980) that in asthmatics the number of α -receptors are increased and β -receptors decreased; the fact that the asthma of our patient improved rather than deteriorated in the presence of high concentrations of circulating NA militates against this suggestion. It seems that if asthma disappears as hypertension develops then the possibility of a catecholamine secreting tumour should be considered.

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