Octreotide for Treatment of Intraoperative Hypotension Due to an Unexpected Neuroblastoma in an Adult

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EXTRACEREBRAL neuroblastoma, a neuroendocrine tumor, is exceedingly rare in adults. Its secretory products include catecholamines. We describe a patient in whom a pheochromocytoma was diagnosed and treated until a major intraoperative hypotensive crisis forced rapid revision of the initial diagnosis and treatment. Octreotide stopped the crisis. This case represents a novel application of a somatostatin agonist.

Case Report

The patient was a 75-yr-old man with a 4-month history of 14-kg weight loss, fatigue, persistent hiccoughs, nausea, and a few vague episodes of feeling “flushed.” Other than mild hypertension, he had been healthy. Evaluation revealed a large retroperitoneal mass involving the right adrenal gland and inferior vena cava. Plasma epinephrine was 272 pg/ml (normal <90 pg/ml), norepinephrine 1,512 pg/ml (normal <700 pg/ml), and dopamine 4,912 pg/ml (normal <200 pg/ml). β-Human chorionic gonadotropin was increased, at 10 IU/ml (normal <2.9 IU/ml). Serum cortisol, α-fetoprotein, and urinary 17-hydroxysteroids and 17-ketosteroid concentrations were within normal limits. His hematocrit was 51%. Metoprolol 50 mg daily and phenoxycamine 10 mg twice daily were begun.

After 4 weeks of therapy the patient was scheduled for resection of the pheochromocytoma, including resection and repair of the inferior vena cava. Premedication included intramuscular morphine sulfate 6 mg and scopolamine 0.2 mg. Radial artery and pulmonary artery catheters were inserted before induction, and midazolam 5 mg was administered for sedation. General anesthesia was induced with etomidate 0.5 mg/kg and fentanyl 2 μg/kg and muscle relaxation with pipercuronium. After tracheal intubation, anesthesia was maintained with fentanyl (total 10 μg/kg before incision) and isoflurane. The procedure was eventful until 30 minutes after incision.

Until this point, superficially manipulating the tumor mass produced slight increases in blood pressure. After the tumor had been exposed, the surgeons began dissecting its superior portion. The patient’s systolic blood pressure abruptly decreased from 120 to less than 70 mmHg, accompanied by an increase in heart rate from 82 to 130 beats/min. His face was flushed and the carotid pulse strong. Diphenhydramine 50 mg and cimetidine 300 mg were given for a possible allergic reaction, although no new drugs had been given within the preceding 0.5 h. Phenylephrine was administered immediately, but there was no response even with frequent 200-μg boluses and continuous infusion of more than 100 μg/min. The ST segment of the electrocardiogram in leads II and V₅ became significantly depressed. As the ST-segment depression progressed, esmolol administration in a bolus of 0.5 mg/kg and infusion of 100 μg·kg⁻¹·min⁻¹ was begun to attempt to control his heart rate, but without effect. While norepinephrine was being prepared, we reassessed his diagnosis.

Events were transpiring too rapidly to obtain thermodilution cardiac output data, but on examination the circulation appeared to be hyperdynamic (characterized by tachycardia, flushing, and bounding pulse). His tumor, however, had been thought to be dopamine predominant. Hypotensive crisis may occur in patients with pheochromocytoma, but usually it is caused by catecholamine-induced cardiogenic shock or a hyperdynamic vasodilated state in an epinephrine-dominant tumor.† Because the patient was not in cardiogenic shock and did not have an epinephrine-dominant tumor, we turned our attention to the possibility of a misdiagnosed neuroendocrine tumor, many of which secrete catecholamines. Several of these tumors are known to produce hypotensive crisis with pronounced skin flushing. Although we could not guess the type of neuroendocrine tumor, we knew that these tumors share many common characteristics, including, frequently, somatostatin receptors.

Based on this differential diagnosis, an ampule of octreotide acetate was obtained from our pharmacy and 50 μg given intravenously, less than 10 min after the hypotension had begun. Within a few seconds the patient’s blood pressure increased and his heart rate decreased. We stopped bolus doses of phenylephrine and stopped the esmolol infusion. The remaining 50 μg of octreotide was given. Within 90 s of the initial dose, we were able to stop the phenylephrine infusion, and his heart rate, blood pressure, and ST segments returned to normal.

Tumor invasion was too extensive for resection so the operation was limited to biopsy and hemostasis. Surgical time was 3 h. During this time the patient had two more episodes of sudden hypotension and tachycardia. On each occasion, a 100-μg bolus of octreotide corrected the perturbation within seconds.

After wound closure, an epidural catheter was placed for postoperative pain control. The trachea was extubated in the recovery room. Octreotide, 100 μg every 6 h, was continued, and the patient had no additional episodes of hypotension and tachycardia. The biopsy specimen was later identified as that of a neuroblastoma.

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Discussion

Neuroendocrine tumors are a varied group with functional and physiologic similarities, including the ability to produce amino acid–derived hormones. This class of tumors is also known as “apudoma” (where “apud” = amine precursor uptake and decarboxylation). These tumors were formerly thought to be of neural crest origin, but only a few (such as neuroblastoma and pheochromocytoma) indisputably are of that origin. Included among the neuroendocrine tumors are carcinoid, medullary thyroid carcinoma, pituitary and pancreatic islet cell tumors (e.g., insulinoma), melanoma, and oat cell carcinoma. Some tumors secrete, in large amounts, only the hormone produced by its parent cells, as is typical of most pituitary tumors. Others, however, produce a mélange of substances including catecholamines, peptide hormones or neurotransmitters, prostaglandins, histamine, and serotonin. The number of pharmacologically active products these tumors are known to secrete seems limited only by the number of assays used. Even pheochromocytomas secrete various peptide hormones.

Common to many neuroendocrine tumors is the ability to express a cell-surface somatostatin receptor that through a G-protein reduces intracellular cyclic adenosine monophosphate and free calcium concentrations. Receptor stimulation inhibits tumor product release and cell replication. Somatostatin and its analogues thus present an attractive possibility for inhibiting paraneoplastic syndromes and tumor growth. Unfortunately, these have been effective in only some of the syndromes, possibly because hormone production is decreased yet still greater than symptom threshold. Inhibition of tumor growth may be only transient, even with concentrations too high to be clinically practical.

Neuroblastomas are rare neuroendocrine tumors found almost exclusively in young children. In fact, it is one of the most common pediatric solid tumors. It is much rarer in adults, and we have found only about 50 published cases. Neuroblastomas may produce vasoactive intestinal peptide, adrenocorticotrophic hormone, melatonin, substance P, neuropeptide Y, calcitonin and somatostatin. These tumors also produce catecholamines and their metabolites, which can be assayed in mass screening efforts in infants. Neuroblastomas frequently produce dopa, dopamine, and its metabolite homovanillic acid, as well as vanillylmandelic acid, whereas pheochromocytomas usually produce norepinephrine, epinephrine and vanillylmandelic acid. Unfortunately, increased homovanillic acid is not a feature solely of neuroblastoma; some pheochromocytomas do produce dopa and homovanillic acid.

Some neuroblastomas have functioning somatostatin receptors. Indeed, somatostatin has been used once before in neuroblastoma, to attempt to control intractable vasoactive intestinal peptide–induced diarrhea. Although the plasma concentration of vasoactive intestinal peptide varied inversely proportionally to plasma somatostatin concentration, the effort was unsuccessful; the vasoactive intestinal peptide concentration was never low enough to reduce symptoms.

Hypertension due to neuroblastoma-produced catecholamines is uncommon except perhaps intraoperatively. Tumor-induced hypotension has not been reported with neuroblastoma. Our patient’s α-adrenergic receptor blockade could have unmasked the effect of vasodilatory tumor products by blocking the vasoconstriction effect of dopamine. Some of these products also cause tachycardia through non-β-adrenergic mechanisms, rendering β-adrenergic blockade ineffective.

Octreotide is a somatostatin analogue with slower clearance (200 vs. somatostatin’s 3,000 ml/min) and prolonged binding to target receptors. Thus, whereas somatostatin needs to be given by continuous infusion, octreotide can be given in intermittent boluses to produce the desired effect. Octreotide has few acute side effects: mainly mild transient hypo- or hyperglycemia from decreased insulin, glucagon, and growth hormone secretion. At an acquisition cost of $6.35 per 100-μg ampule it is relatively inexpensive. It may be worthwhile to administer octreotide empirically to attempt to control severe hypotension associated with flushing when other causes, particularly anaphylaxis, are ruled out, if it is possible that a neuroendocrine tumor responsive to somatostatin is the cause.

References

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Resistence to Injection May Predict Spinal Catheter Breakage

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破损的脊髓或硬膜外导管，离开一个导管段，这在一个中段或硬膜外的外国体，是相对稀有的。1-6 因为预测破洞的导管破洞是困难的，Hurley和Lambert建议撤除的导管而当患者是在在的腰椎的以弯曲的位置与脊柱最大屈曲到减少的可能的绑定的导管和撤除它的破洞。1 我们报告两病例在其中我们有证据的破洞的导管。在破洞的导管的撤除后的随后的破洞的导管的检查中，压缩和摇晃，这可能已经增加了破洞的机率。我们建议破洞到注射可能是一个警告的标志破洞的压缩或损坏，这可能导致破洞的破洞的撤除。

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持续的脊柱麻醉是使用了两个患者（70岁和73岁）进行的在的股动脉的血管操作。在一块案例

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