A new variant of Carney’s triad: phaeochromocytoma and chondrosarcoma

S T Wahid, R Jones, S L Chawla, V M Connolly, W F Kelly, R W Bilous

Abstract

A 61 year old hypertensive woman presented in 1986 with a right scapular chondrosarcoma. She developed type 1 diabetes mellitus in 1991 and suffered a stroke in 1991. Chest radiography showed pulmonary metastases in 1997. Further radiological staging detected a right sided phaeochromocytoma, which was subsequently removed in 1998. Before this, repeated urine estimations of vanillylmandelic acid had been normal. Her diabetes was cured by adrenalectomy. It is believed that the combination of phaeochromocytoma and extrapulmonary chondrosarcoma represents a new variant of Carney’s triad. (Postgrad Med J 2001;77:527–528)

Keywords: chondrosarcoma; phaeochromocytoma; Carney’s triad

Case report

The patient presented as an emergency in 1991 with severe headaches and labile blood pressure. She had hypertension since 1972 and phaeochromocytoma was suspected in 1974. However, an intravenous urogram and 24 hour urine estimation of vanillylmandelic acid gave normal results. Hypertension required treatment with three different agents, but still remained labile with systolic readings ranging from 115 to 180 and diastolic from 70 to 110 mm Hg. Family history included a younger sister with hypertension, and the deaths of her father and another sister from cerebral haemorrhage aged in their 40s. In 1986 she had undergone a right scapulectomy with adjuvant chemotherapy and radiotherapy for a chondrosarcoma. Chest radiography and computed tomography at that time revealed no metastases. On examination in 1991 there was a marked postural drop in blood pressure: 240/110 mm Hg supine, falling to 140/80 mm Hg upon standing, cachexia, and dehydration. Investigations (table 1) revealed diabetes and dehydration. Treatment was started with insulin and intravenous fluids. During the next few days she developed a right hemiparesis due to a left parietal lobe infarct. Treatment was aspirin, nifedipine, and atenolol. Urine vanillylmandelic acid concentrations were normal (table 1). Blood chemistry returned to normal, blood pressure stabilised at 144/90 mm Hg and she made a good recovery from her stroke.

From 1991 to 1997 diabetes control was good with a glycated haemoglobin (HbA1c) of 6.4%, but blood pressure remained difficult to control. In 1997 a left mid-lung lesion was noted on routine chest radiography. Computed tomography (fig 1) suggested pulmonary metastases and a right adrenal mass. It was felt she had metastatic lesions from her chondrosarcoma. Computed tomography guided biopsy of the right adrenal gland showed histological features of a phaeochromocytoma.

Direct questioning revealed no symptoms often associated with phaeochromocytoma and

Table 1 Pertinent investigations

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose (mmol/l)*</td>
<td>28.6</td>
<td>4.5–5.6</td>
</tr>
<tr>
<td>Serum urea (mmol/l)*</td>
<td>15.6</td>
<td>2.5–7.2</td>
</tr>
<tr>
<td>Plasma creatinine (µmol/l)*</td>
<td>203</td>
<td>45–121</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)*</td>
<td>180</td>
<td>115–155</td>
</tr>
<tr>
<td>Electrocardiogram*</td>
<td>Left ventricular hypertrophy</td>
<td>&lt;32</td>
</tr>
<tr>
<td>24 Hour urine VMA 1 (µmol/l)*</td>
<td>9</td>
<td>&lt;32</td>
</tr>
<tr>
<td>24 Hour urine VMA 2 (µmol/l)*</td>
<td>26</td>
<td>&lt;32</td>
</tr>
<tr>
<td>24 Hour urine metadrenaline 1 (µmol/l)</td>
<td>20.6</td>
<td>&lt;15</td>
</tr>
<tr>
<td>24 Hour urine metadrenaline 2 (µmol/l)</td>
<td>30.2</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

*These investigations relate to the admission in 1991, when the patient developed diabetes and suffered a stroke. The 24 hour urine metadrenaline measurements are from 1997 when the patient was under investigation for a possible phaeochromocytoma.
Learning points

- Urine vanillylmandelic acid measurements have a poor sensitivity in the diagnosis of phaeochromocytoma, and other more sensitive investigations (urine metadrenaline or catecholamines measurement) should be utilised.
- Diabetes, induced by excess circulating catecholamines, in phaeochromocytoma is often cured by adrenalectomy.
- When patients present with a phaeochromocytoma, the association with Carney’s triad should be borne in mind and appropriate screening investigations (chest tomography, 24 hour urine collection for catecholamine estimation, and computed tomography of the stomach with contrast) should be considered.

Discussion

We believe the above combination of phaeochromocytoma and chondrosarcoma is an unreported variant of Carney’s triad. Carney’s triad comprises gastric leiomyosarcoma, pulmonary chondroma, and functioning paragangioma.\(^1\) Not all features need to be present for diagnosis, each component may present at different times in the same patient and each component may behave in a different manner in individuals,\(^1\) therefore suggesting that there is a spectrum of disease still to be fully characterised. Our patient demonstrates several unusual features. Firstly, it was a phaeochromocytoma accounting for the hypertension rather than a paragangioma, but in a review of 79 cases of Carney’s triad there was one patient who had an adrenal mass as well as multiple parangliomas.\(^1\) Our patient had a pulmonary chondrosarcoma not a chondroma, and in the latter review, of the 61 cases with a pulmonary neoplasm, the histological reports revealed a wide range of pathological tumours. Moreover, even if these tumours were resected, most patients developed further pulmonary lesions. It could be argued that in our patient the pulmonary chondrosarcoma was metastatic in nature, but our case is also consistent with the multicentric nature of the lesions making up Carney’s triad, as the pulmonary lesion was discovered 11 years after the diagnosis of scapular chondrosarcoma. There was no evidence of a gastric leiomyosarcoma in our patient. In a case review, 70 out of 79 patients had gastric tumours,\(^3\) but only 17 cases had all three components of the triad. Many patients presented with one component, only to develop a further manifestation during follow up to 26 years.\(^3\) Carney’s triad is commoner in females and it normally presents before 25 years.\(^3\) A phaeochromocytoma may have been present in our patient at age 36 years when she first had hypertension. Our case does not therefore have all the classical features, but does fit into the overall spectrum of the condition.

The aetiology of Carney’s triad is unknown. Because of the strong family history of hypertension and cerebral haemorrhage in our case, there is the possibility of genetic inheritance. However, both her son and younger sister have had negative screening investigations for phaeochromocytoma, but pulmonary and gastric screening has not been done. There is no evidence of familial inheritance of Carney’s triad and no candidate gene or gene product has been identified,\(^3,4\) but the multicentric nature, occurrence at young age, and the rarity of these tumours support a genetic defect.

This case demonstrates several other important points in the diagnosis and treatment of phaeochromocytoma. Urine vanillylmandelic acid measurements have a poor sensitivity of 65%, and should be replaced either with urine metadrenaline measurements (reported sensitivity of 93%) or, ideally, with specific urine catecholamines measurements (reported sensitivity \(\cong 100\%\)).\(^4\) MIBG imaging is helpful, but not infallible, with a sensitivity of 80%–90%.\(^5\) The message is that in the face of convincing symptoms of a phaeochromocytoma one should continue along the diagnostic path, up to and including provocative testing. Hyperglycaemia complicating phaeochromocytoma is well known, and it usually resolves after adrenalectomy.\(^6\)

Patients with phaeochromocytoma are usually screened for several associated syndromes (multiple endocrine neoplasia 2, von Hippel-Lindau disease, Sturge-Weber syndrome, and neurofibromatosis). Carney’s triad should now be added to this list. We also believe that the use of the term “triad” is a misnomer and we suggest “Carney’s syndrome” would be a more appropriate description.

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