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CASE REPORT

Bronchial asthma improved after removal of a phaeochromocytoma

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ABSTRACT: It is uncommon for bronchial asthma to be a symptom of phaeochromocytoma. We describe a patient with a phaeochromocytoma who presented with worsening of her asthma and persistent dyspnoea between attacks. She had markedly elevated levels of catecholamines. After surgical resection of the phaeochromocytoma there was a lasting improvement of the bronchial asthma.

We hypothesize that worsening of bronchial asthma in phaeochromocytoma patients may be due to catecholamine-induced deterioration of asthma.

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Phaeochromocytoma is an unusual but by no means rare tumour. The paroxysm or crisis is the classic manifestation of phaeochromocytoma [1, 2]. It is the physiological consequence of catecholamine release from the tumour and the subsequent stimulation of adrenergic receptors. One would expect that this release of catecholamines protects against the occurrence of bronchial asthma attacks in phaeochromocytoma patients. Bronchodilatation by $beta_2$-adrenergic sympathicomimetics is one of the cornerstones of medical therapy for asthma.

We report the history of a woman who presented with bronchial asthma attacks, which seemed to be triggered by phaeochromocytoma. A possible explanation for this phenomenon is discussed.

Case history

A 67 yr old woman was admitted for dyspnoea. She had neurofibromatosis (Recklinghausen's disease), chronic asthmatic bronchitis (existing for 10 yrs) and aspirin idiosyncrasy (detected 5 yrs previously). She did not smoke. In the last 3 yrs the attacks of dyspnoea occurred more frequently. Hence, treatment had been commenced with salbutamol inhalations and theophylline orally. Nevertheless, in the last month before admission the breathlessness persisted even between attacks. On admission, there were also complaints of chronic cough with copious production of sputum. There was no history of a recent airway infection.

On physical examination an-ill-looking, severely dyspnoeic woman with generalized cutaneous neurofibromatosis was seen. She had a tremor and excessive sudation. There was a peripheral cyanosis. The pulse rate was 96·min^{-1}. The arterial blood pressure was 180/100 mmHg. On auscultation of the lungs we found an expiratory wheeze. Further physical examination was unremarkable.

Complete blood count and routine chemical laboratory investigations did not reveal any significant abnormality. A specimen of arterial blood, drawn while the patient was breathing room air, revealed that the arterial oxygen tension (Pao_2) was 8.2 kPa (normal 10.0–13.3 kPa), the arterial carbon dioxide tension ($Paco_2$) was 5.2 kPa (normal 4.7–6.4 kPa) and the pH was 7.42 (normal 7.35–7,45).

Microscopic examination of sputum showed numerous eosinophilic granulocytes, but no microorganisms.

X-ray films of the chest were normal. Spirography showed an obstructive pulmonary function. The forced expiratory volume in one second (FEV_1) was 0.93 *l* (52% of predicted), the forced vital capacity was 1.88 *l* (87% of predicted) and the peak expiratory flow rate 2.27 *l*·s^{-1} (45% of predicted).

A diagnosis of acute bronchial asthma was made. Salbutamol inhalation, intravenous administration of theophylline and high dose corticosteroids with supplemental oxygen therapy were started.

The patient initially showed some improvement. However, 5 days after starting this treatment her blood pressure was 180/130 mmHg and she had a regular tachycardia of 120–130·min^{-1}.

The diagnosis of phaeochromocytoma was considered. We found gross elevations of noradrenaline 2,621 pg·ml^{-1} (normal 100–600 pg·ml^{-1}), adrenaline 4,438 pg·ml^{-1} (normal below 100 pg·ml^{-1}) and dopamine 273 pg·ml^{-1} (normal below 100 pg·ml^{-1}) in the serum (all measured by radio-immunoassay). A computed

tomography scan of the abdomen, showing a tumour in the right adrenal gland with a diameter of 6 × 10 cm, was in agreement with this diagnosis. Iodine-131 Metaiodobenzylguanidine scanning of the body did not reveal any catecholamine producing tumours other than that in the right adrenal gland.

After preoperative treatment with phenoxybenzamine a tumour with a diameter of 8 × 7 cm was surgically removed from the right adrenal gland. Postoperatively the tachycardia, the hypertension and the raised catecholamine levels in the serum disappeared (noradrenaline 234 $pg \cdot ml^{-1}$, adrenaline 55 $pg \cdot ml^{-1}$, dopamine 27 $pg \cdot ml^{-1}$).

The spirometry values returned to baseline (FEV_1 2.22 *l* (124% of predicted), vital capacity (VC) 2.88 *l* (133% of predicted), although the patient had to continue salbutamol and corticosteroid inhalations. Two years after operation the patient is persistently well, and there has been no recurrence of severe asthmatic attacks.

Discussion

Most phaeochromocytomas produce noradrenaline either alone or mixed with smaller quantities of adrenaline [3]. On rare occasions, as in the patient described, adrenaline is the major secreted catecholamine. In most patients the clinical picture is dominated by signs of excessive beta-adrenergic stimulation such as tachycardia and hypermetabolism [4]. Noradrenaline and adrenaline are endogenous catecholamines with alpha- and beta-adrenergic effects. Stimulation of $beta_2$-adrenergic receptors in the lung causes bronchodilatation. The massive release of catecholamines into the circulation by phaeochromocytoma would be expected to alleviate bronchoconstriction by $beta_2$-adrenergic stimulation, hence, preventing asthmatic attacks in phaeochromocytoma patients. The asthmatic patients described in five earlier case reports, who showed reappearance of bronchospasm following resection of their phaeochromocytoma, are an argument for this view [5–9]. In contrast to these cases, the acute attacks of bronchospasm in our patient disappeared after resection of the tumour. The clinical course of this patient suggests that catecholamines released by phaeo-chromocytoma into the bloodstream are responsible for the occurrence of attacks of bronchial asthma.

Stimulation of post-junctional alpha-adrenoceptors located on bronchial smooth muscle and submucosal glands in the lung can mediate bronchospasm in some patients [10–12]. Alpha-adrenergic blockade can reduce bronchospasm partially or completely in exercise-induced asthma [13]. Recently, clinical studies have shown that regular treatment with $beta_2$-adrenergic agonists can exacerbate asthma [14]. $Beta_2$-adrenergic agonists can be responsible for an increased antigen load and acute inflammatory response in the lower airways by inhibiting mast cell degranulation [15].

Thus, the release of noradrenaline and adrenaline into the bloodstream by phaeochromocytoma may not always protect against the occurrence of asthmatic attacks, as is suggested in the earlier mentioned case reports.

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Asthme bronchique amélioré après résection d'un phéochromocytome. Janssen J, Tjiong H.
RÉSUMÉ: L'asthme bronchique n'est que rarement un symptôme de phéochromocytome. Nous décrivons l'observation d'une patiente atteinte de cette affection, qui s'est traduite par une aggravation de son asthme et une dyspnée persistante entre les crises. Elle avait des taux très élevés de catécholamines. Après résection chirurgicale du phéochromocytome, l'on a noté une amélioration persistante de l'asthme bronchique.

Nous émettons l'hypothèse que l'aggravation de l'asthme bronchique chez les patients atteints de phéochromocytome pourrait être due à une détérioration de l'asthme, induite par les catécholamines.
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