Catecholamine-Secreting Paragangliomas: Recent Progress in Diagnosis and Perioperative Management

Tahl Y. Colen, M.D.,¹ Frederick G. Mihm, M.D.,³ Theodore P. Mason, M.D.,² and Joseph B. Roberson, M.D.¹

ABSTRACT

Catecholamine-secreting paragangliomas (CSPs) present challenges for the managing team of surgeons and anesthesiologists. Without proper preoperative management and planning, the patient is at high risk for complications and significant morbidity. A review of the literature looking at all aspects of the care of patients with CSP was performed to provide a consensus on the comprehensive care of these difficult patients. A case study is also provided to illustrate the management algorithm. Specific recommendations are made with regards to preoperative workup, including serum and urine testing, tumor localization, angiography, and embolization. Preoperative and intraoperative management techniques by the surgical and anesthesiology teams are discussed, including pharmaceutical interventions and fluid management. Aspects of postoperative care are also discussed. Management of patients with CSP requires significant attention to detail by a multidisciplinary team of surgeons and anesthesiologists. By following the recommendations included within this article, the morbidity associated with removal of these tumors can be significantly reduced or eliminated.

KEYWORDS: Paraganglioma, glomus tumor, catecholamine, perioperative management, diagnosis

Catecholamine-secreting paragangliomas (CSPs) are relatively rare entities. Unfortunately, the failure to diagnose a secreting tumor can result in serious perioperative morbidity or mortality. In

recent years, significant advances have improved the diagnosis and treatment of CSP, greatly reducing the risk of major complications. The key to improved outcome is maintenance of a high index

¹California Ear Institute, E. Palo Alto, California; ²Ear, Nose & Throat Surgeons of Western New England, Springfield, Massachusetts; ³Stanford University Department of Anesthesia, Stanford, California.

Address for correspondence and reprint requests: Tahl Y. Colen, M.D., California Ear Institute 1900 University Ave., Ste 101, E. Palo Alto, CA 94303 (e-mail: tcolen@calear.com).

Skull Base 2009;19:377–386. Copyright © 2009 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1 (212) 584-4662.

Received: January 20, 2009. Accepted: February 27, 2009. Published online: May 26, 2009.

DOI 10.1055/s-0029-1224771. ISSN 1531-5010.

of suspicion along with a proactive workup that will uncover catecholamine-secreting tumors, allowing for appropriate and methodical intervention. This review will discuss the diagnostic evaluation of a patient with a CSP and the appropriate perioperative management.

MATERIALS AND METHODS

A Medline literature search was performed using the terms “glomus tumor” and “paraganglioma” in combination with “catecholamine.” Each step of patient care was reviewed, including biochemical and radiological diagnostic workup, preoperative interventions, intraoperative treatment algorithms, and postoperative care. Using this input and case study, specific recommendations to minimize the morbidity associated with CSP are proposed.

RESULTS OF LITERATURE REVIEW

Characteristics of Secreting Glomus Tumors

The commonly accepted term, “glomus tumor,” is often used interchangeably with “paraganglioma,” but “paraganglioma” is a more precise term in that the chief cells of these tumors arise from the paraganglia and not from the pericytes of glomus bodies. These chief cells, which are derived from the neural crest, are widely distributed throughout the autonomic nervous system and are capable of producing a variety of biologically active amines via decarboxylation. Paraganglia are found in the aortic and carotid bodies, jugular foramen and middle ear, vagus nerve, lung, adrenal medulla, and bladder. The exact function of the paraganglion system is unknown except for the carotid and aortic bodies, which function as chemoreceptors sensitive to changes in arterial pH and oxygen tension.

CSPs are found primarily in the adrenal medulla where they are referred to as “pheochro-

mocytomas.” However, all paragangliomas can potentially secrete catecholamines. Approximately 3 to 4% of head and neck paragangliomas secrete catecholamines.^{1,2} The majority of CSPs produce norepinephrine, with only a very few secreting epinephrine or dopamine.

Multicentricity has traditionally been reported in ~10% of patients with sporadic paragangliomas.³ More recently, with more sensitive localization studies, this number appears to be rising; one review of over 200 cases found multiple tumors in 17%, with two-thirds of the multicentric sites occurring in the head and neck.¹ As many as 78% of familial paragangliomas demonstrate multiple tumors.⁴ Familial paragangliomas have been linked to mutations in the succinate dehydrogenase (SDH) gene⁵ and represent ~35% of head and neck cases.⁶ Furthermore, the SDH-subunit D gene-linked head and neck tumors are associated with an increased prevalence of catecholamine excess.⁷ The overall incidence of metastasis, which denotes malignancy, approximates 3%.³

Preoperative Diagnostic Workup

Glomus tumors often present to the otolaryngologist with a diagnosis already suggested by prior magnetic resonance imaging (MRI) or computed tomography (CT), found as a neck mass or incidentaloma. Rarely will the discovery of catecholamine secretion have been made by this time, and it is the duty of the intervening surgeon to evaluate the patient for this potentially lethal variant.

Clinically, the most common finding is hypertension (~90% of CSPs), either paroxysmal (lasting minutes to days) or sustained.^{2,8} Patients who only experience hypertensive paroxysms (some may be asymptomatic) are easily overlooked by a casual blood pressure (BP) measurement that is normal. Hypertension is often accompanied by the classic triad of headache, palpitations, and sweating. Patients should be questioned carefully for any episodic symptoms, frequency, duration, and most importantly, BP and heart rate checks during these episodes.

Figure 1 Catecholamine synthesis, breakdown products and excretion pathways.

Diagnostic Testing

Catecholamine assays are fundamental to the diagnosis of CSP. Figure 1 demonstrates the basic pathways of catecholamine production, breakdown, and excretion. Although catecholamine breakdown occurs in the liver, kidney, and peripheral tissues, the vast majority of excretion occurs via the kidney. Classically, a 24-hour urine collection is evaluated for concentrations of catecholamine metabolites such as metanephrine, normetanephrine, and vanillylmandelic acid (VMA). Recent recommendations for biochemical testing of secreting tumors include high-performance liquid phase chromatography measurements of plasma free metanephrines (metanephrine and normetanephrine) or 24-hour urine fractionated metanephrines.⁹ Unlike catecholamines which may be secreted episodically, metanephrines are continuously produced by tumor cells via catechol-O-methyltransferase.¹⁰ The sensitivity and specificity of plasma free metanephrines are 99% and 89%, respectively, for sporadically occurring tumors. Urinary fractionated metanephrines are the next best choice with a sensitivity of 97% and specificity of 69%.⁹ When urine catecholamines are additionally tested, the specificity increases. Urine VMA has a low sensitivity (but very high specificity when positive) and should not be used for

screening purposes.¹¹ Patients with CSP almost always excrete these metabolites in excess, usually exceeding the normal range by threefold. There are some medications that can cause modest increases in catecholamine production (Table 1).

Tumor Localization

Once the diagnosis of CSP has been established with biochemical testing, the next step is tumor localization. CT and MRI are both useful in the preoperative evaluation of glomus tumors for localizing and analyzing the extent of the lesion for surgical planning. MRI, however, appears to be more accurate than CT for extra-adrenal tumors.¹²

Table 1 Drugs That Can Increase Catecholamine Measurements

Caffeine/chocolate
Tricyclic antidepressants
Phenothiazines
Calcium channel blockers
Sympathomimetics (pseudoephedrine)
Labetalol
Buspirone
Dopaminergic drugs (levodopa)
Acetaminophen

In addressing the issue of multicentricity, both have been used successfully in the localization of adrenal and extra-adrenal paragangliomas, but total-body CT and MRI can be prohibitively expensive to use as a screening tool.

A safer and less expensive alternative to angiography is ^{131}I -iodine- or ^{123}I -iodine-metaiodobenzylguanidine (MIBG) scintigraphy. This technique was first described in the evaluation of pheochromocytomas but has recently gained popularity in the evaluation of glomus tumors.¹²⁻¹⁴ The molecular structure of MIBG resembles norepinephrine and is therefore taken up preferentially by adrenergic tissues.¹⁴ Although the majority of the reports are from the pheochromocytoma literature, ^{131}I -MIBG scintigraphy demonstrates a sensitivity of 64 to 90% and a specificity of 99 to 100% in detecting extra-adrenal tumors.¹²⁻¹⁴ ^{131}I -MIBG scintigraphy is particularly useful in the setting of multicentric tumors and/or postoperative management.¹³

Other authors advocate the use of ^{111}In -pentetreotide²⁸ and ^{111}In -octreotide²⁹ scintigraphy in detecting CSP.^{15,16} This modality is based on the numerous somatostatin receptors expressed in different neuroendocrine tumors. Octreotide scintigraphy is reported to have a sensitivity of 88 to 97% and specificity of 75 to 82% in the detection of paragangliomas.¹⁴⁻¹⁶ Some reports recommend somatostatin receptor scintigraphy (SRS) over MIBG scintigraphy for head and neck paragangliomas.^{16,17} Furthermore, SRS can be useful in screening for familial paragangliomas and for detecting potential recurrence following surgery. SRS additionally limits the need for angiography, which has inherent risks for the patient, as a screening tool. Most recently, ^{18}F -DOPA positron emission tomography has shown promise in detecting subcentimeter glomus tumors with the added benefit of being a functional study as well.¹⁸

Medical Workup

Prior to removing a CSP, a thorough medical workup should be performed. The hematocrit in

these patients will often be elevated as a result of catecholamine stimulation. We advocate the preoperative donation of autologous packed cells, which not only will reduce the increased blood viscosity but also can serve as a source of blood should intraoperative blood loss warrant transfusion. Care should be used in washing these cells to avoid intraoperative infusion of catecholamines.¹⁹

Of particular importance is a complete cardiac workup. Left ventricular hypertrophy is seen in virtually all patients with CSP. Furthermore, prolonged exposure to increased concentrations of circulating catecholamines may result in a form of dilated cardiomyopathy linked with ventricular failure in one third of patients.²⁰ Evaluation by chest X-ray, assays for creatine kinase, electrocardiography, and echocardiography will diagnose those patients with significant catecholamine-induced myocarditis or cardiomyopathy and those at risk for congestive heart failure under the physiological stress of surgery. Cardiac enzyme elevations consistent with a myocardial infarction have been observed with myocarditis²¹ and may complicate the clinical presentation in patients with known coronary artery disease. It is wise to wait for cardiac recovery after adrenergic blockade if acute electrocardiogram/enzyme changes have occurred or if evidence of severe cardiomyopathy (ejection fraction <35%) are present.

Tumor Embolization

Preoperative embolization of glomus tumors not only reduces intraoperative blood loss but also shortens operative time.²² However, with a CSP, there is a significant risk of complications associated with embolization. Several reports document hypertensive crisis or wide fluctuations in BP,²³ theoretically from tumor necrosis and subsequent release of catecholamines into systemic circulation. Other authors have described marked hypotension, asystole, and even death with embolization.²⁴ Still others report uneventful embolizations.²⁵

Preoperative Strategy

Alpha adrenergic blockade should be accomplished with the following endpoints: to normalize BP or eliminate episodic hypertension and any symptoms related to such events (headaches, diaphoresis, palpitations, etc.); to achieve a mild degree of postural hypotension; and to observe normalization of both the blood sugar and hematocrit. All of these goals can usually be achieved with α blockade alone in most patients. The most commonly used agent is phenoxybenzamine, which is a noncompetitive, irreversible α -adrenergic antagonist. It blocks both postsynaptic α_1 receptors and presynaptic α_2 receptors. Newer, more selective α_1 antagonists like prazosin or its derivatives have also been used. Phenoxybenzamine is usually started at a dose of 10 mg twice a day and gradually increased every 2 to 3 days until the desired endpoint is reached. Some patients will require over 200 mg/d. This drug should be titrated carefully with close management by an endocrinologist or anesthesiologist. As there are differences of opinion about how much blockade to induce, the anesthesiologist must be involved because this decision influences the patient's intraoperative responses. If this is done as an outpatient, the patient must have access to an automatic BP device and track both BP and heart rate responses to this medication.

Frequent BP monitoring with both lying and standing measurements is crucial during the titration of these potent drugs. After optimal titration of adrenergic blocking drugs (may take several weeks in some patients), patients should be maintained for 1 to 2 weeks prior to surgery. This period allows time for normalization of the pressure autoregulation responses in vital organs, cardiac recovery, and recovery from chronic vasoconstriction and ischemia to other organs. Beta blockade is rarely needed in patients with tumors that only secrete norepinephrine. If necessary, β blockade should be used for persistent tachycardia (heart rate >120) or arrhythmias. Beta blockers should *not* be used to control hypertension in these patients. Beta blockade before establishment of α blockade is dangerous

and may result in myocardial infarction, organ ischemia, and death from unopposed α agonism.

Premedication should be used to sedate the patient with a CSP unless there are specific contraindications, such as airway compression from a large glomus tumor. Typical agents include hydromorphone (Dilaudid; Abbot Laboratories, North Chicago, IL), which does not release histamine, and an anxiolytic such as midazolam (Versed, Dormicum; Roche Laboratories, Basel, Switzerland). Premedication is given to make the patient comfortable during placement of invasive catheters before induction of anesthesia. Agents that should be avoided include narcotics that are known to release histamine (morphine, demerol) and anticholinergic agents (atropine, scopolamine, glycopyrrolate). The antiemetics droperidol and metoclopramide (Reglan; Baxter Healthcare Corporation, Deerfield, IL) are especially dangerous in patients with a CSP and should *never* be administered.²⁶

Perioperative/Intraoperative Management

Monitoring should be established before starting a general anesthetic. Minimal monitoring would include an arterial catheter and a central venous catheter. The use of a pulmonary artery catheter can provide additional useful information that may be important in some patients.²⁷ Anesthesia can be induced with several agents. Induction with thiopental or propofol, paralysis with vecuronium, and maintenance with isoflurane with or without nitrous oxide is one of the safer combinations. Supplementation with narcotics like fentanyl or hydromorphone, and the use of lidocaine, should make a routine intubation fairly uneventful.

Hypertension predictably occurs during tumor resection and can be treated with a spectrum of rapidly acting agents (Table 2). The α blocker phentolamine does not share the rapid pharmacological profiles of nitroprusside, nitroglycerin, and fenoldopam and is therefore not the first-line drug for the swiftly changing operating room environment. In the typical case, a plan for controlling

Table 2 Intraoperative Antihypertensive Agents

Drug	Class	Onset	Duration
Na Nitroprusside	Nitric oxide donor	1 min	3–5 min
Nitroglycerin	Nitric oxide donor	2–5 min	5–10 min
Fenoldopam	DA ₁ agonist	4–5 min	<10 min
Phentolamine	α_1 α_2 blocker	15 min	1 h
Nicardipine	Ca channel blocker	1–5 min	3–6 h
Labetalol	α_1 β_1 β_2 blocker	<5 min	3–6 h

hypertension includes nitroprusside, fenoldopam, and nitroglycerin, with or without β blockade with esmolol to control reflex tachycardia. If hypertension is still not reasonably controlled, then the anesthesiologist should ask the surgeon to stop the surgical dissection. Because the half-life of circulating catecholamines is only 1 to 2 minutes, even brief interruptions of the surgery may be the most effective way to control BP. Surgical finesse rather than speed is more important in this type of surgery. The nature of glomus tumor removal requires prolonged periods of continuous tumor manipulation, which makes the intraoperative management of hypertension significantly more difficult in comparison with the removal of an abdominal pheochromocytoma.²⁸

Although traditional dictum emphasized the need to volume load CSP patients prior to surgery to restore intravascular volumes, more recent consideration proposes intraoperative fluid management guided by invasive hemodynamic monitoring to ensure safe endpoints.²⁷ The goal is to optimally fluid load these patients intraoperatively *before* tumor removal to best prevent postresection hypotension. Clinical series that have followed this strategy report a reduction in the incidence and severity of hypotension after tumor removal.

Hypotension during glomus resection may occur as a result of severe bradycardia from carotid sinus stimulation. This can be treated with atropine and local infiltration with lidocaine. Hypotension after tumor removal is the most dangerous perioperative event for these patients. It is important that the surgeon communicate with the anesthesiologist so that prior to removing the last portion of the tumor, the following

can be performed: (1) controlled volume expansion with physiologic endpoints, (2) decreased anesthetic depth, and (3) elimination of vasodilators/ β blockers. If hypotension occurs despite these steps, additional fluid may be required if indicated, followed by the appropriate use of a vasopressor/inotrope. If the patient's cardiac output is inadequate, then epinephrine should be used for inotropic support. If cardiac output is adequate, then vasopressin or phenylephrine should be titrated to achieve an acceptable mean arterial BP.

Postoperative Management

Resuscitation of the patient may continue into the postoperative period and should be performed in an intensive care unit. Patients who require vasopressor agents usually can be tapered off in a few hours, as long as any ongoing fluid resuscitation is not overlooked. If the patient is hemodynamically stable, fluid restriction should be instituted.

Hypoglycemia is common postoperatively as a rebound effect from chronic catecholamine excess and its effects on glucose metabolism. These patients should have frequent blood sugar checks in the first 24 hours postoperatively and also receive a 5% dextrose-containing solution infusing at 125 mL/h.

Hypertension may occur in the postoperative period. Although the cause may be the result of unresected tumor or another tumor location, more likely explanations such as hypervolemia, pain, and anxiety should be considered. Coexisting essential hypertension in some patients may require a modest antihypertensive regimen.

CASE STUDY

A 65-year-old woman presented to the emergency room with a severe headache, left neck pain, and a BP of 255/145. An MRI of the brain was obtained, revealing a large tumor of the left skull base consistent with a glomus jugulare tumor.

After referral to our institution, additional workup revealed a 24-hour urine normetanephrine level of 1616 nmol/dL (normal 50 to 650) and VMA level of 17.4 mg/d (normal 0 to 7). Further assessment with a CT scan of the temporal bone demonstrated the classic radiological characteristics of a glomus tumor. MRI of the chest and abdomen revealed a small adrenal mass. Subsequent total-body MIBG scanning showed uptake in the left skull base region only.

After evaluation by the anesthesiology service, her previously prescribed antihypertensive medications (labetalol) were discontinued, and she was started on phenoxybenzamine 10 mg twice a day. Over the next 2 weeks, this regimen was increased to 20 mg twice a day, and then propranolol 60 mg every day was added to control tachycardia. This regimen kept her BP and heart rate relatively stable and eliminated her episodic symptoms.

The patient was admitted 2 days prior to her planned surgical date for embolization. The procedure took place in the interventional radiology suite under local anesthesia with fentanyl and midazolam and was closely monitored with an a-line and central pulmonary catheter by the anesthesia team that participated in her preoperative care. The embolization was uneventful, with no major swings in BP, and she was transferred to the intensive care unit for observation.

That night after the embolization, the patient had an acute hypertensive event with transient mean arterial BPs to 150. Sodium nitroprusside and esmolol drips were started, which were able to control her pressure but required constant attention to keep them properly titrated.

The patient was taken to the operating room the following day, where the tumor was excised via a combined transmastoid/transcervical approach. Intraoperatively, the patient's BP was controlled primarily with sodium nitroprusside. When pressures began to elevate sharply, the surgeons were asked to pause until the pressure was better controlled. These breaks in tumor manipulation allowed for reductions in BP within 60 to 90 seconds.

Postoperatively, the patient was transferred intubated to the intensive care unit, where her still somewhat elevated pressures were again controlled by sodium nitroprusside and esmolol drips. The following day, she was extubated without incident. Her BP regimen was changed over to scheduled metoprolol and hydralazine doses with good result.

Over the next 5 days, her antihypertensives were quickly tapered off. During this time, she experienced significant periods of hypotension and lightheadedness, which resolved over 2 days once she was off medications. She was discharged home on postoperative day 7 with no antihypertensive medications. One year later she continues to require no antihypertensive medications and is tumor-free by repeat MRI.

CONCLUSIONS

It is our belief as well as others that all cervical and skull base paragangliomas, including glomus jugulare, glomus vagale, and carotid body tumors, should undergo a preoperative workup for catecholamine secretion. The one exception is a glomus tympanicum, which in review of the literature has been only cited once to produce catecholamines. Plasma free metanephrines or urinary fractionated metanephrines appear to be the most accurate and useful as screening tools. The case example preceded the above biochemical recommendations. Because elevated BP measurements and other symptoms are often not apparent until the catecholamine level is 4 to 5 times normal levels, they are not reliable indicators to decide who gets screened.

Once catecholamine secretion is documented, appropriate imaging should be performed to rule out a synchronous tumor, which can be present 10 to 78% of the time, especially in vagal and familial paragangliomas.⁴ Usually CT and/or MRI of the skull base and neck have already been done at this point, so further workup with either SRS or ¹³¹iodine-MIBG scanning appears to provide the most cost-effective and sensitive screening

tool for additional tumors. Faced with the possibility of two or more secreting sites, the next step should be selective venous sampling.² Using this protocol, risk to the patient is minimized and diagnostic costs are kept within reason.

In preparation for surgical excision, a team, consisting of surgeon, endocrinologist, and anesthesiologist, must institute proper BP control. Phenoxybenzamine is the preoperative drug of choice for this endeavor, owing to its unique pharmacological profile. Additional β blockade may be useful in select cases for tachycardia. Proper titration of these medicines will significantly reduce the possibility of morbidity/mortality associated with CSP.

We feel that the benefits of embolization with respect to reducing blood loss and shortening operative time outweigh the potential risks associated with CSP. We therefore advocate embolization whenever possible. An experienced anesthesiology team in this setting is as critical as in the operating room to provide safe control of any BP events. Similarly, close postoperative monitoring is required due to the unpredictability of postembolization hemodynamic events.

Intraoperative BP control can range from routine to extremely harrowing. Proper preoperative BP control will reduce the chance of the latter situation. Rapidly acting agents such as sodium nitroprusside, nitroglycerin, and fenoldopam will aid the anesthesiologist in controlling large swings in BP. Constant communication between the surgeon and anesthesiologist is essential, stopping tumor manipulation as needed to allow the anesthesiologist to regain BP control.

Postoperative care requires close monitoring not only of BP, but also of fluid resuscitation and blood sugars. Most patients do not require long-term BP control after complete tumor removal.

Modern advances in the workup and perioperative management of secreting glomus tumors have the potential to virtually eliminate the historical morbidity associated with their resection. Maintenance of a high index of suspicion along with a proactive workup and careful perioperative

management will ensure an optimal outcome in this challenging disease process.

REFERENCES

1. Erickson D, Kudva YC, Ebersold MJ, et al. Benign paragangliomas: clinical presentation and treatment outcomes in 236 patients. *J Clin Endocrinol Metab* 2001; 86:5210–5216
2. Schwaber MK, Glasscock ME, Nissen AJ, Jackson CG, Smith PG. Diagnosis and management of catecholamine secreting glomus tumors. *Laryngoscope* 1984;94:1008–1015
3. Spector GJ, Ciralsky R, Maisel RH, Ogura JH. IV. Multiple glomus tumors in the head and neck. *Laryngoscope* 1975;85:1066–1075
4. Nettekville JL, Jackson CG, Miller FR, Wanamaker JR, Glasscock ME. Vagal paraganglioma: a review of 46 patients treated during a 20-year period. *Arch Otolaryngol Head Neck Surg* 1998;124:1133–1140
5. Baysal BE, Ferrell RE, Willett-Brozick JE, et al. Mutations in SDHD, a mitochondrial complex II gene, in hereditary paraganglioma. *Science* 2000;287:848–851
6. Drovdic CM, Myers EN, Peters JA, et al. Proportion of heritable paraganglioma cases and associated clinical characteristics. *Laryngoscope* 2001;111:1822–1827
7. van Houtum WH, Corssmit EPM, Douwes Dekker PB, et al. Increased prevalence of catecholamine excess and pheochromocytomas in a well-defined Dutch population with SDHD-linked head and neck paragangliomas. *Eur J Endocrinol* 2005;152:87–94
8. Amar L, Servais A, Gimenez-Roqueplo AP, Zinzindohoue F, Chatellier G, Plouin PF. Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma. *J Clin Endocrinol Metab* 2005;90:2110–2116
9. Lenders JWM, Pacak K, Walther MM, et al. Biochemical diagnosis of pheochromocytoma: which test is best? *JAMA* 2002;287:1427–1434
10. Eisenhofer G, Keiser H, Friberg P, et al. Plasma metanephrines are markers of pheochromocytoma produced by catechol-O-methyltransferase within tumors. *J Clin Endocrinol Metab* 1998;83:2175–2185
11. Bravo EL, Tagle R. Pheochromocytoma: state-of-the-art and future prospects. *Endocr Rev* 2003;24:539–553
12. Jalil ND, Pattou FN, Combemale F, et al. Effectiveness and limits of preoperative imaging studies for the localization of and paragangliomas: a review of 282 cases. French Association of Surgery (AFC), and The French Association of Endocrine Surgeons (AFCE). *Eur J Surg* 1998;164:23–28
13. Maurea S, Cuocolo A, Reynolds JC, Neumann RD, Salvatore M. Diagnostic imaging in patients with paragangliomas. Computed tomography, magnetic resonance and MIBG scintigraphy comparison. *QJ Nucl Med* 1996; 40:365–371

14. Brink I, Hoegerle S, Klisch J, Bley TA. Imaging of pheochromocytoma and paraganglioma. *Fam Cancer* 2005;4:61–68
15. Bustillo A, Telischi F, Weed D, et al. Octreotide scintigraphy in the head and neck. *Laryngoscope* 2004;114:434–440
16. Telischi FF, Bustillo A, Whiteman MLH, Serafini AN et al. Octreotide scintigraphy for the detection of paragangliomas. *Otolaryngol Head Neck Surg* 2000;122:358–362
17. Muros MA, Llamas-Elvira JM, Rodríguez A, et al. 111In-pentetreotide scintigraphy is superior to 123I-MIBG scintigraphy in the diagnosis and location of chemodectoma. *Nucl Med Commun* 1998;19:735–742
18. Hoegerle S, Ghanem N, Althoefer C, et al. 18F-DOPA positron emission tomography for the detection of glomus tumours. *Eur J Nucl Med Mol Imaging* 2003;30:689–694
19. Smith DF, Mihm FG, Mefford I. Hypertension after intraoperative autotransfusion in bilateral adrenalectomy for pheochromocytoma. *Anesthesiology* 1983;58:182–184
20. Van Vliet PD, Burchell HB, Titus JL. Focal myocarditis associated with pheochromocytoma. *N Engl J Med* 1966;274:1102–1108
21. Gupta KK. Letter: Pheochromocytoma and myocardial infarction. [letter] *Lancet* 1975;1:281–282
22. Murphy TP, Brackmann DE. Effects of preoperative embolization on glomus jugulare tumors. *Laryngoscope* 1989;99:1244–1247
23. Matishak MZ, Symon L, Cheeseman A, Pamphlett R. Catecholamine-secreting paragangliomas of the base of the skull. Report of two cases. *J Neurosurg* 1987;66:604–608
24. Pandya SK, Nagpal RD, Desai AP, Purohit AV. Death following external carotid artery embolization for a functioning glomus jugulare chemodectoma. Case report. *J Neurosurg* 1978;48:1030–1034
25. Nelson MD, Kendall BE. Intracranial catecholamine secreting paragangliomas. *Neuroradiology* 1987;29:277–282
26. Plouin PF, Menard J, Corvol P. Hypertensive crisis in patient with phaeochromocytoma given metoclopramide. [letter] *Lancet* 1976;2:1357–1358
27. Mihm FG. Pulmonary artery pressure monitoring in patients with pheochromocytoma. *Anesth Analg* 1983;62:1129–1133
28. Farrior J. Surgical management of glomus tumors: endocrine-active tumors of the skull base. *South Med J* 1988;81:1121–1126