Pathologic Quiz Case

A Retroperitoneal Mass in a 44-Year-Old Woman With Recurrent Myocardial Infarctions

Irina Mikolaenko, MD; Michael G. Conner, MD

A 44-year-old black woman suffered myocardial infarctions 1 and 2 years prior to her most recent admission. A computed tomographic scan of the abdomen (Figure 1) performed during evaluation of her sustained hypertension revealed a 3.6 × 2.7-cm mass immediately inferior to the duodenum at the aortic bifurcation. Metaiodobenzylguanidine (mIBG) scan (Figure 2) demonstrated abnormal activity just to the right of the lower thoracic or upper lumbar spine region. The patient had the following laboratory findings: serum dopamine, 101 pg/mL (reference range, 100–440 pg/mL); epinephrine, 4 pg/mL (0–15 pg/mL); norepinephrine, 96 pg/mL (11–86 pg/mL); total catecholamines, 201 pg/mL (<540 pg/mL); and urine metanephrine, 0.40 mg/24 h (0.0–1.30 mg/24 h). Her past medical history was significant for asthma and migraines. The maximal blood pressure reading observed during the course of surgery was 180/110 mm Hg. Grossly, the tumor was well circumscribed, weighed 23.2 g, and measured 4.5 × 4.0 × 3.1 cm. It had the consistency of a rubbery mass and was brownish-tan, well vascularized, and encapsulated. Microscopically, the tumor was characterized by proliferation of a rather homogenous population of round to oval cells with eosinophilic granular cytoplasm containing a round, slightly vesicular nucleus with a single nucleolus. The lesion exhibited a predominantly trabecular architectural pattern consisting of anastomosing cords and bands of tumor cells (Figure 3, original magnification ×20). On the evening of the first postoperative day, the patient experienced midsternal chest pain that radiated down her right arm. Pain was controlled with sublingual nitroglycerin. Cardiac enzymes were markedly elevated above their normal ranges. Electrocardiography showed ST elevation consistent with inferior injury or acute infarct. The patient was successfully treated by a cardiology team and was referred to her primary cardiologist for subsequent follow-up after her discharge.

What is your diagnosis?
Paragangliomas arise from dispersed collections of specialized neuroendocrine cells of neural crest origin in close association with autonomic nervous system. These segmentally and symmetrically distributed paraganglia may be classified according to their anatomic distribution as branchiomeric, intravagal, aorticosympathetic, and visceral autonomic. An anatomic classification of the neoplasms arising from these paraganglia has considerable utility, since tumors in certain locations tend to possess common clinical characteristics. The area known as the organ of Zuckerkandl (aorticosympathetic group) encompasses all extra-adrenal chromaffin tissue near the origin of the inferior mesenteric artery and the aortic bifurcation. It was first described by a professor of anatomy at the University of Vienna, Emil Zuckerkandl, in 1901. The physiologic role of the organ of Zuckerkandl is considered to be the homeostatic maintenance of blood pressure in early fetal life. These ganglionic bodies involute between the eighth month of gestation and the first year of life, leaving only a loose plexus of sympathetic fibers along the anterior surface of the abdominal aorta. The organ of Zuckerkandl is the most common site of occurrence of extra-adrenal paraganglioma. Most patients are between the ages of 30 and 45 years, and women are affected more frequently than men.

The behavior of paragangliomas of the organ of Zuckerkandl is known to be more malignant than in those found elsewhere. A malignancy rate of 22% to 50% has been reported. By comparison, about 10% of paragangliomas of the adrenal gland are malignant. These tumors demonstrate evidence of both hematogenous and lymphatic spread, with the most common sites of distant metastasis being bone, liver, and lung. Extra-adrenal paragangliomas, specifically paragangliomas of the organ of Zuckerkandl, may present a diagnostic problem to the surgical pathologist. The “zellballen” pattern is a characteristic feature in many tumors, but in some cases it may be obscured by broad anastomosing bands, an alveolar pattern, a predominance of round to oval cells, and the presence of giant multinucleated cells. In these cases, the differential diagnosis has to be made with alveolar sarcoma, fibrous malignant histiocytoma, alveolar rhabdomyosarcoma, liposarcoma, variant of malignant melanoma, and some large carcinomatous metastases (especially from kidney, thyroid, adrenal medulla, and liver). Carcinoid and islet cell tumors may pose a greater problem in the differential diagnosis, especially when the biopsy material is limited.

The histologic appearance of paragangliomas is an unreliable predictor of their ultimate behavior. Pleomorphism, mitotic figures, and bizarre nuclear forms are common findings in paragangliomas and do not necessarily indicate aggressive behavior.

The symptoms of tumor arising in the organ of Zuckerkandl may be those related either to the growth of a retroperitoneal mass or to excessive catecholamine secretion. In most cases, paragangliomas of the organ of Zuckerkandl elaborate an excess of norepinephrine over epinephrine. The greater epinephrine-producing capacity of adrenal pheochromocytoma can be explained by glucocorticoid dependence of the enzyme phenylethanolamine-N-methyltransferase activity.

Paragangliomas traditionally are divided into chromaffin paragangliomas (associated with the sympathetic nervous system) and nonchromaffin paragangliomas (associated with the parasympathetic nervous system and derived from structures presumed to function as chemoreceptors). Tumors originating from the nonchromaffin system usually are endocrinologically inactive. In some instances, tumors presumed to be connected with the sympathetic system on the basis of location appear nonchromaffin and nonfunctioning and otherwise. Most paragangliomas of the organ of Zuckerkandl are endocrinologically active (chromaffin paragangliomas). Several cases of nonfunctional paragangliomas of the organ of Zuckerkandl have been described in the literature.

Catecholamines, particularly norepinephrine, are known to have a toxic effect on the myocardium, which may account for various cardiovascular manifestations in patients with norepinephrine-secreting tumors of the organ of Zuckerkandl. Myocardial infarction, serious arrhythmias, congestive heart failure, cardiomyopathy (active catecholamine myocarditis), dissecting aneurysm, and sudden death have been reported. A classic pathologic feature most commonly observed in the heart exposed to toxic effects of catecholamines is myocardial contraction band necrosis.

An accurate preoperative clinical diagnosis of paraganglioma of the organ of Zuckerkandl is rarely made without overt symptoms produced by catecholamine secretion. Although computed tomographic scan is also the first modality used to localize functional tumors, mIBG scan may help delineate multiple tumors and small tumors not seen on computed tomographic scan. Once the diagnosis is established, every attempt should be made to perform a complete surgical resection.

References