Pheochromocytoma metastatic to the mandible presenting as a large jaw mass

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In this case report of an unusual presentation of a metastatic pheochromocytoma as a large jaw mass, the anesthetic management of the resection of a vasoactive tumor in close proximity to the airway is described. The strategy to maintain a stable hemodynamic profile is explained, and a review of current management techniques is given with a discussion of the benefits or contraindications of each method. In summary, this case highlights the importance of preoperative alpha-adrenergic blockade and preparation for rapid fluctuations in blood pressure when operating on patients with pheochromocytoma.

The perioperative management of a patient with a pheochromocytoma may be challenging for the anesthesiologist. Between 10% and 30% of pheochromocytomas are malignant, with primary extra-adrenal tumors exhibiting malignant characteristics more often than adrenal tumors (1–3). Reported sites of metastasis for these tumors include bone, liver, lymph nodes, lungs, brain, and omentum (3). We report the perioperative and anesthetic management of a patient with a pheochromocytoma that had metastasized to the mandible and presented as a large left-sided jaw mass. The anesthetic management of this particular manifestation of metastatic malignant pheochromocytoma has not been previously reported.

CASE REPORT

A 23-year-old, 75-kg man was scheduled for radical resection of a large (10 x 5 cm) mandibular tumor and reconstruction with a free fibular bone graft. At age 11, the patient had undergone resection of a large periaortic, subdiaphragmatic pheochromocytoma. Persistent hypertension, occasional tachycardia, and elevated catecholamine levels followed that surgery. Over the next 10 years, the patient had a slowly enlarging, bony left jaw mass in addition to possible tumor sites in the liver, right femur, and left ischium. The patient sought alternative medical therapy during this time. However, as the left mandibular tumor continued to grow, the patient returned for conventional medical treatment.

A preoperative 131I meta-iodobenzylguanidine scan showed a markedly localized mandibular mass, suggesting the presence of an active, metastatic pheochromocytoma.
Figure 1). In the weeks preceding the operation, the patient's blood pressure, historically difficult to control, was adequately controlled with atenolol, 37.5 mg orally twice a day; phenoxybenzamine, 30 mg orally twice a day; and a clonidine patch, 0.05 mg. Preoperative arterial blood pressure was 140/78 mm Hg with a heart rate of 70 beats per minute. Laboratory data showed a normal chemistry profile, with a glucose concentration of 88 mg/dL, normal liver function, a normal thyroid profile, and a hematocrit of 46%. His preoperative electrocardiogram displayed a normal sinus rhythm. Plasma norepinephrine levels were elevated at 12,490 pg/mL, and plasma dopamine levels were elevated at 5010 pg/mL. Urinary catecholamines were elevated with a norepinephrine level of 2020 ?g/day and a dopamine level of 1361 ?g/day. Both plasma and urine epinephrine levels were normal. On physical examination the only abnormality was a large bony tumor protruding from the left jaw line (Figure 2). The airway itself was unobstructed and was designated Mallampati class 1, with a normal thyromental distance and adequate cervical spine mobility.

The patient was premedicated with intramuscular midazolam, 7.5 mg; famotidine, 20 mg; and metoclopramide, 10 mg orally, prior to arrival in the operating room. A 16-gauge peripheral intravenous catheter and a 20-gauge left radial arterial catheter were placed. Electrocardiography and pulse oximetry were also monitored. Midazolam, 2 mg intravenously, was administered in the operating room for additional sedation. The jaw mass was carefully avoided during face mask placement and airway maintenance. Hemodynamic responses prior to induction were closely observed. Blood pressure and heart rate were minimally elevated with gentle face mask ventilation. Induction was achieved with intravenous propofol, 100 mg, and fentanyl, 250 ?g. Muscle relaxation was attained with vecuronium, 7 mg. Laryngoscopy with a #3 Miller blade revealed a grade 1 view of the glottis, and an 8.0-mm endotracheal tube was placed in the trachea. Pressure on the jaw mass during face mask ventilation and laryngoscopy was avoided, and no hypertension was noted in response to induction, laryngoscopy, or intubation. A pulmonary artery catheter was placed via the right internal jugular vein, and a cardiac index of 2.7 L/min/m² and a systemic vascular resistance (SVR) of 1014 dynes?cm?sec⁻⁵ were recorded after induction. A tracheostomy was performed before resection of the jaw mass and harvest of the fibular bone graft from the left leg by a second surgical team. Anesthesia was maintained with isoflurane, fentanyl, and a propofol infusion, and relaxation was maintained with vecuronium. Hemodynamically, the patient was stable initially except for a tendency toward hypotension following fentanyl administration, which was easily correctable with intravenous phenylephrine given in 100-?g increments. Blood pressure was stable, despite intensive tumor manipulation. After 4 hours of operating time, the venous drainage of the tumor was surgically ligated. This was quickly followed by marked hypotension with a mean arterial pressure of 50 mm Hg, a decreased SVR of 437 dynes?cm?sec⁻⁵, and a cardiac index of 5.5 L/min/m². The hypotension was corrected with an infusion of norepinephrine, 0.1 ?g/kg/min to 0.2 ?g/kg/min. The SVR remained well below baseline for the remainder of the operation, and the norepinephrine infusion was maintained (Table). Estimated blood loss during the surgery was 1500 cc. Two units of packed erythrocytes, 8700 cc of crystalloid solution, and 500 cc of hetastarch solution were transfused during the 12-hour procedure, maintaining the pulmonary artery occlusion
pressure between 9 and 14 mm Hg. Urine output throughout the case was excellent. The patient's hematocrit on arrival at the intensive care unit was 26%. The patient returned to the operating room the next morning because of continued bleeding and formation of a left facial hematoma, and 2 units of additional packed erythrocytes were given at that time. On postoperative day 1, the patient was weaned off the norepinephrine infusion. He did well subsequently, with an unremarkable hospital course. The pathology report obtained from the operative specimen confirmed the diagnosis of metastatic pheochromocytoma with 1 of 2 lymph nodes positive for tumor cells.

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<th>Table: Hemodynamic changes during pheochromocytoma resection</th>
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<td>CVP (mm Hg)</td>
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CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVR = systemic vascular resistance; MAP = mean arterial pressure.

The patient had a follow-up visit with his endocrinologist 6 weeks postoperatively. Urinary metanephrines were slightly elevated at 1.4 mg/day (normal value upper limits, 1.3 mg/day); vanillylmandelic acid was mildly increased at 9.3 mg/day (normal value, <8 mg/day). This was evidence that some pheochromocytoma tissue still existed and was producing catecholamines. He was to be seen in 3 months for more testing and possible location of other active tumor sites.

DISCUSSION

This case reports the unusual occurrence of a pheochromocytoma metastatic to the mandible. In addition to the expected challenge of hemodynamics associated with a pheochromocytoma, this case posed the additional consideration of a potentially difficult airway management. Although succinylcholine is often quite useful in the management of a difficult airway, its use has been discouraged in cases of pheochromocytoma. Succinylcholine-induced fasciculations may liberate catecholamines and may contribute to ventricular ectopy by stimulating sympathetic ganglia (2, 4). In this particular case, we confirmed the ability to face mask ventilate without manipulating the large tumor mass prior to administration of vecuronium. This muscle relaxant was selected because of its stable hemodynamic properties and lack of histamine release (5). While monitoring arterial and central venous pressures may be adequate in managing some patients with pheochromocytoma and uncompromised cardiac function (2), the information obtained from the pulmonary artery catheter was useful in differentiating potential causes of progressive hypotension during the surgery. The declining SVR after ligation of the venous return of the tumor with relatively constant cardiac filling pressures pointed toward catecholamine deficit as the source of hypotension.
Pheochromocytomas usually secrete norepinephrine and epinephrine, with norepinephrine predominating in most circumstances. Occasionally, the tumor secretes dopamine, and there are reports of secretions of a multitude of other substances, including somatostatin, vasoactive intestinal peptide, enkephalins, adrenocorticotropic hormone, serotonin, calcitonin, parathyroid-like hormone, neuropeptide Y, and atrial natriuretic peptide (3, 6). It is doubtful that the ratio of norepinephrine to epinephrine secreted by a tumor has predictable effects on an individual's hemodynamic profile (6, 7). Patients with norepinephrine-secreting tumors may be predisposed to sustained hypertension, while those with epinephrine-secreting tumors may experience paroxysmal hypertension (8). The hallmark of the hemodynamics in patients with pheochromocytoma-induced hypertension, regardless of the specific catecholamine secreted, is an increase in SVR (6, 7). For this reason, alpha-receptor inhibition has been advocated prior to surgery for patients with an active pheochromocytoma. To date, there are no randomized, controlled trials specifically addressing the effect of preoperative alpha-receptor inhibition on perioperative morbidity and mortality. However, since the advent, in the 1960s, of alpha-receptor blocking agents to preoperatively control hypertension, mortality associated with pheochromocytoma resection has markedly declined (9).

In addition to substantial doses of phenoxybenzamine, our patient required clonidine preoperatively to control hypertension, as well as atenolol for tachycardia. Profound receptor block was achieved in this instance, as evidenced by the minimal response to various noxious stimuli during the procedure, including induction, intubation, skin incision, and, most impressively, direct manipulation of the tumor. Although various agents, including phentolamine, nitroglycerin, prazosin, and magnesium sulfate, have been advocated to control hypertension in operations for pheochromocytoma, we elected to have sodium nitroprusside and esmolol immediately available in case of sudden hypertension as the rapid onset of action of both drugs and their short duration allow close control.

Noteworthy in this patient was the rapid drop in blood pressure and SVR associated with the surgical ligation of the venous drainage of the tumor. The patient had 3 other sites of probable metastatic tumor, so this significant fall in blood pressure was surprising. This decline may have resulted from the fact that the other tumors were not pheochromocytomas or were too small to produce enough catecholamines to have a systemic effect. Along with volume expansion as the case progressed, the norepinephrine infusion was critical in restoring the arterial blood pressure to acceptable levels. The patient was weaned off norepinephrine infusion early in the postoperative period, presumably as the down-regulation of adrenergic receptors due to prolonged high catecholamine levels in the preoperative period resolved.

The patient's follow-up examination, 6 weeks after surgery, demonstrated evidence that further catecholamine-secreting tumor sites still remained.
References


