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Adrenal Radiography: Problems and Pitfalls in Adrenal Localization

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The traditional preoperative localization of adrenal tumors has employed one or more of the following radiographic techniques: plain abdominal films, intravenous urography, adrenal venography and venous sampling, arteriography, ultrasonography, computed tomographic scanning, and scintiscanning. These localization techniques may be divided into invasive or noninvasive types with each technique having different degrees of sensitivity and specificity for the establishment of adrenal disease. The diagnostic accuracy of these radiographic techniques is reviewed for a 5-year series in a university hospital with special emphasis on false-positive localization. The techniques employed in localization and their sequence vary and depend on whether adrenal medullary or adrenal cortical disease was suspected, and whether or not the patient was protected by pharmacologic preparation.

Before the advent of noninvasive scanning techniques, the adrenal gland could hide in the retroperitoneum, a clinically silent area of the body. When clinical and chemical evidence of adrenal hyperfunction suggested the presence of adrenal neoplasm, invasive techniques were required for tumor localization. Adrenal arteriography has been the gold standard by which other localization techniques have been measured and was usually applied only to those patients who had prelocalization studies that confirmed the clinical diagnosis with confidence.

With the advent of a new noninvasive technique of computed tomography (CT) and ultrasonography (US), our ability to detect mass lesions in the suprarenal fossa has remarkably improved. Because these studies are noninvasive, they are often ordered before there is biochemical confirmation of a particular clinical syndrome. In some instances, the localization techniques not only preceded but also substituted for the confirming biochemical data. In addition, the use of sophisticated localization techniques for screening patients without proven adrenal clinical syndromes has led to the discovery of many abnormalities in the suprarenal fossa that may be incidental to the patient's clinical problem. In addition to these "incidentalomas," discovered by imaging techniques, nonfunctioning, benign masses may also be imaged in patients who have clinical and chemical evidence of adrenal hyperfunction. However, the lesions demonstrated by either invasive or noninvasive radiography are not the basis for a patient's complaints. Many of the problems in adrenal tumor localization in the current era are related to the successful detection of space-occupying masses with uncertain correlation between mass and pathophysiology. In addition to the positive detection of adrenal lesions that have no bearing on the patient's ultimate diagnosis, there are numerous possibilities for the false-positive localization of adrenal disease. These errors in preoperative diagnosis and methods for their prevention are the subject of this review of the current state of the art in adrenal radiography.

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Adrenal Localization Methods

Abdominal X-ray

A plain abdominal film taken on a Bucky grid can distinguish retroperitoneal calcification or large soft tissue densities. In some instances, the abdominal plain film may be diagnostic, such as the incidental discovery of the calcified adrenal gland (Fig. 1). The abdominal film is of such low sensitivity, however, that very few of the adrenal lesions demonstrated in this fashion have any clinical relevance.

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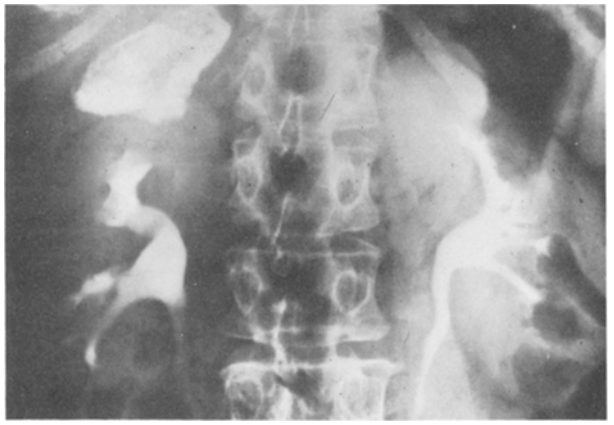

Fig. 1. The abdominal radiograph may be diagnostic in making some diagnoses of low clinical relevance, such as this demonstration of a calcified adrenal gland.

Retroperitoneal Pneumography

Gas insufflation of the retroperitoneum is mentioned only to consign this technique to historical interest alone. It was a hazardous, invasive procedure and could be a strong, provocative challenge to the patient who might have an adrenal medullary neoplasm that was functional. This technique was obsolete long before the advent of CT scanning.

Excretory Urography

Excretory urography is a useful examination for screening patients with hypertension thought to have either renovascular or renoparenchymal basis. As a method to detect masses in the suprarenal fossa, the examination is insensitive except when masses cause recognizable displacement of the kidneys or adjacent organs by virtue of size. The excretory urogram is a useful screening test for related conditions in the differential diagnosis of adrenal tumors, but it is more indicated for these disorders than for localization of adrenal masses.

Adrenal Venography

Adrenal venography is a sometimes useful procedure with rapidly decreasing indications. It is usually performed in conjunction with adrenal vein sampling. As there is only one principal vein from each adrenal gland in contrast to the 3 arteries supplying each gland, adrenal mass localization can often be carried out more easily with venography than with arteriography (Fig. 2). Prior to CT scanning, an important function of venography in the evaluation of endocrine tumors was to detect the intravenous

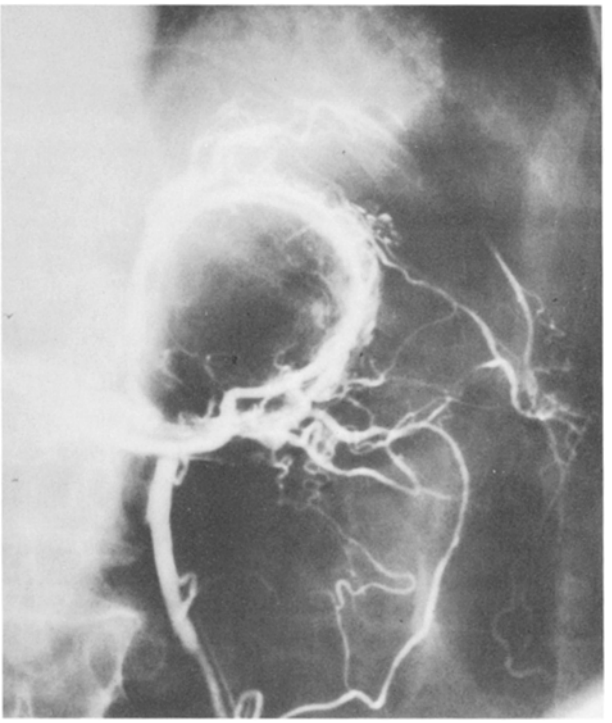

Fig. 2. Adrenal venography is simpler and faster than arteriography because of the singular and more nearly constant venous anatomy; it may result in excellent localization of adrenal tumors as seen in this example.

extension from a primary tumor [1]. For particularly large tumors, such as adrenal cortical carcinoma (Fig. 3), invasion into the inferior vena cava—sometimes all the way to the heart—is a not uncommon occurrence. Currently, this technique has been largely supplanted by CT scanning which has been shown to be very accurate in detecting intracaval extension of tumors. One of the possible complications of adrenal venography, which has been advocated by some as a possible therapeutic maneuver, is the over-injection of contrast into the adrenal vein in an attempt to extravasate contrast directly into the gland. This has been shown to cause adrenal infarction and ablation of glandular function. The extent of the hematoma that can be caused is demonstrated in Fig. 4, which shows a gland removed surgically shortly following venography.

Adrenal Venous Sampling

Sampling of the adrenal effluent blood through catheters placed at the adrenal vein orifice through the percutaneous transfemoral approach might seem an ideal resolution to the hazards of retrograde adrenal venography. Adrenal venous sampling has been attempted for both catecholamine

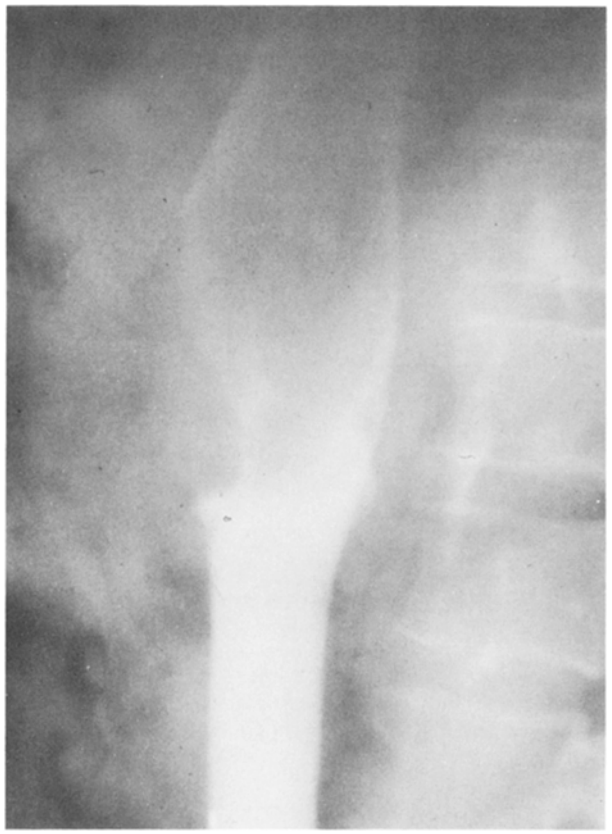

Fig. 3. Venography may be useful in planning resection for those malignant adrenal tumors that give rise to intravenous extension as detected in this case of adrenocortical adenocarcinoma.

assay in searching for adrenal medullary chromaffin tumors and corticosteroid assays in the localization of adrenal cortical tumors.

A serious pitfall in the interpretation of sampling data obtained via this route may occur through the overreliance on absolute levels of hormones determined by chemical assay. By reading the absolute numbers and blood concentrations, a sampling error may be obtained usually suggesting localization to the left adrenal gland. This is because the left adrenal vein is much easier to catheterize than the right. The left adrenal venous sample may represent pure adrenal effluent on the left, but may be mixed with caval blood on the right and an absolute left-to-right stepdown may result that is purely a matter of sampling concentrations, an error that can be avoided by relying on 2 other techniques.

In the instance of adrenal venous sampling for specific cortical adenomas, one steroid should always be checked against another as a control. For example, if one is seeking to localize a suspected adenoma in a patient who exhibits the features of primary aldosteronism, aldosterone concentration should be assayed against the control of cortisol. The ratio of the 2 steroids then becomes the determining factor in a true stepup. An example of such a sampling error and its control is seen in Table 1. Attempts at adrenal catheterization and reliance on absolute values of concentrations led to the false localization studies illustrated in Fig. 5.

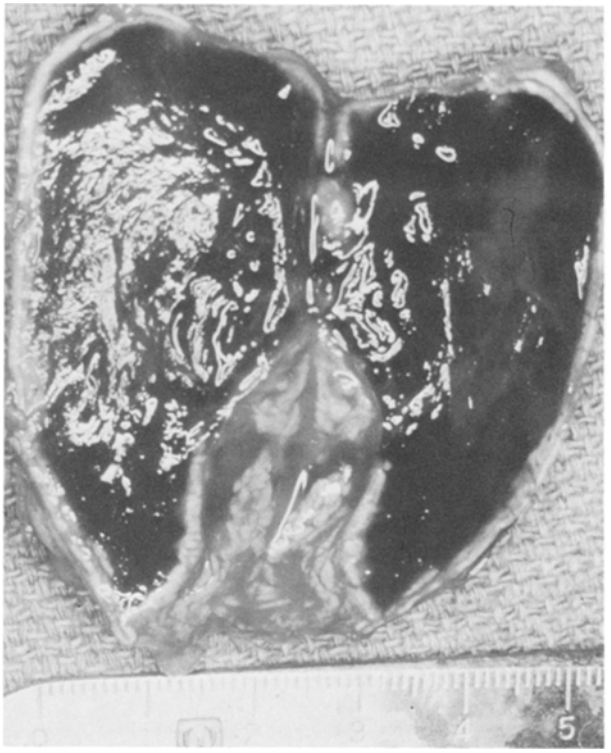

Fig. 4. Adrenal hematoma resulted from the retrograde injection of contrast required in venography which in this case was followed by extravasation.

A second technique for the prevention of this pitfall in sampling technique is the use of caval catheterization and the laminar flow principle of blood collection rather than the directed adrenal venous catheterization. As seen in Fig. 6, a catheter is advanced up the inferior vena cava and samples are taken in the effluent stream alongside the left cava up over the entrance of the left renal vein. The catheter is then placed in the right side of the cava up over the level of the right adrenal vein. Blood is allowed to flow under gravity, rather than through suction, and these blood samples are assayed for hormone concentrations with at least 2 species of hormones obtained to allow comparison of ratios. Further samples are obtained at the level of the right atrium and at the lower level of the inferior vena cava to check peripheral hormone ratios.

Adrenal Arteriography

Long the touchstone of precision localization of adrenal pathology, adrenal arteriography has been

Table 1. Adrenal venous sampling error results from interpretation of absolute values of concentrations rather than ratios of one hormone against a second adrenal hormone as a control.

	Right	Left	Interpretation
Absolute Aldosterone	1:	6	Non-lateralizing
Ratio Aldosterone: Cortisol	1:	6[a] 40	Lateralizing aldosteronoma on right

As an example, a patient with primary aldosteronism is sampled, yielding nonlocalizing information from sampling error originally thought to prove a *left*-sided adenoma; the ratios of cortisol and aldosterone indicate a *right*-sided tumor.

[a]This indicates a 6.8:1 ratio, right compared to left when aldosterone:cortisol ratios are used.

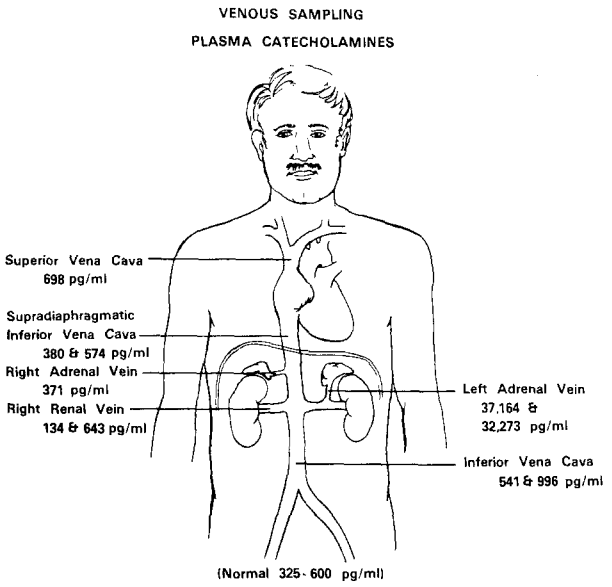

Fig. 5. Absolute values of adrenal venous hormone concentrations yielded false localization information in this patient, since catheterization of adrenal veins was attempted—successfully on the left, and incompletely on the right. In addition to this error in sampling technique, ratios were not obtained controlled against, for example, cortisol.

declared "dead and gone" as of 1981 (J.L. Doppman, personal communication). The disadvantages of this procedure that led to this rapid decline include the high degree of technical expertise required in catheterizing the 3 adrenal arteries, as well as the potential complication that may result from performing arteriography in a patient with pheochromocytoma who has not been blocked with pharmacologic agents.

Ultrasonography

Sonography is a noninvasive technique not requiring the use of ionizing radiation. If the sensitivity of the procedure were high enough, sonography might be the procedure of choice for adrenal localization. At the present time, sonography is useful as a screening procedure but does not have the precise discrimination of CT scanning. Ultrasonography is able to demonstrate whether a mass is solid or cystic, but beyond this, no functional information can be obtained by the demonstration of an adrenal mass.

CT Scanning

Computed tomography (CT) is the localization method of choice for adrenal tumors. As opposed to ultrasound, CT requires the use of ionizing radiation. It has a degree of spatial and contrast resolution unapproached by other imaging techniques. The only hazard that CT may present to the patient with pheochromocytoma occurs when intravenous glucagon is administered during the scan in order to lessen the effects of bowel peristalsis. Glucagon has been shown to be one of the more provocative agents that can be employed to stimulate the release of catecholamine [2]. If the radiologist is alerted to the possibility of the patient's having a pheochromocytoma prior to the CT examination, glucagon will not be administered and the examination will carry no risk to the patient. As is true with any pure imaging technique, the CT demonstration of a space-occupying mass lesion cannot provide any information as to its functional status. This may result in clinically misleading information when an adrenal mass is identified but biochemical confirmation of biological activity cannot be confirmed.

Scintiscanning

Adrenal scintiscanning is the "coming thing" in adrenal localization. It shares the advantages of the noninvasive techniques, but adds a considerable advantage of correlation with functional characteristics of the tumor. The scintiscans depend not so much on the space-occupying nature of the lesion as on its biochemical activity. This is their major strength and weakness.

An example of the scintiscanning for adrenal cortical tumors is the iodine-labeled cholesterol scan. The newest agent in use is iodine-labeled benzyl guanidine for the localization of pheochromocytomas. The latter remains an experimental procedure, but is very promising in the localization of pheochromocytoma, particularly the ectopic pheochromocytoma. It is even capable of uniformly

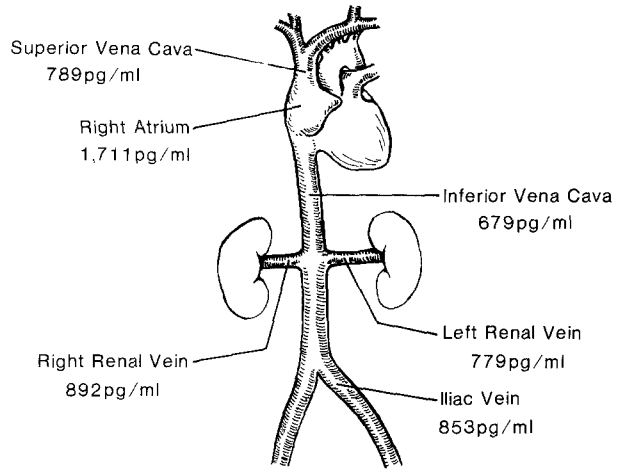

Fig. 6. The "laminar flow" principle of blood sampling by means of caval catheterization in the stream of effluent from each adrenal gland.

identifying normal adrenal glands. It has taken some time for the isotope labeling of various pharmacologic agents taken up in the vesicles of the chromaffin tissue to be developed, but the clinical trials have been very promising with the newer agent and the technique should become the procedure of choice if a stable isotope can be made available.

The indications for, problems of, and present status of the various localization techniques are summarized in Table 2.

Clinical Examples of Misleading Localization Information

Adrenal Medullary Tumors

False-positives. An example of venous localization studies by means of catecholamine assay on a venous sampling is shown in Fig. 5 in which the absolute values were thought to localize a tumor to the left adrenal gland, where none was found by further study. In another patient who had hypertension, equivocal urinary metabolite data were followed by localization studies including a CT scan which showed a fullness in the left adrenal gland. This was confirmed by subsequent arteriography which showed an enlarged left adrenal (Fig. 7). The arteriogram was interpreted as localizing a left adrenal mass and further diagnostic confirmation was not awaited in a patient who had both a demonstrable left adrenal mass and hypertension. Surgical exploration showed a small, nonfunctioning cortical adenoma, and further results of plasma catecholamine and other diagnostic information tended to exclude pheochromocytoma as a source of the patient's hypertension. The patient remained unchanged postoperatively.

This case illustrates the danger of sending a patient for a noninvasive localization study without biochemical evidence indicating a functional adrenal tumor. This patient had both essential hypertension and an adrenal mass which were coincident, without the one being the cause of the other. It is a disservice to such a patient to have a discovery of such a lesion and its operative resection without the firm evidence of linkage between the symptoms and a probable anatomic source.

Another patient with hypertension had as his initial study an abdominal CT scan. The scan revealed an adrenal mass (Fig. 8A). At this time, the assays of urinary catecholamine levels did not indicate the presence of pheochromocytoma. A renal venogram was also performed as part of an evaluation of a suspected right adrenal mass. Reflux into the right adrenal vein confirmed the finding of an adrenal mass. At surgery, this lesion proved to be a nonfunctioning cortical adenoma (Fig. 8B).

The insensitivity of the excretory urogram, even when enhanced by nephrotomography, is reflected in Fig. 9A. A patient suspected of having pheochromocytoma by convincing biochemical data underwent nephrotomography which, even in retrospect, is normal. CT scan suggested a left adrenal mass (Fig. 9B), and this rather large left adrenal mass was confirmed on venography with appropriate localization on catecholamine/cortisol ratios, to confirm a left adrenal pheochromocytoma. A bonus of this venous sampling study is the remarkable venogram exhibited in Fig. 2. Without the convincing evidence of the biochemical confirmation of her diagnosis, localization studies may not have proceeded beyond the negative nephrotomogram. The CT scan demonstrated the lesion well, but with the negative nephrotomography, further confirmation was sought through venous sampling. The remarkable venogram appearance (Fig. 2) clinches the diagnosis with some redundancy. Important questions that follow from these multiple examinations include: which tests are necessary with the highest degree of specificity and sensitivity, in which sequence should they be run, under what conditions of patient preparation, and at what point is diagnostic certainty sufficient to suspend further localization and proceed directly to treatment?

This sequence of questions was incorrectly answered in a patient with hypercalcemia, hypertension, and an elevated catecholamine excretion rate. The initial CT scan is seen in Fig. 10A, which suggested a left adrenal mass. Adrenal arteriography under less than adequate alpha-receptor blockade was thought to confirm this adrenal mass (Fig. 10B). A positive response to a Regitine test satisfied

Table 2. Localization techniques: Indications, problems, and present status.

Localization technique	Indication	Problems/pitfalls	Status
Plain abdominal film	Retroperitoneal density	Insensitive Non-specific	
Retroperitoneal pneumography			Obsolete
IVP	Renovascular hypertension Parenchyma or collecting system lesions	Gross technique for suprarenal fossa	Under-diagnosis
Nephrotomography	Unexpected encounter in IVP	Insensitive	
Adrenal venogram	Intravenous tumor extension	Extravasation of contrast and ablation	
Adrenal venous sampling	Functional assay of hormone output	Extravasation Sampling error	
Adrenal arteriography	Precise	Painstaking	
Ultrasonography	Noninvasive	Sensitivity is operator dependent	
CT scanning	Noninvasive, precise	Pharmacologic provocation[a]	
Scintiscanning	Correlates with function	Isotope pharmacology	

[a]Glucagon should not be utilized.

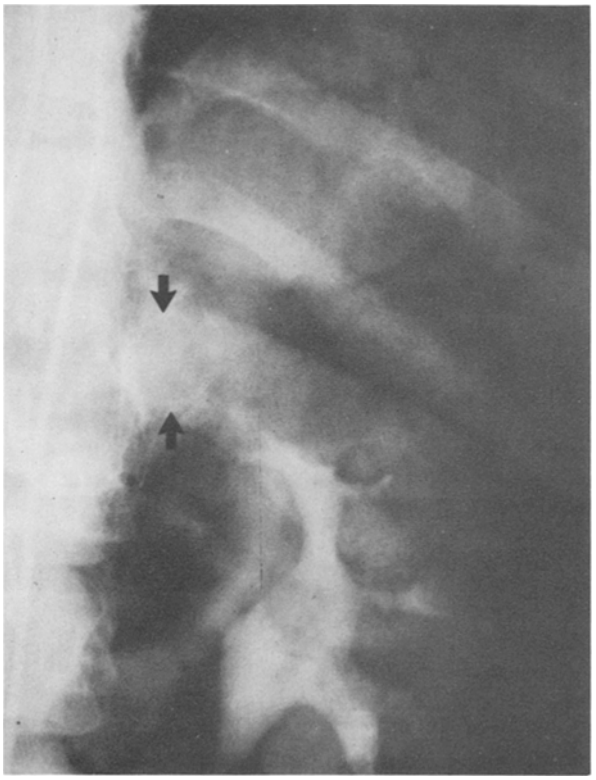

Fig. 7. CT scanning and this arteriogram demonstrated a left adrenal mass in a hypertensive patient; this localization information preceded diagnostic confirmation of the suspected pheochromocytoma, and adrenalectomy revealed a nonfunctioning cortical adenoma with no postoperative change in the patient.

the physician who referred this patient for a later follow-up after an adrenalectomy which yielded a normal left adrenal by histologic examination. The patient's final diagnosis was hyperparathyroidism owing to a parathyroid adenoma, and no other endocrine abnormality could be confirmed.

One explanation for false-positives is that patients sometimes have findings that are present, even though they are not causally related to the problems for which the patient is undergoing localization testing. Examples of cortical adenomas that were uncovered in a search for adrenal medullary tumors have been illustrated in the patients whose radiographs are displayed in Figs. 7 and 8. Another reason for a false-positive is in the acquired pathology displayed in Fig. 4 in a patient who has an adrenal hematoma. More distressing are the patients in whom pheochromocytoma is suspected and there is ambiguous or suggestive evidence of multiple localization tests (typically without congruence among the tests employed for the given patient and site of the presumed adrenal pathology) but who had normal adrenal glands on exploration or pathologic review.

False-negatives. An example of one false-negative test is the nephrotomogram exhibited in Fig. 9A with the true localization by the CT scan and venogram (Figs. 2 and 10B). False-negative examinations have been frequent for studies with limited resolution, such as the ultrasonogram and some of the arteriograms performed for adrenal medullary disease. The instances in which arteriography was misleading and yielded false-negative information occurred when inferences were drawn regarding the morphology of the whole adrenal gland from the injection of one of the arterial feeding vessels. A conclusion from this review is that it is not possible to study the whole gland from a single arterial injection and rule out small lesions in that adrenal gland.

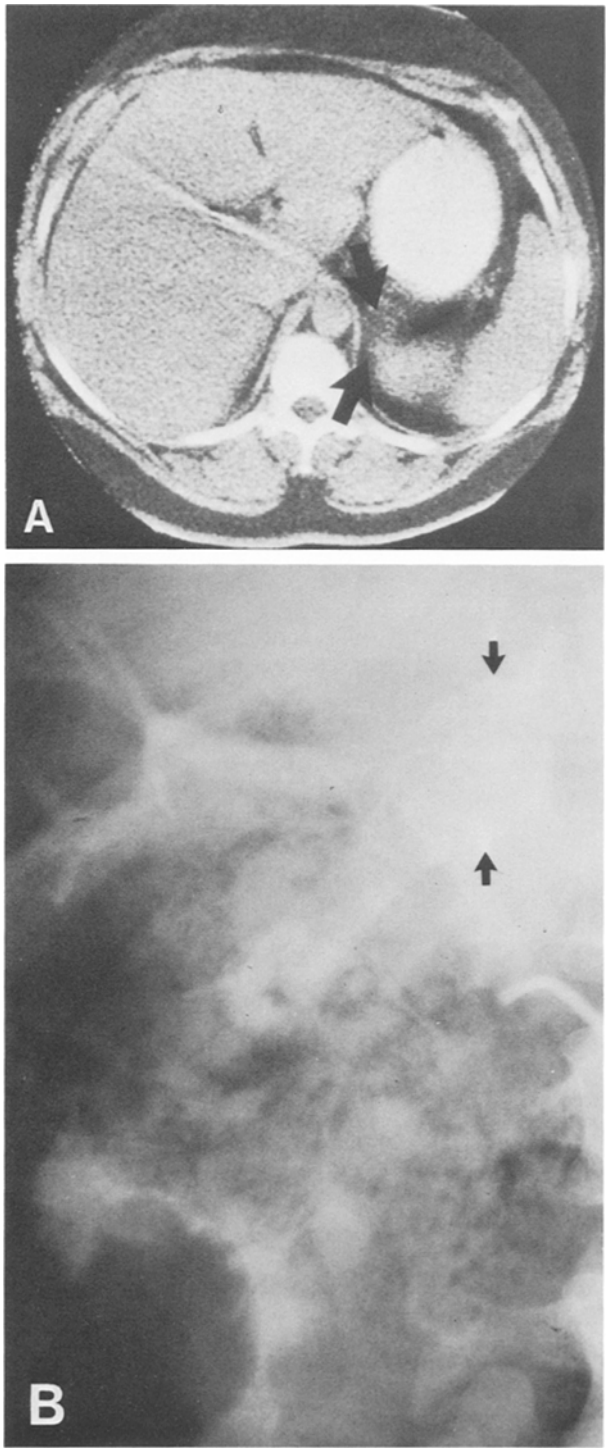

Fig. 8. Another patient had CT scan evidence of an adrenal mass (**A**), but a venogram was done, which in late phase shows the mass to be cortical in location (**B**), and nonfunctional on further study.

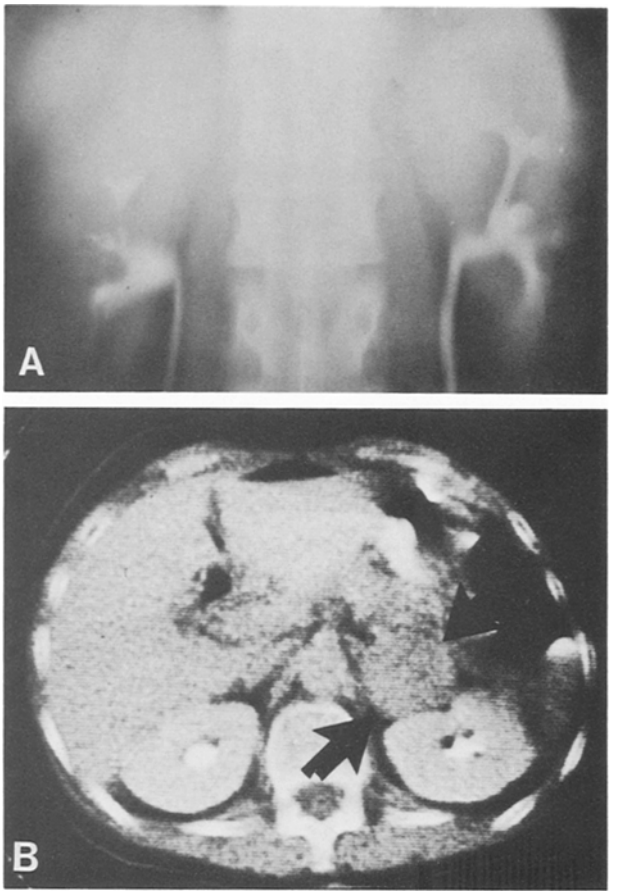

Fig. 9. A non-revealing IVP nephrotomogram (**A**) was followed by a convincing CT scan imaging of a left adrenal pheochromocytoma (**B**) in a patient with convincing biochemical proof of the diagnosis. The adrenal venogram of this mass in seen in Fig. 2.

If false-negatives have been the problem with several of the adrenal localization studies just mentioned, follow-up of the patient and later repetition of these studies might be a lesser evil than that seen with the localization tests that gave false-positives, because this information compels treatment. The latter hazard is thought to represent a greater risk for the patient than is under-diagnosis. Some combination of the greater and lesser sensitivity imaging tests might be beneficial to the patient, particularly if coupled with data that imply the function of the lesion demonstrated.

Adrenal Cortical Masses

False-positives. Adrenal cortical masses may also be studied by means of the same techniques reviewed for adrenal medullary tumors, with the additional benefit that the cortical tumors are generally strictly adrenal in location, unlike the more widely scattered anatomic locations of tumors in the chromaffin system. An additional advantage is that the patient rarely requires special preparation before even the invasive studies, and greater phys-

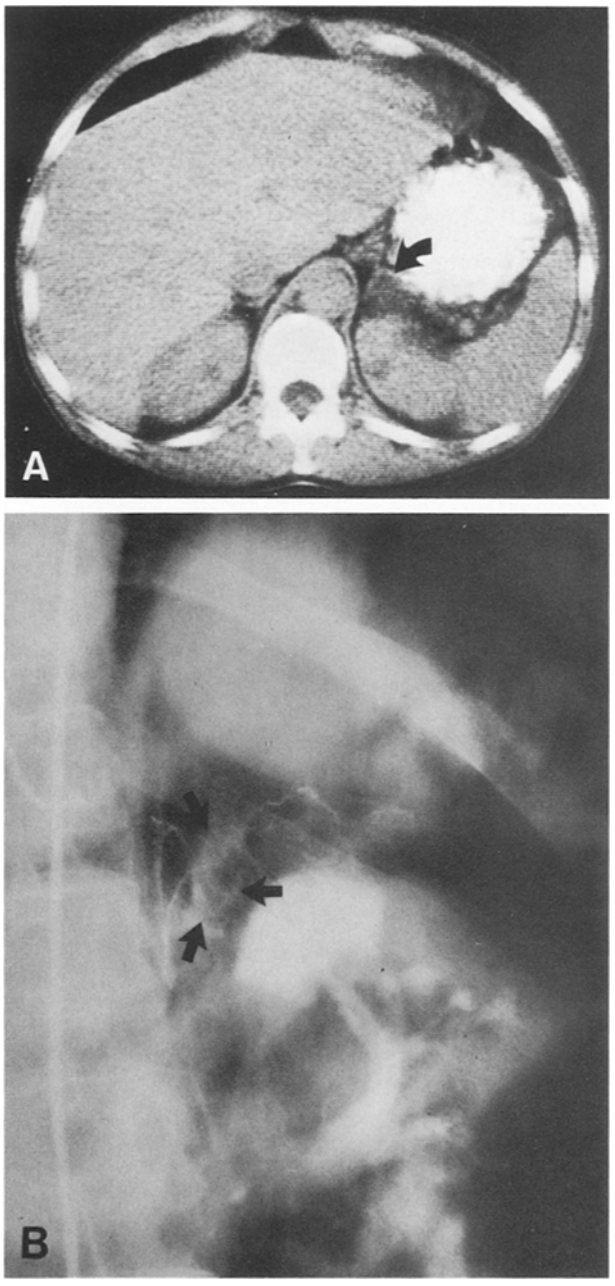

Fig. 10. A CT scan left adrenal enlargement (**A**) was reinforced by arteriography (**B**) in a hypertensive patient thought to have symptoms of pheochromocytoma, but without biochemical confirmation. Adrenalectomy of a normal left adrenal left the patient unimproved.

iologic stability has meant that some of these patients have more aggressive manipulation for localization. A disadvantage is that some adrenal cortical tumors can be symptomatic at very small dimensions of the primary tumor, straining the imaging techniques to the limit of the present resolution of these localization methods.

A patient with hypokalemia and hypertension had the clinical and biochemical diagnosis of primary

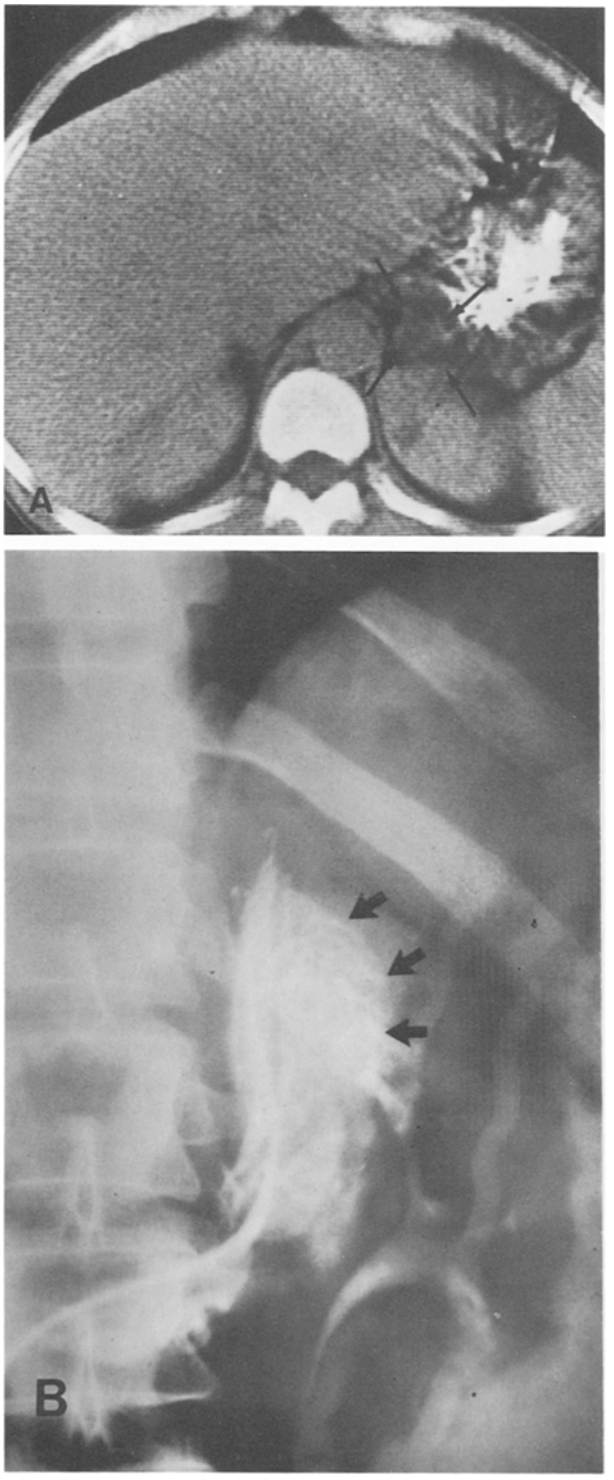

Fig. 11. CT scan-demonstrated lesion in left adrenal cortex (**A**) is confirmed by venous sampling and venogram (**B**) as the source of this patient's primary aldosteronism.

aldosteronism. A contrast-augmented CT scan showed an abnormality in the left adrenal gland (Fig. 11A). Venous sampling studies were carried out to confirm the functional nature of this lesion

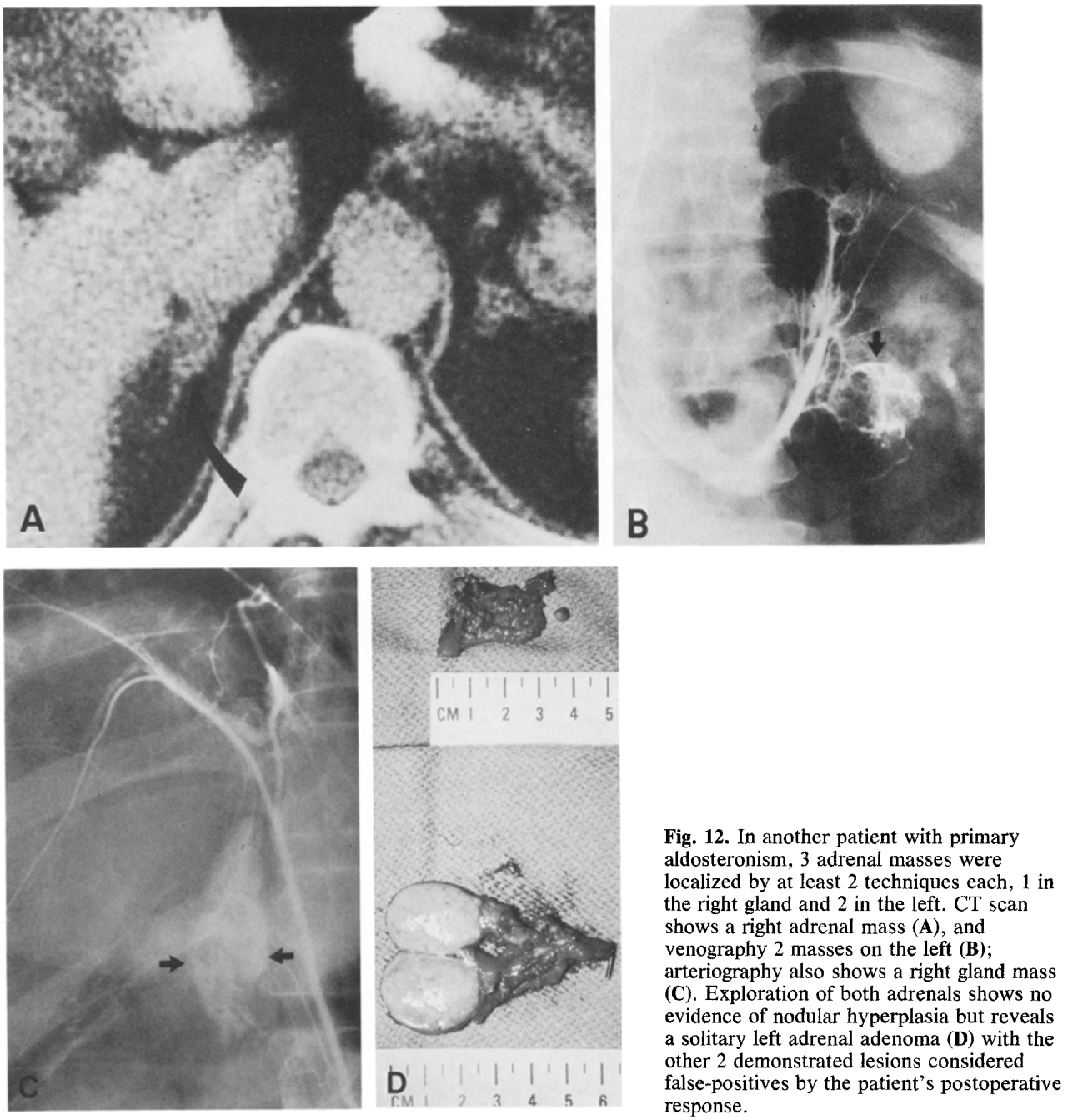

Fig. 12. In another patient with primary aldosteronism, 3 adrenal masses were localized by at least 2 techniques each, 1 in the right gland and 2 in the left. CT scan shows a right adrenal mass (**A**), and venography 2 masses on the left (**B**); arteriography also shows a right gland mass (**C**). Exploration of both adrenals shows no evidence of nodular hyperplasia but reveals a solitary left adrenal adenoma (**D**) with the other 2 demonstrated lesions considered false-positives by the patient's postoperative response.

and to rule out bilateral origin of excessive aldosterone production. The adrenal venogram associated with the sampling studies confirmed the presence of the lesion seen on CT scan by demonstrating the adenoma seen in Fig. 11B, which was confirmed by unilateral adrenalectomy yielding a 3 × 2.5 cm cortical adenoma. The patient was cured of the metabolic consequences of excess aldosterone, as well as hypertension, postoperatively.

The same approach, however, was employed in another patient with primary aldosteronism with misleading results on the basis of false-positive information on both left and right adrenal glands. With satisfactory clinical and biochemical evidence of primary aldosteronism, the patient underwent CT scan imaging of the adrenal glands which demonstrated a mass in the right adrenal gland (Fig. 12A). When venography and venous sampling were carried out, two nodules were demonstrated in the left adrenal gland with nothing suspicious seen in the right adrenal (Fig. 12B). To confirm or deny the presence of bilateral disease, an arteriogram was performed, which again demonstrated a mass on the right side (Fig. 12C) as well as suggesting the two

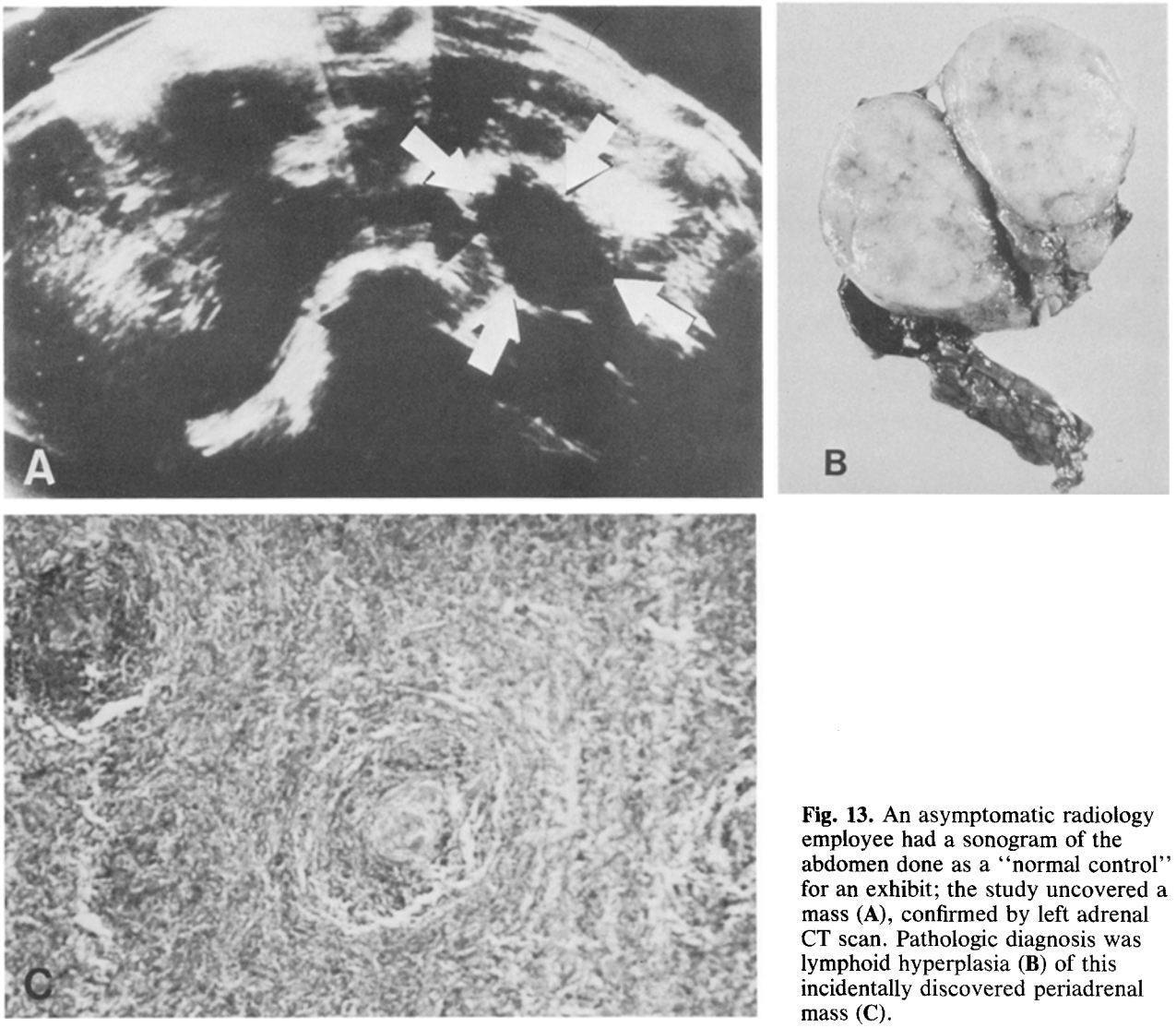

Fig. 13. An asymptomatic radiology employee had a sonogram of the abdomen done as a "normal control" for an exhibit; the study uncovered a mass (**A**), confirmed by left adrenal CT scan. Pathologic diagnosis was lymphoid hyperplasia (**B**) of this incidentally discovered periadrenal mass (**C**).

adrenal lesions on the left that were seen in the venogram. The diagnosis of bilateral nodular hyperplasia of the adrenal glands was not supported by evidence of suppression and postural changes, and a preoperative diagnosis of bilateral adrenal cortical adenomas was made on the basis of these localization tests which seemed to reinforce each other. For that reason, the operation performed was a simultaneous exploration of both adrenal glands via the posterior approach. The right adrenal gland was carefully examined, and no evidence of any gross pathology was encountered. To be sure of the normalcy of this gland, a section of the gland was biopsied and confirmed to be normal without evidence of nodular hyperplasia. The biopsy was taken in the portion of the gland which by CT scan and the arteriogram had had the appearance of a mass lesion, and no such lesion was apparent on study of the specimen. The left adrenal gland contained a clearly visible cortical adenoma in the inferior portion of the gland as demonstrated in the venogram (Fig. 12B). However, the nodule shown to be in the superior portion of the gland (Fig. 12B) could not be confirmed. The preoperative demonstration, therefore, had shown a total of 3 adrenal cortical nodules, 1 on the right and 2 on the left, each being demonstrated by at least 2 techniques. The actual operative yield and pathologic confirmation were that of a solitary adrenal cortical adenoma (Fig. 12D). The patient did well after the procedure with a cure of hypertension and hypokalemia, and has been normal with respect to cortisol secretion. The "phantom nodules" that were clear on localization studies remain unexplained even in retrospect.

A special consideration of adrenal cortical lesions, particularly of the large and bulky tumors that might represent adrenal cortical cancer, is the advisability of venography in their preoperative

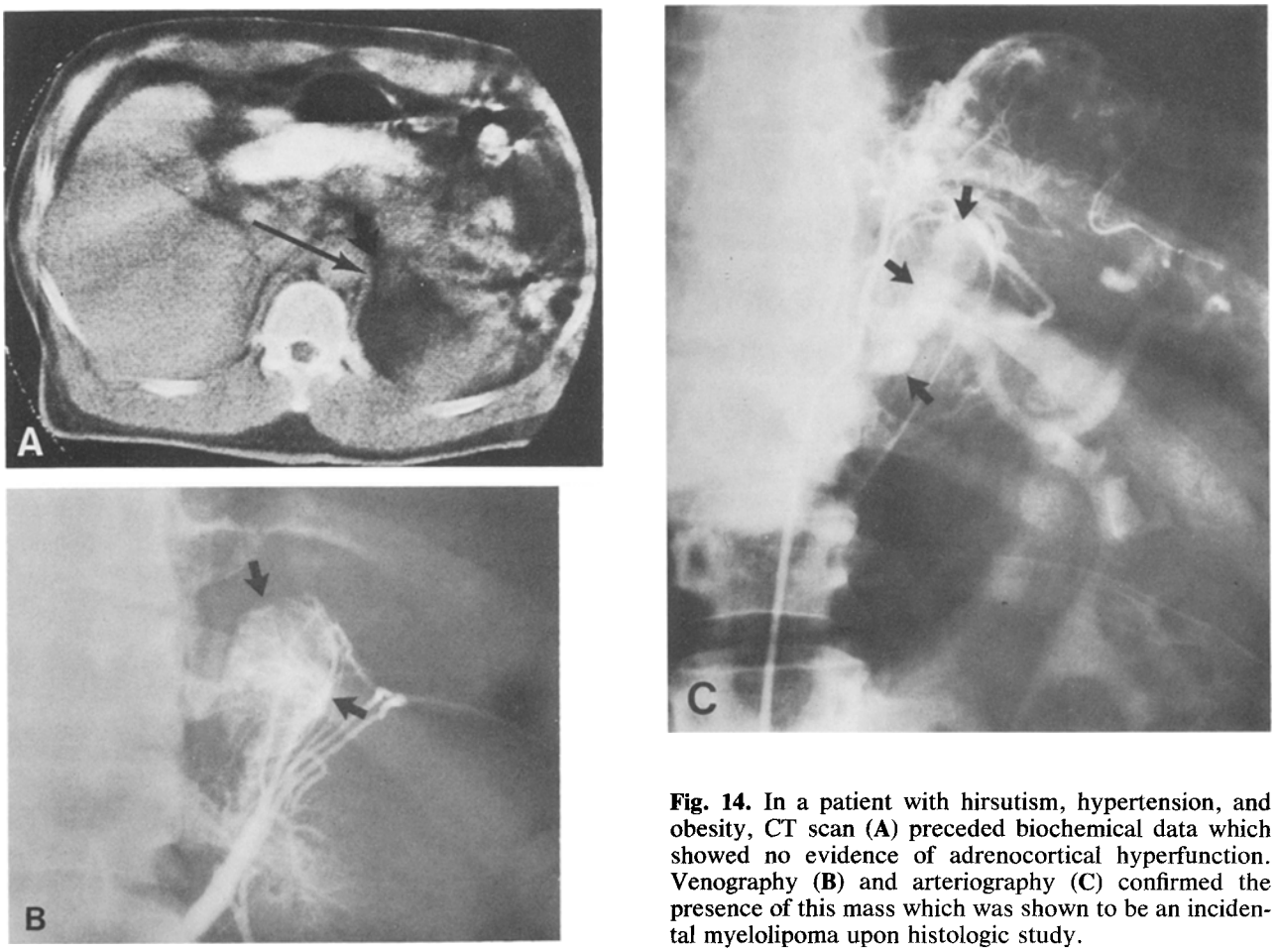

Fig. 14. In a patient with hirsutism, hypertension, and obesity, CT scan (**A**) preceded biochemical data which showed no evidence of adrenocortical hyperfunction. Venography (**B**) and arteriography (**C**) confirmed the presence of this mass which was shown to be an incidental myelolipoma upon histologic study.

evaluation to help plan the surgical approach if intravenous extension of the tumor is present [1]. As seen in Fig. 3, the extensive intravenous extension of this adrenal cortical cancer encouraged an operative approach that obtained early distal venous control and extirpation of the intravenous extension without embolization of this component of the tumor in the bloodstream.

False-negatives. Patients with Cushing's syndrome or evidence of metastatic disease to the adrenals often present with larger adrenal tumors that are more easily localized than the patients who may be symptomatic with primary aldosteronism. Particularly the patients who have normokalemic primary aldosteronism have very small adrenal cortical neoplasms at the limit of the resolution of our imaging techniques. The reason for the application of the localization methods for these patients is to avoid bilateral operative exploration of both adrenals. In at least one instance, a combination of our imaging techniques compelled bilateral adrenal exploration (Fig. 12) which may have been unnecessary. The more physiologically useful study for adrenal cortical localization might be the iodocholesterol scanning technique. This technique should "light up" the gland with a focal lesion and suppress the imaging of the opposite gland. Particularly when coupled with dexamethasone suppression, iodocholesterol imaging is an excellent technique not only for localizing tumors but also for judging their presumed functional status on the basis of the isotope uptake.

The Adrenal "Incidentaloma"

Some patients have no complaint that would arouse suspicion of adrenal disease, but have undergone a localization study that incidentally uncovers evidence of mass lesion in or around the adrenal gland. One such patient was an employee of the radiology department who was a volunteer for an ultrasound study of the normal female abdomen. A CT scan was employed for confirmation of the presence of this mass (Fig. 13A). After endocrinologic evaluation, which showed no abnormality in cortical or medullary adrenal function, exploration was undertaken to determine the nature of this mass. At the

Table 3. Trends in adrenal localization utility.

Increasing
Computed tomography
Ultrasonography
Biochemical venous sampling
Decreasing
Nephrotomography
Arteriography
Venography
Future—isotopic scanning
Cortical: iodocholesterol
Medullary: iodobenzylguanidine

time of the retroperitoneal dissection of this large mass, the left adrenal gland was found to be wrapped around and contiguous with a retroperitoneal mass that was adjacent to smaller masses, probably of lymphatic origin (Fig. 13B). The intraoperative diagnosis was probable lymphoma, but the final pathologic diagnosis revealed a benign lymphoid hyperplasia.

Another patient presented with evidence of hirsutism, hypertension, and obesity, and before the biochemical information from urine collections had returned, she had undergone CT scan (Fig. 14A) which revealed a left adrenal mass. This left adrenal mass was confirmed by venography (Fig. 14B) and arteriography (Fig. 14C). The biochemical data returned without evidence of adrenal cortical hyperfunction, but adrenal exploration was now planned to identify the mass encountered by the localization studies. The diagnosis of this adrenal mass when resected was "myelolipoma"—an incidental finding in this adrenal gland, unrelated to the patient's presenting complaints.

The incidental cortical adenomas discovered in patients thought to have adrenal medullary disease are also classified as incidental discoveries of the localization tests (Figs. 7 and 8). At least one additional patient had the incidental discovery of adrenal metastasis from a lung cancer before the primary was discovered.

Discussion

Adrenal radiography has remarkably increased in precision, particularly with the wider application of noninvasive techniques. An increase in precision has not necessarily implied specificity for adrenal disease. The increased sensitivity of the localization tests has also brought with it the hazards to the patient of false-positive studies and the discovery of adrenal "incidentalomas."

Trends in adrenal localization are shifting according to the utility of the tests employed to uncover mass lesions with greater sensitivity and decreased false-negative localization testing. However, at the current state of the art, some of the imaging tests are so sensitive as to uncover "adrenal non-disease" and the sensitivity of these studies is being tempered with the addition of tests with high correlation with the functional nature of the adrenal tumors discovered. Examples of these latter studies with their inference of a functional nature of the adrenal tumors are seen in Table 3—the wider application of biochemical venous sampling and hormone ratios, and isotopic scanning with function-specific labeled compounds being selectively taken up in the endocrine tumors.

With respect to catecholamine-producing tumors in adrenal or extra-adrenal sites, the advent of specific isotopic scanning is a considerable advance [3]. Not only does it promise a much higher degree of specificity in localizing pheochromocytoma, but it can also image the normal adrenal glands much more regularly than can sonography or CT scanning. In addition, it offers the promise of being able to deliver sufficient radioisotope to be used as specific therapy in some cases of functioning metastatic pheochromocytoma [4]. At the present time, the isotope is not available for widespread application, but it is anticipated that this study will be the most specific localization test for chromaffin neoplasms when released for general use.

CT scanning is both the star and the enigma of adrenal localization procedures. Many advocates are promoting its use as the first and only adrenal localization test necessary and sufficient for confident predication of adrenal tumors, particularly pheochromocytoma. "CT is recommended as the initial radiographic procedure in the evaluation of patients with clinical suspicion of pheochromocytoma" [5]. "CT offers final assessment of certain adrenal masses even when their size is 1–2 cm" [6]. "CT is the examination of choice in the localization of a pheochromocytoma" [7]. A poll taken by one of the authors of the membership of the American Association of Endocrine Surgeons in April, 1981, showed that 50% of the membership of the AAES would accept localization of a pheochromocytoma by CT scan alone, possibly modifying their approach to excise it via a posterior retroperitoneal exploration on the basis of the CT scan information [8].

Perhaps some of this enthusiasm for CT scan localization of pheochromocytoma is uncritical; although the sensitivity of this test is not doubted, the lack of specificity may have caused misdirected exploration and therapy in several patients in this series. Several centers have voiced reservations about the cost-effectiveness and necessity of CT scanning, particularly as the single procedure of choice for pheochromocytoma localization. One

group suggests that sonography is a good localization technique and CT scanning adds nothing beyond the ultrasound noninvasive testing [9]. Another group suggests that venous sampling is far more specific in pheochromocytoma localization and should be preferred over imaging studies [10], and some groups advocate no preoperative localization studies whatever, since the intraoperative localization by the pressor effect of surgical exploration finds even those small tumors that CT scanning would miss and uncovers them by the most unreliable method, that is, their biologic effect [11].

For adrenal cortical masses, CT scanning is also advocated as the procedure of choice [12, 13]. Even in the small adrenal cortical lesions of primary aldosteronism [14], CT scanning has been useful in identifying some adenomas, and in some instances distinguishing primary aldosteronism on the basis of aldosterone-producing adenomas from idiopathic bilateral hyperplasia. However, in our experience, some false-negative scans have been seen with very small lesions, and false-positives have not been eliminated, as seen in Fig. 12. The functional study that might be more helpful in directing unilateral adrenal exploration might be venous sampling as has been practiced for some time [15], modified for interpretation of aldosterone:cortisol ratios for lateralization.

The propensity of endocrine neoplasms to invade veins makes venography a significant preoperative study for large tumors, those known to be malignant or recurrent. This is especially helpful for cortical neoplasms [1] or for recurrent pheochromocytoma [16].

If a single radiographic procedure is often not sufficient to localize a tumor and may be unnecessary even if it can demonstrate the lesion, in what sequence should these procedures be performed and how much localization study is enough? The single feature that should precede localization studies is the clinical and biochemical confirmation of the diagnosis. Patients should not be sent for localization studies ahead of diagnostic confirmation workups, because often localization will produce findings that are incidental to a complaint the patient has, and "adrenal non-disease" is demonstrated compellingly, with treatment of this non-disease offering no benefit to the patient. Consequently, in a patient who has secured the more difficult diagnostic information before the less troublesome noninvasive studies, localization procedures have a high yield. If a localization procedure is clearly positive in a patient with a clear-cut syndrome, this may give the clinician confidence enough to proceed with therapy. However, if there are any doubts as to the diagnosis—*even in the presence of a radiographically demonstrated mass*—such a patient should undergo a further study to correlate function with the finding. Suggestions for such studies would be the venous sampling for biochemical assay or radioisotope scanning. When widely available, these studies may be both necessary and sufficient as primary localization tests offering a margin of safety when each of the tests is reliable, and the physician and patient are willing to accept the cost and risk of the test in exchange for a lower margin of error [17]. However, even congruent redundant localization tests are not a substitute for diagnosis, which should still precede localization for adrenal cortical and medullary tumors.

Résumé

La détermination du siège des tumeurs de la surénale nécessite de recourir à une ou plusieurs méthodes radiologiques: clichés à blanc de l'abdomen, urographie intraveineuse, veinographie surrénalienne et échantillonage veineux, artériographie, ultra-sonographie, tomodensitométrie et scintigraphie. Ces techniques peuvent être divisés en deux types: invasives et non invasives, chacune possédant des degrés différents de sensibilité et de spécificité. La précision diagnostique des différentes méthodes a été étudiée sur des séries concernant cinq années en soulignant spécialement les localisations faussement positives. En fait, la précision de la localisation varie selon que l'affection intéresse la médullaire ou la corticale de la surrénale et selon que les malades ont été ou non protégés par une préparation pharmacologique.

Abstracto

La localización preoperatoria tradicional de los tumores suprarrenales ha empleado una o más de las siguientes técnicas radiográficas: placas simples de abdomen, urografía intravenosa, venografía suprarrenal y muestreo de sangre venosa, arteriografía, ultrasonografía, escanografía computadorizada (CAT) y centelleoescanografía. Estas técnicas de localización pueden ser clasificadas como de tipo invasivo o de tipo no invasivo, con cada técnica poseedora de diferentes grados de sensibilidad y especificidad para establecer la presencia de enfermedad suprarrenal. La precisión diagnóstica de estas técnicas radiográficas es revisada a partir de una serie de 5 años en un hospital universitario, con especial énfasis sobre localización positiva falsa. Las técnicas empleadas en la localización y su secuencia varían y dependen de si se sospechaba la presencia de enfermedad suprarrenal medular o cortical, y de si el paciente estaba o nó protegido por preparación farmacológica.

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