Background: Although pheochromocytomas are believed to account for fewer than 0.3% of all cases of hypertension, aggressive diagnostic and surgical intervention is recommended whenever a pheochromocytoma is suspected because uncontrolled catecholamine release from the tumors can lead to catastrophic consequences. Many biochemical diagnostic and imaging localization tests exist for detecting pheochromocytomas. We sought to evaluate the sensitivity of these tests used over a 35-year period at a single institution.

Methods: Thirty-five patients with complete medical records who had pathologically confirmed pheochromocytomas between 1962 and 1997 at the University of Chicago Hospitals were identified. Sensitivity and 95% confidence intervals were calculated for 12 laboratory diagnostic tests and 5 imaging studies.

Results: The most sensitive laboratory diagnostic tests in our study were plasma total catecholamines (95%) and urine total metanephrines (100%). Testing for urine vanillylmandelic acid, while less expensive and easier to perform than many other tests, had a slightly lower sensitivity (89%). The most sensitive imaging tests in the study were magnetic resonance imaging (100%) and iodine I-131 metaiodobenzylguanidine scintigraphy (100%). The more often used computed tomography had only 88% sensitivity. Localization was safely and successfully performed on two pregnant patients using magnetic resonance imaging and ultrasound.

Conclusions: By properly choosing from the wide array of laboratory diagnostic and imaging tests, pheochromocytomas can be identified and localized with nearly 100% sensitivity. These tests should be performed in any patient for whom the diagnosis of pheochromocytoma is being considered.

Arch Intern Med. 2000;160:2521-2524

PHEOCHROMOCYTOMAS arise from pheochromocytes, the primary cells of the adrenal medulla, which are also found in the paraganglia near the aorta and in the sympathetic nervous system ganglia. Most frequently, symptoms are present when large amounts of catecholamines enter the circulation, which can be triggered by changes in position, increased abdominal pressure, trauma, labor, anesthesia, surgery, stress, or the ingestion of certain drugs or foods. Although pheochromocytomas are believed to account for fewer than 0.3% of all cases of hypertension, aggressive diagnostic and surgical intervention is recommended whenever a pheochromocytoma is suspected because the uncontrolled catecholamine release from the tumors can lead to malignant hypertension, cerebrovascular accidents, or myocardial infarction. Because approximately 10% of pheochromocytomas are extra-adrenal and 10% are bilateral (with a higher percentage in familial syndromes), accurate pre-operative localization of the tumor is imperative for safe, expeditious surgical management. Older imaging techniques, including retroperitoneal air insufflation, angiography, and venography, have largely been replaced by ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and iodine I-131 metaiodobenzylguanidine (MBG) scintigraphy. Computed tomography is believed to be the best available technique for detecting adrenal lesions, and ultrasound and MRI are useful in pregnant patients; MBG scintigraphy has been especially useful in localizing extra-adrenal and recurrent pheochromocytomas.

Biochemical diagnosis of pheochromocytoma is traditionally performed by examining plasma and total urinary lev-
METHODS

After institutional review board approval, all patients who were treated for pheochromocytoma at the University of Chicago Hospitals were identified from records found in the tumor registry and the surgery, pathology, and anesthesia departments. Of the 31 cases identified, 37 had complete records available from the medical records department. Of these 37 patients, 2 died before referral to surgery (and before diagnosis of pheochromocytoma). Therefore, 35 patients met our inclusion criteria. All of these patients had pheochromocytomas confirmed by pathologic examinations.

We computed sensitivity and 95% confidence intervals for routine, commercially available laboratory diagnostic tests (serum epinephrine, norepinephrine, dopamine, and total catecholamines; urine epinephrine, norepinephrine, dopamine, total catecholamines, vanillylmandelic acid [VMA], metanephrine, normetanephrine, and total metanephrines) and localization tests (MRI, CT, MIBG scintigraphy, ultrasound, and angiography).

RESULTS

Of the 35 patients, 18 (51%) were women, and the median age of all patients was 40 years (interquartile range, 32-54 years). Two patients had multiple endocrine neoplasia (MEN) type IIA, one patient had MEN type IIB, and three patients had neurofibromatosis. Two patients were pregnant at the time of diagnosis and surgery.

Sensitivity and 95% confidence intervals of the 12 laboratory diagnostic tests are listed in Table 1. Sensitivity and 95% confidence intervals of the 5 imaging tests are listed in Table 2.

COMMENT

Because of the rarity of pheochromocytomas (believed to exist in fewer than 0.3% of hypertensive patients), this analysis was performed as a retrospective study in which only true pheochromocytoma cases were examined.12 Thus sensitivity could be measured, but not other variables, such as specificity, predictive value of positive test results, and predictive value of negative test results. We have included a table from representative literature sources that compares the specificity of biochemical and imaging studies for pheochromocytomas (Table 3). Because of the difference in controls between studies (normal patients, patients with other chronic diseases, patients with other causes for hypertension), such specificity data have substantial variability.6,7,13-18

Twenty-four-hour urine tests are widely considered superior to plasma tests in the diagnosis of pheochromocytoma, mainly because pheochromocytomas often secrete catecholamines only intermittently. This fact, along with the short half-life of catecholamines, can result in relatively normal plasma catecholamine levels even in the presence of a functional tumor.7

In our study utilizing commercial laboratory assays, however, plasma total catecholamines proved to be one of the most sensitive tests, with a sensitivity of 95% (95% confidence interval, 74.0%-99.9%), representing the highest lower confidence limit value in our study. Plasma epinephrine and norepinephrine values were relatively comparable in sensitivity (77% and 86%, respectively) with urine epinephrine and norepinephrine values (81% and 75%, respectively).

Several studies have found urine metanephrines to be the most sensitive test in pheochromocytoma diagnosis.1,6,7,10 Measurement of VMA in urine is generally believed to have lower sensitivity. However, since VMA has acceptable specificity (Table 3) and sensitivity (Table 1) and is relatively inexpensive and easy to perform by colorimetry, some might choose it as an initial “case finding” test.6,9

In our study, urine total metanephrines correctly revealed a diagnosis of pheochromocytoma in all 10 patients for whom the test was ordered. Urine VMA measurement was the test ordered most frequently (n = 28), but it was less sensitive than testing for urine normetanephrine, total metanephrine, or plasma total catecholamines.

Several studies report a sensitivity at or near 100% for CT scans, but in our study CT scans failed to localize the tumor in 3 of 26 patients (88% sensitivity).1,5,9 Sensitivity for both MRI scans and MIBG scintigraphy was 100% in our study, correctly identifying tumors in 12 of 12 and 8 of 8 patients, respectively. Recent studies have found sensitivity ranging from 90% to 100% for MRI scans and 88% to 94% for MIBG scintigraphy.1,5,9

Treatment of pregnant patients with pheochromocytoma is high-risk and must be individualized.20 Magnetic resonance imaging and ultrasound are the preferable methods for localization of tumor in pregnant patients to avoid exposing the fetus to ionizing radiation.7 In our study, one pregnant patient underwent MRI localization and the other underwent ultrasound localization, with effective localization of the tumor in each case.

Because pheochromocytomas are life-threatening without treatment, it is important that a diagnostic test exclude false-negative results as efficiently as possible. False positives are relatively less important because additional testing (including clonidine suppression and glucagon stimulation) can be performed to rule out the disease.7,21 We found that urine total metanephrines, se-
rum total catecholamines, and urine VMA were the most sensitive laboratory diagnostic tests, and that MRI scans and MIBG scintigraphy were the most sensitive imaging tests.

Accepted for publication March 8, 2000.

All financial support for this project was provided by the University of Chicago Hospitals.

Corresponding author: Michael F. Roizen, MD, Department of Anesthesia and Critical Care, University of Chicago Hospitals, 5841 S Maryland Ave, MC 4028, Chicago, IL 60637.

**REFERENCES**


