Near and Far: Multi-modal imaging presentation of a case of malignant carotid body tumor with systemic metastases

Abstract

Carotid Body Tumours (CBT) are rare neoplastic paragangliomas that are typically benign, however, 10-15% are malignant with local invasion and in rare cases, metastases systematically. A 45-year-old female with a familial history of CBT presented following a syncopal episode. Multi-modal imaging confirmed the presence of bilateral CBTs. DOTATE-PET scans revealed distant systemic metastases in the liver and vertebra. Surgical intervention was undertaken to excise the less complex right CBT. This report presents a rare case of malignant CBT with distant metastases, describing the post-intervention multi-modal imaging findings with a focus on the Duplex ultrasound features.

Key Words: carotid body tumor, metastatic paraganglioma, duplex ultrasound, multi-modal imaging

Introduction

Carotid Body Tumours (CBT) are rare neoplastic paragangliomas that are vascular in nature located in the bifurcation of the common carotid artery, affecting predominantly young to middle age people, with an incidence of 1:30 000\(^1\). CBT’s represent 70% of the extra-adrenal paragangliomas and are more predominant in females \(^1,2\). Bilateral occurrence is considered rare and presents in only 10% of patients commonly with familial origins \(^2,3\). The majority of cases of carotid body paraganglioma are benign, with malignancy considered rare, occurring in 10% of cases \(^4\). Malignancy in CBTs is unpredictable and can present with local vascular and
neural invasion and in rare instances, distant systemic metastases can occur in multiple sites including bone, liver, and lung.5.

The major structural consequence of CBTs is an encasing of the internal and external carotid arteries which although may not initially narrow these vessels, will tend to result in the internal carotid artery (ICA) and external carotid artery (ECA) being spread apart, resulting in extensive local invasion.2 The extent of the invasive pattern of CBTs and their anatomical relationship to the carotid vessels was first described by Shamblin’s and colleagues. Shamblin’s classification system is based on gross examination and surgical notes and organises CBTs into three categories: type I (a small localized tumor easily excised and minimally attached to the vessels), type II (larger more adjacent tumours with partial surrounding of vessels) and type III (completely surrounded/encapsulated vessels)6,7. The extent of circumferential encapsulation of the carotid vessels by the paraganglioma is a key predictor of surgical morbidity.

CBTs are typically slow-growing tumors that may be present for several years prior to symptomatic presentation. The extrinsic compressive nature of the mass will eventually result in the patient experiencing symptoms such as syncope and headaches.8 Due to their infiltrative nature and malignant potential, management and/or surgical treatment is necessary for the patient’s best outcome.

**Case Description**

One month prior to the examination, a 45-year-old, Caucasian female presented to the emergency department reporting left occipital headaches, along with nausea and intermittent left ear hearing disturbance, that was slightly relieved with left cervical flexion. The patient gave a history of an undifferentiated neck lump, thought to be swollen glands, which had been
present for approximately two years and were slowing growing. She reports significant growth over the last two months and 5kg weight loss over four weeks. The patient denied any pain, shortness of breath or fevers. A family history of CBT recently diagnosed in her father.

**Multimodal Imaging Findings**

Initially, a computed tomography angiogram was requested of the head and neck to determine the positioning of this palpable mass which suggested a carotid body paraganglioma bilaterally. A subsequent magnetic resonance image (MRI) was performed to define the lesions with IV contrast of the neck (Figure 1). The MRI showed a left-sided mass (30 x 35mm) with avid contrast enhancement, suggesting CBT. This caused splaying of the ICA and ECA (Figure 2). A second lesion at the right bifurcation was noted (7mm diameter).

A diagnostic DOTATATE-PET study (Figure 3) was then completed which revealed large intensity DOTATATE avid left upper neck consistent with a paraganglioma/neuroendocrine tumor. The right carotid artery demonstrates a second paraganglioma, but the differential diagnosis was a nodal metastasis. It was determined that there were hepatic metastasis and DOTATATE avid bone lesions confirming malignancy.

**Interpretation of Ultrasound Findings**

Duplex ultrasound was performed to investigate the anatomical and functional consequences post-CBT excision. Figure 4 shows that there was no obvious recurrence of a mass seen in the right carotid arteries post-excision on B-Mode ultrasound. The right-sided vessels were interrogated to also exclude the presence of luminal obstruction internally from atherosclerotic plaque. There was no hemodynamically significant stenosis noted, though minor smooth and homogenous plaque causing a <20% diameter reduction was observed at the bifurcation as well.
as minimal intimal thickening. Importantly, no intimal dissection was noted on the 2D images post-operatively in the right-sided vessels. Findings on Doppler ultrasound confirmed a <50% diameter stenosis as all peak systolic velocities (PSVs) were below <125cm/s and end-diastolic velocities (EDVs) were below <40cm/s (as per ICA stenosis criteria by the University of Washington and the Moneta ratio)⁹. Table 1 summarises these findings. The Doppler velocities calculated an internal carotid artery to common carotid artery (ICA/CCA) ratio of 1.2. The right vertebral artery showed low resistance, antegrade laminar flow with a PSV of 67cm/s and a diameter of 3.8mm, which by modified criteria of the University of Washington and the Moneta ratio suggest a normal blood flow velocity and vessel diameter.

Table 1: Right-sided peak systolic velocities and end diastolic velocities

<table>
<thead>
<tr>
<th>Artery</th>
<th>PSV (cm/sec)</th>
<th>EDV (cm/sec)</th>
<th>Doppler Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA</td>
<td>89</td>
<td>30</td>
<td>60°</td>
</tr>
<tr>
<td>ICA</td>
<td>112</td>
<td>39</td>
<td>60°</td>
</tr>
<tr>
<td>ECA</td>
<td>125</td>
<td>-</td>
<td>60°</td>
</tr>
<tr>
<td>Vertebral (3.8mm)</td>
<td>67</td>
<td>Antegrade</td>
<td>60°</td>
</tr>
<tr>
<td>Velocity Ratio</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 shows the obtained velocities obtained on the right side at the common carotid artery (CCA), internal carotid artery (ICA), external carotid artery (ECA) and vertebral artery. The peak systolic velocity (PSV) for all right-sided arteries post-surgery were within normal limits.

2-Dimensional ultrasound findings of the left side demonstrated a mass measuring 29.7 x 38.9 mm which encompassed the ECA, caused splaying of the ICA and confirmed the left-sided
mass which was detected with MRI. A space occupying mass that is well-defined and homogenous in appearance on grey-scale ultrasound images is consistent with the presence of a CBT, as was the case in this particular patient. The anatomical association of the mass to the left-sided vasculature is demonstrated in Figure 5 in which the mass can be seen spreading apart the ECA and ICA. The anatomical location of the CBT in this patient has resulted in hemodynamic changes of the left-sided carotid vessels, notably in the ICA with a PSV of 139 cm/s. The left vertebral artery shows low resistant antegrade, laminar flow with a normal PSV of 88cm/s. Table 2 summarises the Doppler velocity findings.

Table 2: Left sided peak systolic velocities and end diastolic velocities

<table>
<thead>
<tr>
<th>Artery</th>
<th>PSV (cm/sec)</th>
<th>EDV (cm/sec)</th>
<th>Doppler Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ICA</td>
<td>139</td>
<td>65</td>
<td>60°</td>
</tr>
<tr>
<td>ECA</td>
<td>160</td>
<td>-</td>
<td>60°</td>
</tr>
<tr>
<td>Vertebral</td>
<td>88</td>
<td>Antegrade</td>
<td>60°</td>
</tr>
<tr>
<td>Velocity Ratio</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 shows the obtained velocities obtained on the left side at the internal carotid artery (ICA), external carotid artery (ECA) and vertebral artery. The peak systolic velocity (PSV) for the ECA and ICA are slightly elevated due to compression of the arteries due to the splaying of the vessels. The vertebral artery PSV was normal. The common carotid artery (CCA) velocities were not obtained.

The splaying of the vessels due to the location of the CBT can result in a typical flow pattern of low resistance accompanied by an elevated velocity in diastole, which was the case in this patient. The velocities in the CCA were not estimated due to inability to obtain the peak velocity due to limitations in patient positioning. Colour Doppler imaging in Figure 6a
demonstrates that the vessels are still patent with flow filling the extent of the width of the vessel. Colour Doppler imaging in Figure 6b demonstrates flow within the ECA as well as color fill in the carotid body tumor representing blood flow confirming vascularisation of the mass. The ECA can be seen in this image to be encapsulated by the tumor.

In summary, the carotid Duplex findings were consistent with a widely patent right carotid bifurcation with no recurrence of CBT or other paragangliomas following surgical excision of the right CBT. A large tumor was present in the left carotid bifurcation which encompasses the ECA, with no hemodynamically significant stenosis from atherosclerotic lesions noted.

Discussion

CBTs are rare paragangliomas found in the head and neck region that present sporadically and familial etiology is uncommon. Linkage studies have identified a common mutation in hereditary cases in the succinate dehydrogenase subunit D gene (SDHD), which contributes to the formation of the glomus type 1 cells. When this gene is suppressed, chemoreceptors react to low oxygen levels, and hypoxia occurs. This promotes factors of angiogenesis and therefore, vasoactive endothelial growth factor (VEGF) and reactive oxygen species (ROS) contribute to the formation of paragangliomas. The ultrasound imaging findings in this patient confirm that the lesion is vascularised (as noted in Figure 6b) and thus supports the presence of angiogenesis.

The preferred treatment of CBTs is complete surgical removal as CBTs are resistant to chemotherapy and although radiation therapy has previously been used for patients with carotid body metastasis, there is insufficient evidence to recommend this as a viable treatment option.
In addition, surgical excision of CBTs is complicated by their anatomical position and degree of encapsulation of neighboring vessels and nerves\textsuperscript{13}.

The patient in this case study reported symptomology included headaches and a syncopal episode both of which are suggestive of a reduction in perfusion to the cerebrum. The left-sided CBT in this patient was large in size and classified as a Shamblin’s type III CBT based on the encapsulation of the neighboring vessels. The hemodynamic consequence of a CBT is an increase in resistance intraluminally and subsequent reduction in blood flow as a consequence of the position of the tumor in the carotid bifurcation which results in splaying of the vessels and alterations of the normal pathway of blood flow. The consequence is a reduction in distal perfusion which is the most likely cause of the symptoms in this patient due to the invasive and compressive nature of the left-sided CBT which was noted to be large in size and extensive in its’ local invasion\textsuperscript{2,14}.

Duplex ultrasound is beneficial in detecting the presence of CBTs and establishing the extent of growth and invasion of the CBT. The utility of ultrasound in the assessment of this pathology lies with its’ ability to detect the morphology and relationship of the tumor to the surrounding vessels with 2D imaging as well as determination of the haemodynamic consequences of the tumor on the vessels it encapsulates and the degree of vascularity of the tumor through interrogation with both colour and spectral Doppler.

Considering the metastatic nature of the CBTs in this patient surgical removal was recommended. The potential for neural dysfunction was increased in this patient due to the presence of bilateral CBTs and this factor was carefully considered in the surgical planning when determining which tumor was to be removed first \textsuperscript{4,15}. A recent study by Kruger and
colleagues suggests that it is more effective to remove the smaller tumor first due to the minimal risk of cranial nerve injury and decreasing the risk of bilateral nerve palsies due to surgery. This has been proven to be an efficacious means of treatment in this particular patient as long-term neural injury was avoided.

**Conclusion**

CBTs can cause severe adverse effects on a patient’s long-term prognostic outcome. This case demonstrates a rare presentation of familial etiology with evidence of systemic metastasis requiring urgent attention due to the rate of progression. Removal of the right-sided CBT in this patient was successful at restoring blood flow in the right-sided vessels with no subsequent neural damage. Multi-modal imaging with MRI was essential in the initial identification of the CBTs in this patient and imaging post-surgical intervention with ultrasound demonstrates the utility of this imaging technique in establishing the success of intervention through the evaluation of anatomical and hemodynamic features.
References


Figure 1

Magnetic resonance image of carotid arteries (A) coronal view and (B) transverse view.

Figure 1 shows two magnetic resonance images of the patient's head. Image A shows the left carotid body tumor (red arrow) in the left carotid bifurcation in a coronal view. Image B shows a transverse view at the level of the carotid bifurcation indicating a right carotid body tumor (yellow arrow) and left carotid body tumor (red arrow).
Figure 2- Computed Tomography scan of carotid arteries with contrast.

Figure 2 shows a computed tomography (CT) scan with contrast indicating the positioning of the right and left carotid body tumors. It is evident that the left carotid body tumor (red arrow) causes splaying of the internal carotid artery (green arrow) and external carotid artery (yellow arrow) due to the large mass sitting in the bifurcation.
Figure 3 shows a DOTATE-PET scan of the full body in the coronal view. Red indicates a high uptake of isotope and blue indicates a low uptake of isotope which is indicative of metastases. There is an uptake of the radioisotope by the right carotid body tumor (green arrow) and left carotid body tumor (red arrow). The liver shows an isotope uptake supporting metastases at this site (yellow arrow).
Figure 4- B-Mode Ultrasound Image of the Right Carotid Bifurcation Post-Surgical Intervention

Figure 4 shows the carotid bifurcation (yellow arrow) on the right side post-surgical removal of the carotid tumor (7mm). The CCA, ICA, and ECA are all patent as illustrated by the anechoic appearance. The ICA shows some intimal thickening (red arrow) and smooth homogenous plaque (green arrow) which is minor and echogenic in appearance.

Figure 5- B-Mode Ultrasound Image of the Left Carotid Bifurcation and Carotid Body Tumour

Figure 5 shows the carotid bifurcation on the left side with a Shamblin type III classified carotid body tumor indicated by the yellow dotted line (47.3mm x 27.6 mm). The CCA is patent whilst the ECA and ICA are encapsulated by the tumor. The ICA appears splayed by the mass.
Figure 6- Color Doppler Image of the (A) Left Internal Carotid Artery and Carotid Body Tumour, (B) Left External Carotid Artery and Vascularised Carotid Body Tumour

Figure 6A shows the internal carotid artery (ICA) with Doppler color fill representing blood flow. The color bar illustrates a high pulse repetition frequency (PRF) of 67.4 cm/s. There is an aliasing appearance indicating turbulence (yellow arrow), which is due to splaying caused by the carotid body tumor (CBT). Figure 6B shows ECA is encapsulated by the CBT with color filling within the carotid body tumor (red arrows) indicating vascularisation.