Pheochromocytoma

March 01, 2006
By Timur M. Roytman, MD [1], Marina M. Roytman, MD [2], and Jinichi Tokeshi, MD [3]

A 49-year-old man presents for a routine examination. He has a 15-year history of essential hypertension and a 7-year history of hypercholesterolemia and type 2 diabetes mellitus. The patient has lost 7.5 lb in the past 3 months. The physical examination is remarkable for a blood pressure (BP) of 168/94 mm Hg and a palpable midline epigastric mass that is nontender, firm, and immobile.

Abdominal CT with contrast demonstrates an 87 × 116-mm necrotic, partially enhancing mass in the region of the left adrenal gland (Figure 1). Chest CT with contrast reveals multiple bilateral noncalcified pulmonary nodules with no other apparent lesions in the thorax. The imaging findings prompt a laboratory evaluation of the adrenals with the following results: urine normetanephrines, 27,787 µg/24 h; total urine metanephrines, 27,861 µg/24 h; urine vanillylmandelic acid, 191.9 mg/24 h; urine norepinephrine, 5401 µg/24 h; and total calculated urine catecholamines, 5415 µg/24 h. Levels of urine dopamine and epinephrine are within normal limits. A tumor marker workup reveals elevated levels of CA 125 (63 U/mL) and carcinoembryonic antigen (6.4 ng/mL). The radiographic findings and the significant elevation of catecholamines and their metabolites support a diagnosis of pheochromocytoma.

The patient undergoes a left adrenalectomy, left nephrectomy, and splenectomy. The cut surface of the 12-cm left adrenal mass reveals pale tan-gray tissue with central edema and fibrosis (Figure 2). The periphery of the lesion demonstrates prominent vasculature and nodularity. Intraoperatively, metastases are found in the left renal hilum and a periaortic lymph node; these are resected. Six weeks after the operation, laboratory results include the following: urine normetanephrines, 1388 µg/24 h; urine metanephrines, 1453 µg/24 h; urine norepinephrine, 371 µg/24 h; and total calculated urine catecholamines, 371 µg/24 h. The level of urine dopamine is within normal limits, and the level of urine epinephrine is below the reportable range of 2 µg/24 h. The plasma chromogranin A level is 36 ng/mL. The BP and serum glucose level are normal.

Two months after the surgery, the patient undergoes a 123I-MIBG SPECT fusion scan, which shows no significant uptake in any of the pulmonary nodules. Consequently, he is not a candidate for high-dose 131I-MIBG therapy. Recently, the patient's levels of catecholamines and their metabolites have begun to rise. This prompts radiologic reevaluation, which demonstrates an increase in the size of numerous pulmonary nodules and the presence of new pulmonary nodules and a new paracaval adenopathy. These findings suggest a recurrence of malignant pheochromocytoma.

**EPIDEMIOLOGY**
Pheochromocytoma occur most commonly between the ages of 30 and 50 years. They are more prevalent in whites than in blacks and somewhat more frequent in women than in men.1,2 The incidence is 1 per 2 million population. Among persons with hypertension, 0.1% have an underlying chromaffin tumor as the primary cause.2

Pheochromocytomas are either sporadic or familial. Familial cases occur in persons with Sturge-Weber syndrome, von Hippel-Lindau syndrome, multiple endocrine neoplasia type II, familial carotid body tumors, tuberous sclerosis (Bourneville disease), and neurofibromatosis type 1.1,3 In persons with these syndromes, the incidence of pheochromocytomas is as high as 23%.1 Most pheochromocytomas are sporadic and unilateral; only 10% are bilateral. About 10% to 20% of pheochromocytomas are malignant.4-7 In children, pheochromocytomas are commonly bilateral; they are more frequently found outside the adrenals than are those in adults.8

**ETIOLOGY AND PATHOGENESIS**

Eighty-five percent of pheochromocytomas arise from the chromaffin cells of the adrenal medulla. The remaining 15%, termed "paragangliomas," arise from extra-adrenal chromaffin cells.9 Pheochromocytomas are typically associated with an excess of catecholamines. However, they may also produce atrial natriuretic peptide, vasoactive intestinal peptide, endothelin, erythropoietin, dopa, neuropeptide Y, and adrenomedullin.9 Pheochromocytomas are not innervated; therefore, catecholamine release is not associated with neural stimulation.

**CLINICAL MANIFESTATIONS**

Pheochromocytoma is typically associated with a symptom triad of headache, palpitations, and diaphoresis. Hypertension, either sustained or paroxysmal, is the clinical hallmark of pheochromocytoma and is commonly attributed to catecholamine excess. The classic triad, combined with hypertension, suggests the diagnosis of pheochromocytoma with 93.8% specificity and 90.9% sensitivity. The absence of hypertension excludes the diagnosis with 99.9% certainty.1 Pheochromocytoma is also associated with certain metabolic abnormalities, such as lactic acidosis. Catecholamines that are produced by the chromaffin cells stimulate glycogenolysis and glycolysis. The by-product of these biochemical pathways is lactate, which may produce lactic acidosis when sufficient amounts accumulate in the serum.8,10 Pheochromocytoma may also be associated with hypercalcemia, diarrhea, hypokalemic alkalosis, and glucose intolerance.11-14 Glucose intolerance may result from a combination of the suppression of insulin release, inhibition of insulin-stimulated glucose uptake by skeletal muscles, and stimulation of hepatic glucose production by excessive catecholamines, particularly epinephrine.8,15-18

**DIFFERENTIAL DIAGNOSIS**

Because pheochromocytoma is a relatively rare condition, always consider a differential that is more likely to explain the patient's symptoms. Such a differential would include intracranial lesions (eg, subarachnoid hemorrhage or posterior fossa tumors), anxiety syndromes, panic attacks, thyrotoxicosis, hypoglycemia, myocardial infarction, essential hypertension, illicit drug use (eg, cocaine), factitious disorder, drug withdrawal (eg, clonidine), and menopause.

**DIAGNOSIS**

Diagnosis relies on the demonstration of excessive catecholamine production. Biochemical testing establishes the diagnosis in 95% of patients.8 Once the diagnosis is confirmed biochemically, localization of the tumor is undertaken for further confirmation and to establish a surgical treatment plan. A recommended algorithm for tumor localization is abdominal CT or MRI, followed by MIBG scanning for confirmation. It is difficult to distinguish between malignant and benign pheochromocytomas on the basis of tissue pathology. The diagnosis of malignant pheochromocytoma is established by the presence of metastases, extent of local invasion, and recurrence.19

**MANAGEMENT**

Surgical resection is the definitive treatment. However, surgery is associated with intraoperative and postoperative complications, which are generally the result of a massive release of catecholamines during the resection or a sudden decrease in plasma catecholamine levels.8 During the preoperative period, pharmacologic control of the potential physiologic effects of the excess of catecholamines—particularly tachycardia, myocardial infarction, stroke, arterial hypertension, glucose intolerance, and cardiac arrhythmias—is crucial. Phenoxybenzamine, an α-adrenoceptor antagonist, has been recommended for blood pressure management.20 Patients should be monitored at 6 weeks and 6 months postoperatively by measurement of plasma free metanephrine levels.3 Regular followup is maintained for at least 5 years because about 10% of pheochromocytomas are malignant and may recur. Common sites of recurrence are the lungs, retroperitoneum, liver, and bone.
PROGNOSIS
About 90% of patients with benign pheochromocytoma can expect a complete cure. The recurrence rate is less than 10%. After tumor resection, resolution of hypertension is achieved in 75% of patients. Malignant pheochromocytoma has a poor prognosis; the 5-year survival rate is less than 50%.1,4-8

References: REFERENCES:

Source URL: http://www.physicianspractice.com/articles/pheochromocytoma

Links: