Carotid body tumours

Carotid body tumours are a rare class of paraganglionoma arising from the upper neck, but should be considered in the differential diagnosis of neck lumps. A wrong diagnosis of cervical lymphadenopathy followed by excision biopsy may have serious consequences. The only way to minimize such risk is to be aware of their existence.

Historically, several obsolete terms have been used to describe carotid body tumours, including chemodectoma, glomus and non-chromaffin-staining paraganglia. More recently the term carotid paraganglionoma has become favoured (Martin, 2006). The carotid body was first described by Von Haller and Taube in 1743. In 1762, Heller introduced the term glomus tumour. In 1880, Riegner carried out the first excision of a carotid body tumour. Unfortunately, this patient did not survive the operation. In 1886, Maydl, removed a carotid body tumour successfully, however, the patient suffered a cerebrovascular accident resulting in hemiplegia and aphasia. It was not until 1889 that Albert carried out the first successful excision without ligating the carotid vessels. Since the 19th century surgery has become the treatment of choice although there is still debate about the potential for malignancy of these tumours and hence the timing of surgical intervention (Farr, 1980).

There are three types: sporadic, familial and hyperplastic forms. Around 85% of carotid body tumours are sporadic in nature, with approximately 10% classified as familial tumours. The familial type mainly involves younger patients and is more likely to be multi-centric and malignant. Hyperplastic carotid body tumours are more prevalent where individuals are exposed to conditions or environments of chronic hypoxia, such as chronic obstructive pulmonary disease, congenital cyanotic heart disease and where people live at high altitudes. Although carotid body tumours are usually non-functioning, sometimes serotonin-, histamine-, adrenaline- or noradrenaline-secreting tumours may occur (Sajid et al, 2007).

The carotid body

Embryological origins

The carotid body is a type of paraganglia. Paraganglia are aggregations of cells derived from the neural crest, which is derived from the neuroectoderm. These paraganglia are located throughout the body. In the abdomen and thorax they are associated with the sympathetic nervous system (and secrete catecholamines), the largest of which is the adrenal medulla. Head and neck paraganglia are associated with the parasympathetic system (and secrete a variety of neurotransmitters including acetycholine, adenosine triphosphate and dopamine), the largest of which is the carotid body. The carotid body has the same histological features as paraganglia in the abdomen but their role is more likely to be sensory than secretory (Lack, 1997). It is no surprise then that head and neck paraganglionomas including carotid body tumours have similar gender profiles, sizes and outcomes to phaeochromocytoma and abdominal paraganglioma. However, they occur at an older age, are more likely to cause local pressure effects and rarely have the functional effects of neurotransmitter release (Al-Harthy et al, 2009).

Anatomy

The carotid body is an oval reddish brown structure, 5–7 mm in length and 2.5–4 mm in width. It is found in the neck lying posterior to the common carotid artery bifurcation or between its branches. It is either attached to these branches or partly embedded in their adventitia. Occasionally it takes the form of separate nodules. The carotid body is surrounded by a fibrous capsule from which septa divide the enclosed tissue into lobules. Within these lobules are contained two types of cells. Type 1 (glomus) cells are separated from an extensive network of fenestrated sinusoids by type 2 (sustentacular) cells which act as supporting cells. The carotid body receives a rich blood supply from innominate branches off the carotid artery bifurcation. It receives sensory innervation through the glossopharyngeal nerve. The bodies are most prominent in children and normally involute with older age, when they are infiltrated by lymphocytes and fibrous tissue (Standring, 2008).

Physiology

The carotid body is critical in the body's ability to acutely adapt to fluctuating concentrations of oxygen, carbon dioxide, pH and blood temperature. The carotid body represents the largest collection of chemoreceptor tissue in the human body. Gram for gram, the carotid body's blood flow and oxygen consumption exceed that of the brain. Oxygen partial pressure changes are detected by type 1 (glomus) cells. Once stimulated, these cells release a variety of neurotransmitters and trigger an action potential through the afferent fibres of the glos-

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sopharyngeal nerve, which carries information to the respiratory centre of the CNS. As a result, organs are protected from hypoxic damage through an increase in the rate, depth and minute volume of ventilation, as well as an increase in sympathetic activity manifested by increased pulse rate, cerebrocortical activity, elevated blood pressure and vasoconstrictor tone. Interestingly, complete loss of hypoxic ventilatory drive has been shown in patients with bilateral carotid body resection (Gonzalez et al, 1994; Lack, 1997).

Epidemiology

Carotid body tumours account for over 65% of head and neck paraganglionomas. However, paraganglionomas account for only 0.6% of neoplasms of the head and neck region. The incidence of carotid body tumours is 1 in 30 000 with increased numbers where people live at high altitude in the south American Andes and the western states of the USA (Wilson, 1970). Nevertheless, carotid body tumours remain rare and most vascular surgeons will encounter few during their careers.

Most carotid body tumours present in middle age between the fourth and sixth decades with an increased incidence in women – the male to female ratio is 1:1.0–2.0. The Joint Vascular Research Group presented the largest ever carotid body tumour cases series in Europe and the UK by retrospectively analysing 95 patients over a period of 26 years. This analysis found the mean age at presentation to be 55 years, an age range of 18–94 years and a male to female ratio of 1:1.9 (Sajid et al, 2007). Although carotid body tumours are often considered a disease of middle age they may rarely occur in children. Only 16 cases of surgically excised carotid body tumours in children under the age of 14 years have been reported in the literature with the youngest being 3 months (Georgiadis et al, 2008).

International carotid body tumour case series are often of small number and show wide variation in patient characteristics. A literature review found the incidence of bilateral carotid body tumour to vary from 0–26%. Rates of malignancy vary from 0–15% and rates of recurrence in 0–5%. Functional tumours are very rare with rates reported at 1–3%; the Joint Vascular Research Group reported only 1 case from 95 patients (Dickinson et al, 1986; Wang et al, 1996; Patetsios et al, 2002; Sajid et al, 2007; Kruger et al, 2010). Rates of familial carotid body tumours vary from 0–28%.These familial types of carotid body tumour generally occur at a younger age, in the second to fourth decade. The mean age of diagnosis of mutation positive cases is 30 years compared to 47 years in paraganglionomas overall. Familial carotid body tumours also exhibit higher rates of bilaterality, multifocality (25–48% cases) and malignancy. Multiple tumours may occur simultaneously or at different times with 6-month to 29-year intervals (Wilson, 1970). It is because of this familial tendency that all members of the family should be examined.

Interestingly, there are significant differences in the epidemiology of carotid body tumours found at altitude *vs* those found at sea level in the cities of the USA or Europe. An early study of the effects of altitude in Peru found that 23 out of 25 (92%) subjects with carotid body tumours had lived at altitudes between 2105 and 4350 metres. Over half of these patients had respiratory conditions including emphysema, pulmonary fibrosis and pneumoconiosis. Comparisons of the prevalence of carotid body tumours at altitude and at sea level have revealed that they are 10 times more frequent at high altitude. Other studies have shown that incidence increases in direct relation to altitude (1/1000 at sea level, 9/1000 between 2000 and 3000 m, and 12/1000 between 3500 and 4000 m). Individuals harbouring mutations in carotid body tumour susceptibility genes and suffering chronic hypoxaemia also develop carotid body tumours at an earlier stage (Kay and Laidler, 1977; Pacheco-Ojeda et al, 1988).

A study of 120 cases in Mexico City found the male:female ratio at altitudes above 2000 metres to be 1:8.3 *vs* 1:1.0–2.0 at sea level. Although poorly understood, it has been suggested that this female preponderance may be the result of hormonal changes during pregnancy, periodic loss of erythrocytes during menstruation as well as men having a greater pulmonary capacity thus avoiding chronic hypoxia. Carotid body tumours found at altitude also show lower rates of bilaterality (5%) and familial tendencies (1%) *vs* rates of bilaterality of 0–26% and familial rates of roughly 0–28% at low altitudes. Incidentally, left-sided carotid body tumours are three times more common at altitude (Dickinson et al, 1986; Pacheco-Ojeda et al, 1988; Wang et al, 1996; Patetsios et al, 2002; Kruger et al, 2010).

Aetiology

Inheritance

Although the majority of cases appear to be sporadic, familial forms exist and are inherited in an autosomal dominant manner. Roughly 10% of carotid body tumours have a familial basis. In rare cases, familial paraganglionomas may be part of genetic syndromes such as von Hippel–Lindau disease, neurofibromatosis and multiple endocrine neoplasia. Three genes have been identified that are associated with genetic susceptibility to paraganglionomas. These are succinate dehydrogenase complex subunits 'D', 'B' and 'C' (SDHD, SDHB, SDHC). The genes most frequently implicated – SDHD and SDHB – also predispose to phaeochromocytoma with the risk highest in SDHB. SDHD shows a complex inheritance pattern. If the mutation is inherited from the mother, tumours do not develop. Patients who present with multiple tumours or a family history of carotid body tumours or early onset (<50 years) should be referred for genetic investigation. Patients in whom a SDH subunit mutation is identified should be followed up regularly for further paraganglionomas and phaeochromocytomas (Martin et al, 2007).

The effect of hypoxia

The impact of environment on the development of neoplasms is well known. For example, increased ultraviolet sunlight exposure leads to increased rates of skin cancer, however, the effect of altitude on the neoplastic process is not as readily recognized. At altitudes higher than 2000 m, atmospheric oxygen is diminished and produces chronic hypoxia. Hypoxia is further compounded by chronic medical conditions such as chronic obstructive pulmonary disease. As a result, carotid type 1 cells become stressed as they compensate for lower oxygen levels. Over time hypertrophy occurs with increased volume of functional glomic tissue and capillary blood vessels. Eventually hyperplasia and neoplasia of the type 1 cells occurs. It appears that carotid body tumours at altitude represent an extreme degree of this process. This concept is supported by their slow rate of growth and benign clinical course and may explain why populations at altitude experience higher rates of carotid body tumours (Saldana et al, 1973; Kay and Laidler, 1977).

Presentation

Signs and symptoms

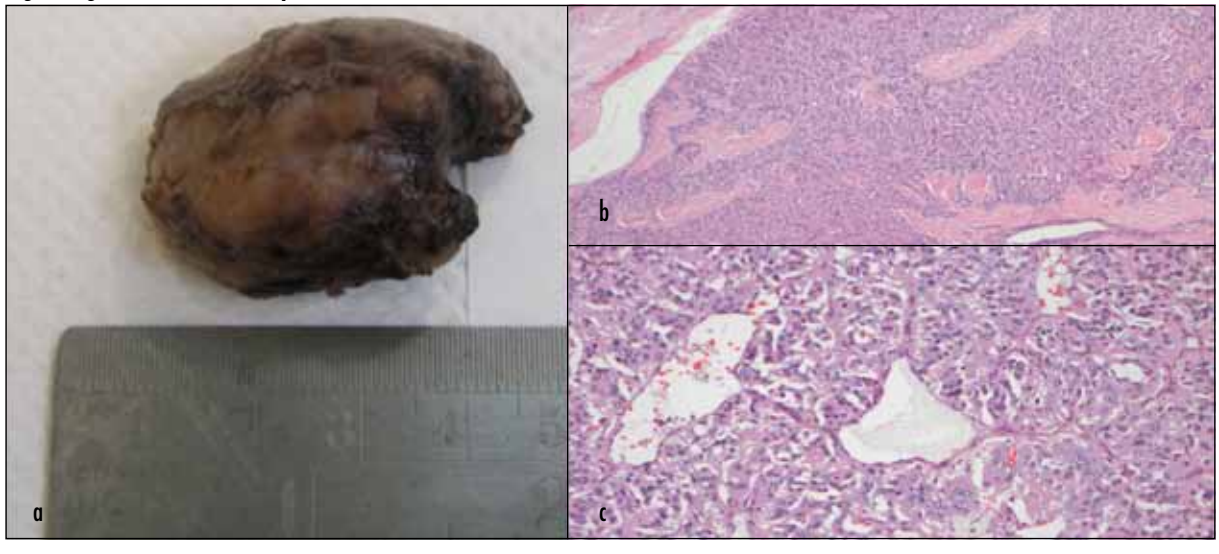
Carotid body tumours are difficult to diagnose clinically, often being mistaken for cases of cervical lymphadenopathy, salivary glands, neurofibromas, branchial cysts or lipomas. They commonly present as an asymptomatic, painless, slow-growing, compressible, rubbery mass in the upper neck. Carotid body tumours are closely associated with the carotid artery pulsation and occur at the carotid bifurcation level with the hyoid bone just in front of the anterior edge of the upper third of the sternocleidomastoid muscle. At presentation, tumour sizes vary greatly. On examination it may be difficult to locate small tumours whereas the largest carotid body tumours may exceed 15 cm in diameter (Patetsios et al, 2002). As they are attached to the carotid sheath, they typically have limited vertical movement and relatively free lateral mobility (Fontaine's sign). Occasionally a bruit may be heard suggesting compression of the carotid arteries. They have usually been present for a considerable time: one series reported a patient presenting after 47 years. The average duration to diagnosis has been reported as 4 years. By plotting size of tumour against duration one can estimate the growth rate as 2 cm in 5 years (Farr, 1980).

Symptoms are reported by approximately 10% of patients. The carotid bifurcation lies close to many important and sensitive structures. Significant expansion and invasion of surrounding cranial nerves may lead to paresis (VII, IX, X, XI, XII) resulting in dysphagia, choking and hoarseness. Other symptoms may be associated with pressure on surrounding structures causing neck pain, dysphonia, stridor, dysphagia, odynophagia, jaw stiffness and sore throat. While all chemoreceptor cells contain neurosecretory cells and are capable of secreting neurotransmitters, carotid body tumours are generally non-secretory. However, rarely functional carotid body tumours may present with symptoms similar to those of phaeochromocytomas with paroxysmal hypertension, palpitations and diaphoresis (Sajid et al, 2007).

Pathology

On gross examination these tumours are usually well-circumscribed and may have a pseudocapsule. The cut surface is typically solid with a smooth, rubbery texture but may display some areas of haemorrhage. Being highly vascular they may have a deep red colour. Histologically, carotid body tumours have a characteristic organoid growth pattern referred to as 'zellballen' where individual tumour cells (predominantly type 1 cells) are polygonal and are arranged in distinctive cell balls. These cell balls are supported by sustentacular cells at the periphery and are separated by a fibrovascular stroma (Wieneke and Smith, 2009) (*Figure 1*).

Figure 1. Carotid body tumour pathology. a. Gross image of excised carotid body tumour with (b and c) histology displaying typical organoid growth or 'zellballen' pattern.



There are no definitive, well-accepted, reproducible histological criteria for malignancy in carotid body tumours. Worrisome histological features include necrosis, extensive capsular or vascular invasion, increased mitotic activity, cellular atypia, loss of the well-differentiated zellbalen pattern and tumour spindling. However, these features tend to be unreliable in predicting tumour behaviour (Wieneke and Smith, 2009).

Investigations

Although carotid body tumours are rarely associated with neurotransmitter release, assessment of urinary catecholamines, vanillylmandelic acid and metanephrines is routine in most centres. In those patients who present with symptoms of a functional carotid body tumour assessment of urinary catecholamines is essential. Owing to their highly vascular nature, incisional biopsy is not recommended as there is a risk of profuse bleeding. In addition, the histological appearance is not predictive of malignant behaviour (Farr, 1980).

Various imaging modalities may be used to identify carotid body tumours. Duplex ultrasound scanning is the primary diagnostic investigation of choice. First, the use of grayscale ultrasound will help to confirm the relationship of the tumour to the carotid bifurcation and demonstrate typical splaying of the carotid bifurcation. Second, colour Doppler will demonstrate the vascularity of the tumour and precisely identify associated vessels and the extent of their involvement. The use of ultrasound may also be used in follow-up and screening of sporadic and familial cases (*Figure 2*).

If ultrasound suggests a carotid body tumour, further modalities are usually used for preoperative assessment and these include digital subtraction angiography, computed tomography, computed tomography angiogram, magnetic resonance imaging and magnetic resonance angiography. On computed tomography scanning, carotid body tumours are easily recognized as hypervascular masses located at the carotid bifurcation, bringing apart the internal and external carotid arteries to resemble a saddle. Computed tomography angiography allows visualization of a tumour blush, the arterial anatomy and any feeding vessels associated with the carotid body tumour. The diagnosis of carotid body tumours using computed tomography angiography is usually based on angiographic criteria, the most reliable of these being the separation and splaying of internal and external carotid arteries (known as the Lyre sign) (*Figure 3*). Magnetic resonance imaging is the most useful imaging modality in evaluating carotid body tumours in relation to the surrounding soft tissues and vascular structures (Morris and Malt, 1994) (*Figure 4*).

Figure 2. Ultrasound imaging. a. Left-sided carotid body tumour, demonstrating (b and c) marked vascularity and (d) splaying of internal and external carotid arteries (red arrows show location of internal and external carotid arteries).

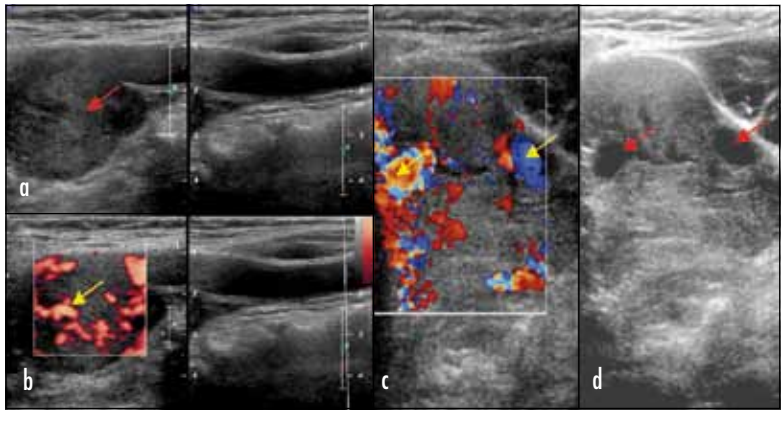
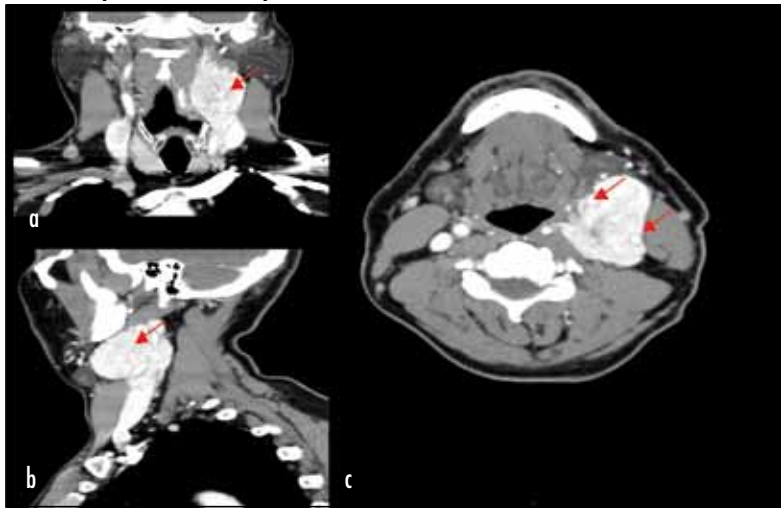


Figure 3. Computed tomography neck (coronal, sagital and axial). a and b. Left-sided carotid body tumour intimately associated with (c) internal and external carotid arteries.



Management

Conservative

Since most tumours are benign, their natural course is of slow enlargement with eventual compression of local structures resulting in symptomatic nerve palsies. In an elderly patient without such symptoms a conservative approach may be advocated. However, it is much safer to remove the tumour before it becomes enlarged and before extensive local invasion. Without treatment, reports suggest that 75% of asymptomatic patients eventually develop symptoms and 30% will die from invasion of local structures or metastatic disease (Morris and Malt, 1994).

Surgical

Surgery is the treatment of choice for carotid body tumours. Surgical treatment usually involves complete excision of the tumour and should be performed early while the tumour is small to avoid progressive local invasion, the risk of metastases and postoperative complication and mortality associated with larger tumours (>5 cm) (Shamblin et al, 1971). The operative plan should be based on tumour location and carotid involvement.

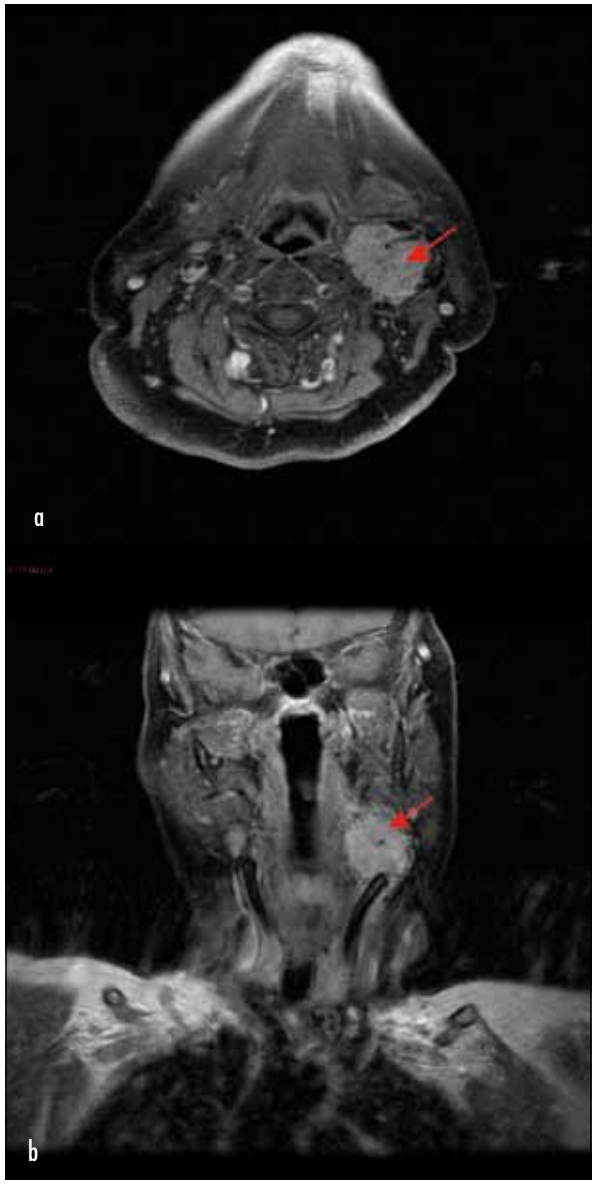
The Shamblin classification is commonly used as a risk management strategy before surgical intervention through the use of imaging studies such as computed

tomography or magnetic resonance imaging. Shamblin's original classification, proposed in 1971, grouped carotid body tumours according to the degree of invasion of the arterial wall. Staging was thus dependant on intraoperative findings, and unrelated to the size of the tumour. More recently, evidence has shown that magnetic resonance imaging can now reliably predict the Shamblin's class preoperatively (Arya et al, 2008). Group 1 are straightforward to remove from the vessels, group 2 require dissection in a subadventitial plane to remove them from the vessel, group 3 tumours encircle and invade the vessel to such an extent that they usually require complete arterial excision and replacement with a length of saphenous vein.

Approximately 50% of carotid body tumours are in Shamblin group 2 and 25% in each of the other groups. Size did not influence Shamblin's original classification, but more recently Luna-Ortiz et al (2006) suggested integrating size into the existing Shamblin classification, proposing that in doing so they can better predict incidences of vascular and neurological injury. In this classification, 'type' 1 (instead of group 1) are tumours less than 4 cm which are clearly separate from the carotid vessels and are easily dissected from the carotid vasculature, 'type 2' are those tumours greater than 4 cm that partially surround the carotid vessels, but dissection is possible without vascular sacrifice, and 'type 3' are those tumours which are intimately associated with the vessel and require vascular repair or sacrifice. Type 3 tumours are further subdivided into type a (greater than 4 cm) and type b (less than 4 cm) (Luna-Ortiz et al, 2006). That said, Shamblin's original classification is still the most widely used system for classifying carotid body tumours.

Bilateral carotid body tumours should not be removed in the same operation. The incidence of nerve damage is sufficiently high to make bilateral recurrent laryngeal nerve and hypoglossal nerve palsies a significant risk factor. In patients who have had a previous carotid body tumour, resulting in nerve palsy or carotid occlusion, the risks of the operation on a contralateral tumour are significant and radiotherapy should be considered (Morris and Malt, 1994; Singh et al, 2006).

Figure 4. Magnetic resonance image of neck: (a) axial and (b) coronal showing left-sided carotid body tumour (arrowed).



Radiotherapy

Surgical excision provides a number of concrete advantages to the patient – the procedure is potentially curative, allows precise pathological diagnosis and in certain cases will have an aesthetic benefit if the tumour is particularly large. However, surgery is not without significant risks. If ligation or replacement of the carotid vessels is likely, if a large tumour is unresectable because of size or patients are at high risk from a general anaesthetic, radiotherapy has been described as an initial treatment in some centres. Hinerman et al (2001) describe their experience with definitive radiotherapy for a variety of paraganglionomas, including 25 carotid body tumours. Within this cohort there was only one recurrence, and the authors estimate a 15-year local control rate following radiotherapy of 92%. However, radiation treatment carries a risk of inflammation of the external auditory canal and middle ear, osteoradionecrosis, cranial nerve neuropathies, direct injury to the brain tissue and acute radiation mucositis. Furthermore, radiotherapy renders subsequent head and neck surgery highly challenging as a result of radiation-induced scarring. As such, a number of authors have advised its use be reserved as a second-line treatment modality, when surgery is either contraindicated or has previously failed (Morris and Malt, 1994; Hinerman et al, 2001; Singh et al, 2006).

Embolization

These tumours are very vascular and, if large, excision may result in excessive blood loss. In dealing with tumours larger than 3 cm, preoperative embolization

may be indicated. Once the tumour has been devascularized, surgery should be performed within the next 72 hours before neovascularization occurs (Morris and Malt, 1994).

Prognosis

Short term

Surgical resection of carotid body tumours is associated with mortality rates of 0–3% (Dickinson et al, 1986; Wang et al, 1996; Patetsios et al, 2002; Kruger et al, 2010).The Joint Vascular Research Group reported postoperative morbidity rates of 35% (Sajid et al, 2007). In the postoperative period, the patient should be closely monitored for central and peripheral neurological deficits, especially of cranial nerves IX, X, XII, cervical sympathetic nerves and the mandibular branch of VII. The incidence of cranial nerve defects is particularly associated with the removal of large tumours (>5 cm) and is reported in 0–27% of cases although most recover in a few weeks with less than <1% of patients left with permanent cranial nerve deficits. Cerebrovascular events occur in less than 3% of cases in most series (Dickinson et al, 1986; Wang et al, 1996; Patetsios et al, 2002; Sajid et al, 2007; Kruger et al, 2010).

Long term

Most patients are 'cured' by surgery with recurrence rates of less than 5%, although patients with a familial basis to their disease are at increased risk of multifocality (Dickinson et al, 1986; Wang et al, 1996; Patetsios et al, 2002; Kruger et al, 2010). Cranial nerve palsies associated with carotid body tumour resection are usually temporary. However, those caused by prolonged compression by the tumour itself are sometimes permanent. Although malignant tumours may be diagnosed histologically, they are usually only identified after metastatic disease develops. If the tumour is known to be malignant because of local or metastatic disease, local radiotherapy can be used to prevent local recurrence or to treat metastatic disease as it occurs. Most tumours are slow growing and survival for many years is possible even with established metastatic disease.

Conclusions

Carotid body tumours, although rare, should be considered in the differential diagnosis of neck lumps. Early diagnosis and treatment avoids symptoms associated with progressive local invasion. If surgical resection is carried out while the tumour is still small good results can be achieved with minimal postoperative complications. BJHM

KEY POINTS

- Carotid body tumours are a rare class of paraganglionoma arising from the neck region.
- They commonly present as a painless, slow-growing, mass in the upper neck.
- Duplex ultrasound scanning is the primary diagnostic investigation of choice.
- Surgical treatment usually involves complete excision of the tumour.
- Early excision achieves good results with minimal postoperative complications.

Conflict of interest: none.

Al-Harthy M, Al-Harthy S, Al-Otieschan A, Velagapudi S, Alzahrani AS (2009) Comparison of pheochromocytomas and abdominal and pelvic paragangliomas with head and neck paragangliomas. *Endocr Pract* **15**(3): 194–202

Arya S, Rao V, Juvekar S, Dcruz AK (2008) Carotid Body Tumors: Objective Criteria to Predict the Shamblin Group on MR Imaging. *AJNR Am J Neuroradiol* **29**(7): 1349–54

Dickinson PH, Griffin SM, Guy AJ, McNeill IF (1986) Carotid body tumour: 30 years experience. *Br J Surg* **73**(1): 14–16

Farr HW (1980) Carotid Body Tumours: A 40 year study. *CA Cancer J Clin* **30:** 260–5

Georgiadis GS, Lazarides MK, Tsalkidis A, Argyropoulou P, Giatromanolaki A (2008) Carotid Body Tumour in a 13 year old child: Case Report and review of the literature. *J Vasc Surg* **47**(4): 874–80

Gonzalez C, Almaraz L, Obeso A, Rigual R (1994) Carotid body chemoreceptors: from natural stimuli to sensory discharges. *Physiol Rev* **74**(4): 829–98

Hinerman RW, Mendenhall WM, Amdur RJ, Stringer SP, Antonelli PJ, Cassisi NJ (2001) Definitive radiotherapy in the management of chemodectomas arising in the temporal bone, carotid body, and glomus vagale. *Head Neck* **23**(5): 363–71

Kay JM, Laidler P (1977) Hypoxia and the carotid body. *J Clin Pathol* **11:** 30–44

Kruger AJ, Walker PJ, Foster WJ, Jenkins JS, Boyne NS, Jenkins J (2010) Important observations made managing carotid body tumors during a 25-year experience. *J Vasc Surg* **52**(6): 1518–23

Lack EE (1997) Paraganglia of the head and neck region. In: Rosai JM, ed. *Atlas of Tumor Pathology: Tumors of the Adrenal Gland and Extra-adrenal Paraganglia.* Armed Forces Institute of Pathology, Washington, DC: 303–6

Luna-Ortiz K, Rascon-Ortiz M, Villavicencio-Valencia V, Herrera-Gomez A (2006) Does Shamblins classification predict postoperative morbidity in carotid body tumours? A proposal to modify Shamblins classification? *Eur Arch Otohinolaryngol* **2:** 171–5

Martin TP (2006) What we call them: the nomenclature of head and neck paragangliomas. *Clin Otolaryngol* **31:** 185–6

Martin TP, Irving RM, Maher ER (2007) The genetics of paragangliomas: a review. *Clin Otolaryngol* **32**(1): 7–11

Morris PJ, Malt RA (1994) *Oxford Textbook of Surgery.* Vol 1. Oxford University Press, Oxford

Pacheco-Ojeda L, Durango E, Rodriquez C, Vivar N (1988) Carotid body tumors at high altitudes: Quito, Ecuador, 1987. *World J Surg* **12**(6): 856–60

Patetsios P, Gable DR, Garrett WV et al (2002) Management of Carotid Body Paragangliomas and Review of a 30-Year Experience. *Ann Vasc Surg* **16**(3): 331–8

Sajid MS, Hamilton G, Baker DM (2007) A multicenter review of carotid body tumout management. *Eur J Vasc Endovasc Surg* **34:** 127–30

Saldana MJ, Salem LE, Travezan R (1973) High altitude hypoxia and chemodectomas. *Hum Path* **4**(2): 251–63

Shamblin WR, DeMine WH, Sheps SG, Harrison EG Jr (1971) Carotid body tumour (chemodectoma). Clinicopathological analysis of 90 cases. *Am J Surg* **122:** 732–9

Singh D, Pinjala RK, Reddy RC, Satya Vani PVNL (2006) Management of carotid paraganglionomas. *Interact Cardiovasc Thorac Surg* **5:** 692–5

Standring S (2008) *Grays Anatomy: The Anatomical Basis of Clinical Practise.* 40th edn. Elsevier Churchill Livingstone, London

Wang DG, Barros D'Sa AA, Johnston CF, Buchanan KD (1996) Oncogene expression in carotid body tumors. *Cancer* **77**(12): 2581–7

Wieneke JA, Smith A (2009) Paraganglioma: Carotid Body Tumour. *Head Neck Path* **3**(4): 303–6

Wilson H (1970) Carotid Body Tumours: Familial and Bilateral. *Ann Surg* **171**(6): 843–8