Twenty-four hour ambulatory blood pressure and heart rate in a patient with a predominantly adrenaline secreting phaeochromocytoma

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Summary: In this report, we present the symptoms, biochemical investigations, 24 hour ambulatory blood pressure and heart rate recordings in a patient before and following removal of a predominantly adrenaline-secreting phaeochromocytoma. The symptoms were of episodic shaking, faintness, nausea, palpitations, sweating and panic, chest and neck pain with headache, and are consistent with previous reports. Ambulatory blood pressure recording demonstrated that mean daily blood pressure was normal, with normal diurnal variation, and two episodes of severe hypertension and bradycardia coincident with symptoms (MAP 150 mmHg and HR 49 beats/minute, MAP 178 mmHg and HR 29 beats/minute, respectively), not reported in predominantly adrenaline-secreting phaeochromocytoma.

Introduction

Predominantly adrenaline-secreting phaeochromocytoma are very rare and present with different symptoms from other phaeochromocytoma. In this report, we present the symptoms, biochemical investigations, 24 hour ambulatory blood pressure and heart rate recordings in a patient before and following removal of a predominantly adrenaline-secreting phaeochromocytoma.

Case report

A 43 year old, previously healthy Caucasian woman first started to complain of episodic shaking, faintness and nausea 18 months prior to presentation. These sensations continued infrequently for approximately a year, but then progressed to more severe attacks of palpitations, sweating and panic, which were associated with chest and neck pain with headache occurring approximately three times per week. These episodes would wake her from sleep. Her condition continued to deteriorate, and at presentation, the episodes were occurring up to five times daily. Over the 18 months prior to presentation, she had been seen frequently by her general practitioner, and had seen a cardiologist and a neurologist. Her symptoms had been attributed to early symptoms of menopause, anxiety and migraine.

On examination she was slightly obese (body mass index 29 kg/m²). She had no tremor and was not sweating excessively. She was normotensive (office blood pressure), and the cardiovascular examination was normal. There was some tenderness in the right upper side of the abdomen. Her electrolytes, full blood count and sedimentation rate were all normal. The random blood glucose was elevated at 12 mmol/l. Examination of her urinary catecholamines by high-performance liquid chromatography (HPLC) with electrochemical detection (ECD) confirmed the clinical diagnosis of a phaeochromocytoma (Figure 1, Table I). Three 24 hour urinary collections demonstrated that the urinary adrenaline levels were between 10 and 15 times normal values, and the noradrenaline levels were marginally raised. Both upper abdominal ultrasound and abdominal computed tomographic scan demonstrated the presence of a large right-sided (5 x 4 cm) adrenal tumour with a necrotic centre. In the immediate preoperative period, following the results from her ambulatory blood pressure measurements, she was treated with phenoxybenzamine 10 mg twice daily to control the hypertensive episodes. This abolished her symptoms, and did not cause her to be faint. During anaesthesia, her blood pressure was controlled using short-acting intravenous α and β-adrenoceptor antagonist agents guided by measurements of her peripheral resistance, central venous pressure and cardiac output. At operation,
no evidence of metastasis was found and the tumour was removed. In the week following surgery, she was extremely somnolent, but otherwise she made an uneventful recovery. Following removal of the tumour, the 24 hour urinary catecholamine levels were all in the normal range. Histological examination of the tumour confirmed that it was a phaeochromocytoma with extensive necrosis.

Twenty-four hour blood pressure monitoring (Figure 2)

Twenty-four hour ambulatory blood pressure and heart rate monitoring was performed (Accutracker II, Suntech Medical Instruments, Raleigh, NC, USA) after diagnosis with the patient on no drug treatment. This was repeated after removal of her tumour. Measurements were made at 15 minute intervals during the day and night. The patient recorded any symptoms during the monitoring period. Prior to removal of the tumour, 104 blood pressure and heart rate measurements were made over 24 hours, two of which were omitted because of errors in measurement. During this period, the mean systolic blood pressure was 113 ± 9 mmHg, diastolic blood pressure 74 ± 6 mmHg, mean arterial pressure 87 ± 6 mmHg and heart rate 72 ± 12 beats/minute. There were two patient recorded events during the 24 hour period. The first occurred at approximately 14.00 hours when blood pressure was 163/144 mmHg, mean arterial pressure 150 mmHg and heart rate 49 beats/minute, the second at 19.30 hours when her blood pressure was 197/169 mmHg, mean arterial pressure 178 mmHg and heart rate 29 beats/minute, respectively. In addition, there was a further asymptomatic episode of diastolic hypertension with bradycardia at around 16.45 hours and a period of asymptomatic hypotension at 13.15 hours.

After removal of her tumour, 96 measurements were made over 24 hours, three of which were omitted because of error in measurement. The mean was not significantly different from the preoperative period, with the systolic blood pressure 116 ± 10 mmHg, diastolic blood pressure 76 ± 8 mmHg, mean arterial pressure 83 ± 14 mmHg and heart rate 83 ± 14 beats/minute, but there were no patient events and the maximum

Table I Twenty-four hour urinary catecholamines results from a patient with a predominantly adrenaline-secreting phaeochromocytoma

<table>
<thead>
<tr>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine volume (ml)</td>
<td>1980</td>
<td>1680</td>
<td>1500</td>
</tr>
<tr>
<td>Noradrenaline (µmol/24 hours)</td>
<td>0.56</td>
<td>0.57</td>
<td>0.54</td>
</tr>
<tr>
<td>Adrenaline (µmol/24 hours)</td>
<td>1.57</td>
<td>1.70</td>
<td>1.61</td>
</tr>
</tbody>
</table>
systolic blood pressure recorded was 148 mmHg, diastolic blood pressure 98 mmHg and the minimum heart rate 64 beats/minute.

Discussion

Our patient’s main symptoms were similar to those previously reported in the adrenaline-secreting phaeochromocytoma,1 the diagnosis being confirmed by the markedly elevated urinary adrenaline levels, and marginally raised noradrenaline levels. In this case, we present unreported features of the condition. Ambulatory recording of blood pressure in noradrenaline-secreting phaeochromocytoma demonstrates a loss of circadian rhythm of blood pressure, and frequent episodes of paroxysmal systolic and diastolic hypertension.2 In predominantly adrenaline-secreting phaeochromocytoma, hypotension rather than hypertension is reported to be the presenting cardiovascular abnormality.3,4 However, there are no data on ambulatory blood pressure and heart rate recording. In this case, mean daily blood pressure was normal, with a normal diurnal rhythm. During the two periods when the patient reported typical symptoms of faintness and headache, there was very severe systolic and diastolic hypertension. This is more characteristic of a noradrenaline-secreting phaeochromocytoma, and may represent the effect of very high levels of adrenaline on α-adrenoceptors. An unexpected finding was that, although there were periods of tachycardia and slight reduction in diastolic blood pressure immediately preceding each reported episode, there was marked bradycardia during these episodes. This bradycardia is likely to be the cause of the symptoms of faintness rather than due to hypotension as in the previously reported cases. Such periods of profound bradycardia have not been previously reported and the mechanism underlying them is not clear. Several mechanisms might be proposed to explain these observations. The increase in circulating adrenaline at the start of each episode will initially act on β-adrenoceptors to increase heart rate, and cause muscle bed vasodilatation reducing diastolic blood pressure. However, as the release of adrenaline increases, the higher concentrations of adrenaline will act on α-adrenoceptors to cause vasoconstriction and increase diastolic and systolic blood pressure. Stimulation of the stretch receptors of the great vessels may induce profound bradycardia through the vagus reflex arc. Catecholamine-secreting tumours may also secrete endothelins, neuropeptide Y and other vasoactive peptides. These were not measured, but might also contribute to the periods of bradycardia. The mechanism of hypertension and bradycardia may have been elucidated by simultaneous measurements of plasma or timed urinary catecholamines measurements, however, we did not make such measurements in this case.

In previous reports of predominantly adrenaline-secreting phaeochromocytoma, treatment with an adrenoceptor blocking agent has resulted in profound hypotension. In this case, because of episodes of severe hypertension, the patient was treated with phenoxybenzamine. This did not result in symptomatic hypotension, although formal measurements were not made. After removal of the tumour, the patients mean blood pressure did not change, and the normal diurnal variation remained. However, no hypertensive episodes or periods of bradycardia were seen.

Thus in this case of a predominantly adrenaline-secreting phaeochromocytoma, ambulatory blood pressure recording demonstrated episodes of severe hypertension and bradycardia coincident with symptoms, and these episodes were not seen following removal of the tumour.

References

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