

## **ANAESTHETIC MANAGEMENT OF CHEMODECTOMA EXCISION**

Dr. Babita Gupta<sup>1</sup>, Dr. Jayanta Kumar Mitra<sup>2</sup>

1. Assistant Professor, 2. Senior Resident  
Department of Anaesthesia and Intensive Care  
All India Institute of Medical Sciences,  
New Delhi – 110029

Correspondence: Dr. Babita Gupta ([drbabitagupta@hotmail.com](mailto:drbabitagupta@hotmail.com))

**About the Author:** Dr. Babita Gupta, a student of Seth G.S. Medical College and KEM Hospital, Mumbai, did her M.D in 1997. She worked as a Lecturer in the same Institution till 1999. She worked as a Senior Resident in G.B. Pant Hospital and gained experience in Cardiac Anaesthesia, and joined as Specialist Cardiac Anaesthesia in 2002. She then worked in Libya as a Consultant Paediatric Cardiac Anaesthesiologist in 2004-05 and subsequently joined AIIMS as Assistant Professor in October 2005.

### **Introduction**

Carotid body tumours (CBTs) or chemodectoma are rare non-chromaffin paragangliomas arising from the chemoreceptor cells found at the carotid bifurcation. About 1000 cases have been reported in the literature<sup>1</sup>. The mainstay of therapy is complete tumour excision. These tumours can present potential anaesthetic problems. There are many reports in the literature on the surgical management of CBT<sup>2-7</sup>. However, reviews on the anaesthetic considerations are sparse<sup>8-12</sup>. We have tried to cover all the aspects of peri-operative management of carotid paraganglioma excision.

### **Historical Overview**

Albrecht Von Haller described the carotid body anatomically in 1743<sup>13</sup>. The first attempt at surgical extirpation of carotid paraganglioma was by Reigner in 1880, and the patient died<sup>14</sup>. In 1886, Maydl successfully removed the tumour, leaving the patient aphasic and hemiplegic<sup>15</sup>. The first removal of a carotid paraganglioma with preservation of carotid artery complex in US was by Scudder in 1903<sup>16</sup>. Just about 40 years ago, in 1957, the mortality and morbidity remained so high, that Hayes Martin recommended abandonment of resection of difficult tumours on proof of diagnosis<sup>17</sup>. Mortality rate was as high as 10% till 1970's<sup>4</sup>. Mortality and morbidity have improved greatly in the current era, largely due to the development of modern imaging and vascular surgical techniques. Recent review of studies shows no mortality. However, perioperative morbidity continues to remain high (20%-40%)<sup>18-23</sup>.

## **Carotid Body Embryology, Anatomy and Physiology**

The carotid body originates from the third branchial arch mesoderm and from ectodermal -derived neural crest lineage. The normal carotid body is an ovoid pink structure approximately 6×4×2 mm in size and is located in the periadventitial tissue. The gland is innervated by glossopharyngeal nerve. Its blood supply is the richest per gram of tissue of any tumour and is derived from vaso-vasorum, branches of the vertebral artery, and predominantly, from the external carotid artery via its branches. Histologically the gland is composed of multiple lobules consisting of three types of cells, each of which is responsive to hypoxia. All three types of cells generate a variety of neurochemicals that serve as first and second messengers and act on target cells by hormonal mechanisms. Epinephrine, Norepinephrine, dopamine, acetylcholine, tyrosine and endothelin are some of the neurochemicals isolated from normal and abnormal carotid bodies<sup>24</sup>. Carotid bodies are primarily responsive to hypoxia and to a lesser degree to hypercapnia and acidosis.

## **Aetiology of Carotid Paraganglioma**

Chronic hypoxemia either sustained or intermittent is a stimulus for hypertrophy and hyperplasia of the gland. Disease accompanied by abnormally low PaO<sub>2</sub> or person residing at high altitudes lead to chronic sustained hypoxic conditions. Chronic intermittent hypoxia results from sleep apnoea or by frequent ventures into hypoxic conditions. Carotid paragangliomas arising from chronic hypoxia are termed nonheritable<sup>25</sup>. Heritable lesions arise in response to familial genetic characteristics of the multiple endocrine neoplasia type II syndrome, to de novo germ-line mutations in tumour susceptibility genes or occur spontaneously in hyperplastic glands<sup>25</sup>. The heritable constitutes approximately 35% of all carotid paragangliomas<sup>26</sup>. An individual who harbours mutant gene and is also subjected to chronic hypoxia, may develop a tumour at an earlier age than otherwise<sup>27</sup>. These tumours are genetically heterogeneous and have been mapped to at least 4 different chromosomal loci. Each of the 4 types seen in carotid paraganglioma has a dominant mode of inheritance<sup>28</sup>.

## **Clinical Presentation**

Patients can present at any age but do so most commonly in fifth and sixth decades. The usual presentation is that of a slow growing painless lump in the neck discovered by the patient or by an examiner incidentally<sup>24</sup>. The presence of a bruit over the mass is uncommonly noted but when present suggests significant compression of the artery. Bulging of the oropharyngeal wall, denoting parapharyngeal space extension occurs in approximately 10% of

tumours<sup>29</sup>. The carotid bifurcation lies close to many important structures and so expansion of the tumour may lead to cranial nerve paresis (VII, IX, X, XI and XII) resulting in symptoms of dysphagia, choking or hoarseness. The incidence of cranial nerve involvement has been estimated to be 20%<sup>30</sup>. Sometimes these tumours are confused with enlarged lymph nodes, branchial cysts, salivary glands, carotid aneurysms or neurofibromas. A useful clinical sign in differentiating a carotid paraganglioma from other lesions is Fontaine's sign: a carotid paraganglioma can usually be displaced laterally but not vertically<sup>5</sup>. Rarely, patient can present with symptoms secondary to the endocrine products of the tumour<sup>31</sup>. Family history of carotid paraganglioma may be present in familial paragangliomas.

## **Diagnosis**

It is vitally important to appreciate the possibility of a carotid paraganglioma in a patient who presents with a neck lump in the region of the carotid bifurcation. A misdiagnosis of lymph node enlargement followed by an attempt of excision biopsy/aspiration cytology can prove to be catastrophic<sup>32</sup>.

Duplex US scanning gives precise identification of the vessels and the extent of their involvement<sup>5</sup>. CT or MRI scan are useful in assessing the extent of the neoplasm, its relationship with carotid arteries and adjacent structures, and the presence of metastasis. Carotid arteriography is the gold standard for the diagnosis, assessment of both carotid circulations when vessel resection is a possibility, and for exclusion of a contralateral tumour<sup>32</sup>. Arteriography also affords an opportunity for preoperative embolisation of feeder vessels to reduce intra-operative blood loss<sup>33,34</sup>. It also gives an opportunity for a balloon occlusion test of internal carotid artery to determine if the patient would be able to tolerate ligation or sacrifice of the artery should it be necessary<sup>33</sup>. Preoperative arteriogram may also include intracranial views to determine whether Circle of Willis is intact. Carotid arteriogram demonstrates splaying of the carotid bifurcation, a tumour flush, and often allows tumour-feeding vessels to be identified (Fig-1). Indium pentetate scanning for the detection of familial paragangliomas<sup>35</sup> and octreotide scintigraphy to detect both primary and concurrent paragangliomas have been considered reliable tests<sup>36</sup>.

## **Malignant Carotid Paragangliomas**

The estimated incidence of malignancy is between 5% and 7%<sup>24</sup>. The risk of malignancy is greatest in young patients with heritable tumours<sup>37,38</sup>. Aggressive local invasion with encirclement of the carotid vessels may suggest the presence of a cancerous lesion; however,

documentation of metastasis to regional lymph nodes, liver or lungs is usually required for a carotid paraganglioma to be designated as malignant. There are no uniform recommendations for their management. There are a few reports of variable results after planned adjuvant radiation and/or chemotherapy for control after excision<sup>38-42</sup>.

### **Functional Carotid Paragangliomas**

All paragangliomas are capable of catecholamine production. The proportion of catecholamine secreting paragangliomas is thought to be high for adrenal pheochromocytomas, intermediate for aortico-sympathetic tumours and low for paragangliomas of the head and neck region<sup>43</sup>. The pheochromocytoma syndrome is exhibited when catecholamines are produced at 4-5 times the normal and 1-4% of paragangliomas of the head and neck can independently secrete sufficient amounts of catecholamine to mimic a pheochromocytoma<sup>44,45</sup>. Symptoms of inappropriate catecholamine secretion include labile blood pressure, headaches, cardiac arrhythmias, weight loss, and unusual flushing or sweating<sup>46</sup>. A high index of suspicion should be held for the presence of an associated pheochromocytoma because of the very significant incidence of associated pheochromocytoma with paragangliomas, especially since pheochromocytomas associated with the polyglandular and neurocutaneous syndromes may be asymptomatic<sup>47</sup>.

### **Treatment**

The treatment modalities for carotid paraganglioma excision are surgery and/or radiotherapy.

Radiotherapy may be used for carotid paragangliomas. In general, the principal indications for the use of radiotherapy as primary treatment for carotid paragangliomas includes extensive tumours where resection would result in significant morbidity as well as patient related factors such as age and medical condition. Evenson et al<sup>48</sup> and Valdagni<sup>49</sup> and Amichetti have reported on radiotherapy as primary treatment for carotid paragangliomas, both studies demonstrating excellent rates of control. However, other authors are of the opinion that radiotherapy is palliative, as recurrence has been observed after initial control and best reserved for unresectable and multifocal tumours<sup>50,51</sup>. Reported complications from radiotherapy include necrosis of the mandible, carotid artery and larynx<sup>52</sup>.

Surgical removal is the treatment of choice. Shamblyn classification<sup>53</sup> is used to assess the difficulty of surgical resection: Class I lesions consist of tumours easily isolated and dissected from the carotid vessels; Class II lesions are more adherent to the adventitial layer and partially encircle the vessel at bifurcation; and

Class III lesions are more densely adherent to the carotid vessels and completely encircle the carotid bifurcation.

The routine use of pre-operative tumour embolisation is controversial because of the potential neurologic complication associated with the accidental reflux of particulate matter into the ophthalmic or cerebral circulation<sup>54</sup>. Some authors advocate its use before the resection of large tumours because it may decrease the vascularity of the tumour, reducing intraoperative blood loss and transfusion requirements<sup>33,34</sup>. The apparent benefits of embolisation should be weighed against the risk of stroke and that its current use be limited to tumours greater than 5 cm in diameter<sup>5</sup>.

**Surgical technique:** A small sized tumour is technically easier to resect. When these lesions are 5cm or greater/Shamblin Class III, their surgical resection becomes difficult because of their extreme vascular nature and their intimate attachments to the carotid vessels. The patient is positioned supine with the neck rotated to the opposite side. Since the need for carotid resection cannot always be predicted one leg is prepared in case the saphenous vein should be required. The carotid artery is exposed through a standard anterolateral cervical incision along the anterior border of the sternocleidomastoid muscle. Control of the common, internal and external carotid arteries is obtained and hypoglossal and vagus nerves are identified. Using the bipolar diathermy, a capsular- adventitial or subadventitial (white line) dissection plane is established at the inferior margin of the tumour at bifurcation and extended cephalad onto the internal and external carotid arteries. Branches of external carotid artery may require division to facilitate the dissection. This technique is usually adequate for excision of Shamblin Class I and II tumours. Tumours completely encasing or infiltrating the internal carotid artery (Class III) are often managed by resection of the involved portion of the artery and replacement with a saphenous interposition vein graft<sup>5</sup>. It may be necessary to either insert a shunt or temporarily clamp the common carotid artery to devascularise these tumours. Although some authors recommend the routine use of a shunt in large tumours, shunts are used only when EEG and CBF studies demonstrate insufficient perfusion during carotid artery occlusion. This minimizes the risks associated with a shunt and avoids an unnecessary arteriotomy.

### **Anaesthetic Management**

Anaesthetic management of carotid paraganglioma excision stems directly from the preoperative concerns.

One of the important concerns involves excess catecholamine secretion. A careful history and physical examination are crucial in identifying functional paragangliomas. Whether all patients of carotid

paragangliomas should test for serum and urine catecholamine levels is controversial. Some authors suggest these investigations should be applicable only to patients with a suggestive history<sup>55</sup>. However, there are cases reported wherein catecholamine levels as high as eight times normal has been found without clinical symptoms<sup>56</sup>. Considering the fact that perioperative morbidity would be high without proper preoperative preparation in undiagnosed functional carotid paragangliomas<sup>57-59</sup>, preoperative measurement of serum and 24-hour urinary catecholamines is justified in all patients with carotid paragangliomas. Blood sugar should also be measured since patients with functional tumours show an inhibition of peripheral uptake of glucose and inhibition of insulin production by pancreatic  $\beta$ -cells<sup>60</sup>. Preoperative administration of  $\alpha$ -blockers and the intraoperative use of propranolol for  $\beta$ -adrenergic blockade have been advocated in the prevention of cardiovascular complications during the induction of anaesthesia and surgery<sup>61</sup>.

Involvement of cranial nerves that may predispose to airway obstruction or aspiration may occur in one of several ways: tumour invasion preoperatively; nerve injury or sacrifice intraoperatively; or tissue oedema causing nerve palsy postoperatively. Ninth, tenth and twelfth cranial nerve dysfunction can predispose to airway compromise, either by aspiration or obstruction. The anaesthesiologist should be aware of pre-operative cranial nerve palsy and/or inadvertent nerve damage during surgery. Postoperatively, the dynamic nature of oedema around cranial nerves, one to three days after the procedure, must be appreciated. Frequent observation for stridor and wheezing is pertinent<sup>56</sup>.

It is important to appreciate the risk of massive and rapid blood loss while resecting the tumour. Besides standard monitors, an arterial line for invasive blood pressure monitoring, central venous pressure monitoring and continuous urinary catheterization are suggested.

Reflex bradycardia from carotid sinus stimulation should respond to intravenous atropine or may be prevented by infiltration around the carotid sinus with local anaesthetic<sup>8</sup>. However, local anaesthetic infiltration needs to be done cautiously as intravascular injection of local anaesthetic during tumour excision has been reported<sup>10</sup>.

Carotid artery may need to be clamped to excise the tumour. Protection of the brain during carotid artery clamping involves monitoring for cerebral ischaemia and management of the same if it occurs. Monitoring for adequacy of cerebral blood flow (CBF) are electroencephalogram (EEG), somatosensory evoked potential (SSEP), measurement of distal carotid stump pressure, transcranial doppler blood flow measurements<sup>62</sup>, and cerebral oximetry<sup>9</sup>. However, the pressures in the common carotid distal to the clamp likely reflects the

pressure in the internal carotid, provide information about cerebral pressure and the effects of the manipulations in the systemic blood pressure.

There are a number of techniques commonly used to protect the brain during carotid artery clamping. Elevation of the blood pressure during carotid artery clamping has been used to promote collateral flow of the ischemic hemisphere. This has the capacity to prevent or reverse changes on the EEG and presumably averts ischemic injury<sup>63</sup>. Prolonged and excessive decreases in blood pressure may jeopardize the cerebral perfusion pressure (CPP) and the adequacy of CBF through collateral channels. Mild hypothermia (34-35°C) has been shown to have a protective effect on the ischemic brain<sup>64</sup>, but is not easy to institute rapidly. Of the many agents proposed for pharmacological protection of the ischemic brain, the barbiturates have been most extensively studied. Mechanisms of action of barbiturates are reduced cerebral metabolic rate of oxygen (CMRO<sub>2</sub>), free radical scavenging, inhibition of calcium uptake and protection from nitric oxide induced cytotoxicity<sup>65</sup>. Other known effects of barbiturates such as reduction of intracranial pressure (ICP) and redistribution of CBF from perfused to ischemic areas (inverse steal) may also play a role<sup>66</sup>. The optimal dose, timing and mode of administration have not been defined. A single bolus of thiopentone causes CMRO<sub>2</sub> suppression for 5-10 minutes<sup>67</sup>. This can cause mild hypotension, which can be treated by judicious volume expansion and use of vasopressors. Granell et al consider cerebral protection to be essential during carotid paraganglioma surgery, which may be provided by drugs such as thiopentone and by temporarily shunting the internal carotid artery<sup>9</sup>.

Several other points need consideration in the anaesthetic management of chemodectoma. Hyperglycemia exacerbates ischemic cerebral damage<sup>68</sup> so dextrose free fluid is recommended if the carotid artery is clamped<sup>8</sup>. Heparin is routinely administered prior to carotid artery clamping to prevent intravascular thrombosis in areas of stasis.

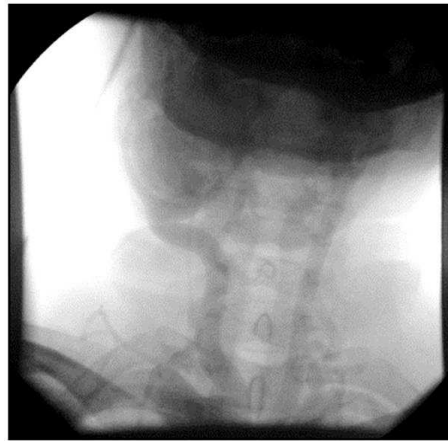
Baroreflex failure is a rare complication, which an anaesthetist should be aware of. Baroreflex failure may arise from denervation of carotid baroreceptor following bilateral carotid paraganglioma excision. Most postsurgical cases occur within days of surgery and if not recognized early it can lead to disastrous postoperative complication such as stroke and myocardial infarction<sup>69</sup>.

Severe postoperative respiratory depression can follow the surgical excision of chemodectoma. The chemodectoma probably functions as a giant peripheral chemoreceptor, which may suppress the chemoreceptor function of the contralateral carotid body. Narcotics depress the central chemoreceptor response<sup>70</sup>. Thus, administration of

opioids to patients undergoing excision of bilateral chemodectoma or even a unilateral chemodectoma may result in serious postoperative respiratory depression<sup>11</sup>. Hence the dose of opioids must be titrated in patients undergoing excision of CBTs. They must be observed for postoperative respiratory depression and for central and peripheral neurological deficits, especially of cranial nerves IX, X, and XII, cervical sympathetic nerves and marginal mandibular branch of VII<sup>5</sup>.

In summary, Chemodectomas are rare tumours. Surgical removal is the treatment of choice. Resection of large tumours may require temporary clamping of carotid artery. Barbiturate therapy or temporary shunting may be used as a means of cerebral protection during carotid artery clamping. The mortality rate has reduced to near zero, however incidence of neurologic deficit is high. Baroreflex failure & postoperative respiratory depression are other anaesthetic concerns.

Fig-1: Pre-operative carotid arteriogram showing right carotid body tumour causing splaying of the carotid bifurcation.



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