Surgical cure of hypertension in a patient with brainstem capillary haemangioblastoma containing neuropeptide Y

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Summary
We describe a 29-year-old woman with persistent arterial hypertension which resolved following complete excision of a capillary haemangioblastoma from within the spinal cord at the cervico-medullary junction. Immunohistochemical staining was positive for neuropeptide Y in capillary walls and nerves in the tumour. This raises the possibility of an association between neuropeptide Y and the central control of blood pressure in man.

Keywords: hypertension, neuropeptide Y, haemangioblastoma, surgery

There is an association between central nervous system tumours and hypertension.1 Neuropeptide Y has a widespread distribution in rat and human brain.23 Central administration of neuropeptide Y increases the blood pressure of anaesthetised or conscious rats.4 We describe a patient who presented with severe hypertension and in whom excision of a brainstem capillary haemangioblastoma resulted in complete resolution of hypertension. The tumour had specific immunoreactivity for neuropeptide Y.

Case report
A 29-year-old Jamaican woman presented to casualty after a head injury, complaining of right facial numbness and weakness, intermittent slurred speech and drooling of saliva. There was a three-month history of sweaty episodes which were not associated with anxiety or palpitations. Arterial blood pressure was 200/105 mmHg sitting. There was no previous history of hypertension with the exception of a single reading of 139/100 mmHg in her first and only pregnancy two years earlier. Her mother had been diagnosed as having essential hypertension aged 54. On examination she had pyramidal weakness and loss of sensation in the right arm with abnormal sensation over the right side of her face. Supine hypertension (130–200/100–126 mmHg) with a marked postural drop in blood pressure (of up to 80 mmHg) on standing but with no change in pulse rate, was a consistent finding during subsequent hospital admission. The remainder of the examination was normal. Initial investigations revealed a neutrophil leukocytosis (total white cell count 16.2 x 10^9/l) and a urinary tract infection due to Proteus spp. The following were normal or negative: serum creatinine and electrolytes, liver function, glucose, syphils serology, urinary vanilmandelic acid to creatinine ratio on two occasions, renal ultrasound. Cerebrospinal fluid examination was acellular with a raised protein (1383 mg/l, normal range <450 mg/l). Autonomic function tests were normal with the exception of supine hypertension and postural blood pressure fall without a significant pulse rise. Magnetic resonance imaging (MRI) showed an enhancing lesion adjacent to the posterior arch of C1 extending down to the...
interspace between C1 and C2 (figure 1), with a cystic area in the upper cervical cord extending into the medulla. The blood pressure was initially managed with nifedipine retard but supine hypertension (140–160 mmHg systolic pressure) and postural hypotension persisted. Oxprenolol 80 mg twice daily was added and the blood pressure improved (130–160/90–100 mmHg). A capillary haemangioblastoma was completely excised from within the cord at the cervico-medullary junction. Immuno-histochemical staining was negative for nitric oxide synthase (inducible, endothelial and neural isoforms), endothelin and vasoactive intestinal polypeptide, but positive for neuropeptide Y in capillary walls (figure 2) and nerves. Post-operatively, she became normotensive off all medication and two months after discharge ambulatory blood pressure recording (Accutrack II, Suntech Medical Instruments) showed an average blood pressure of 123/84 mmHg.

Discussion

Anatomical data regarding the organisation of cardiovascular centres in man are scarce. Langford reported two cases of hypertension developing in young patients following removal of an angioblastoma from the floor of the fourth ventricle in the region of the obex. The second case demonstrated supine hypertension with a significant postural blood pressure drop. Our patient had a haemangioblastoma removed from the caudal part of her medulla and postural symptoms made her blood pressure difficult to control preoperatively. It is possible that raised blood pressure in each case was caused by damage to the nucleus tractus solitarius since hypertension can be produced in rats and cats by electrolytic lesions of this nucleus.

In contrast to Langford’s cases, our patient’s blood pressure was normalised by complete excision of the tumour from the medulla. A similar cure of hypertension by surgery has not been reported previously and in animal models, damage to the brainstem has produced hypertension.

The neurotransmitter neuropeptide Y is widely distributed in rat and in human brains and colocalises to neurons with noradrenaline. In contrast, in our patient neuropeptide Y was concentrated in vascular areas within the tumour. Central administration of neuropeptide Y in the posterior hypothalamic nucleus in the rat can cause a rise in arterial blood pressure. Our patient had hypertension and a tumour with neuropeptide Y immunoreactivity, raising the possibility of an association between neuropeptide Y and the central control of blood pressure in man. Any such association is likely to be complex, since in a series of papers Fuxe et al have demonstrated marked and prolonged vasodepressor and bradycardiac effects of intracisternal or intraventricularly administered neuropeptide Y in the rat. These authors found that neuropeptide Y mimics the central effects of α2-adrenoceptor agonists, and hypothesise that vasodepressor effects of centrally administered neuropeptide Y are caused by activation of high affinity neuropeptide Y receptors in the nucleus tractus solitarius where baroreceptor afferents terminate. The finding in our hypertensive patient of high concentrations of neuropeptide Y in a vascular tumour in the caudal part of the medulla is not necessarily counter to this. There are several possible explanations for the apparent disparity including species variation, opposing actions of neuropeptide Y on closely anatomically related structures, disparate effects of neuropeptide Y when released alone rather than when it is co-released with noradrenaline, and possible neuropeptide receptor down-regulation in neurons adjacent to the tumour.

Figure 1 Gadolinium-enhanced T-1 weighted sagittal image showing an enhancing nodule anterior to the posterior arch of C1 (arrow) with evidence of cyst formation in the medulla and a cyst extending inferiorly through the cervical region

Figure 2 Section of a haemangioblastoma immunostained for neuropeptide Y. Dense immunoreactivity can be seen in the wall of blood vessels (avidin-biotin-peroxidase complex method with haematoxylin counterstain x 200)

Learning points: neuropeptide Y

- 36 amino acid vasoconstrictor peptide, rich in tyrosine (Y = tyrosine)
- isolated from brain, 1982
- widely distributed in central and peripheral nervous systems
- implicated in various physiological processes including:
  - regulation of neuroendocrine secretion
  - circadian rhythms
  - appetite
  - reproductive behaviour
  - sympathetic cardiovascular control

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doi: 10.1136/pgmj.71.836.371

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