Hospital Topics

Role of venous sampling in locating a phaeochromocytoma

D J ALLISON, M J BROWN, D H JONES, J B TIMMIS

Abstract

Selective venous sampling was performed in 31 patients in whom the diagnosis of phaeochromocytoma was suspected on clinical and biochemical grounds. Data from samples assayed for their adrenaline and noradrenaline content using a radioenzymatic technique were used to confirm or refute the suspected diagnosis. In 19 of the 31 patients a phaeochromocytoma was subsequently removed surgically, and the remaining 12 patients are now thought not to have tumours (mean follow up period: four years). Analysis of the assay data shows that selective venous sampling correctly identified the presence of a tumour in all 19 patients, and correctly excluded the diagnosis in 11 of the 12 remaining patients —an overall success rate of 97%. Success rates of 88% for arteriography and 84% for computed tomography were recorded, though these investigations were not performed in all patients. Ultrasound and intravenous urography were much less accurate.

On the basis of this study a sequence of investigation is proposed for patients with a suspected phaeochromocytoma. Computed tomography occupies a central role in this sequence with venous sampling (and occasionally other techniques) being used only as complementary investigations when specific indications for their use exist.

Introduction

Phaeochromocytoma is a rare cause of hypertension but is a life threatening disorder if it remains undiagnosed.[1] The diagnosis and management of very large or active tumours are often straightforward, but there are two circumstances in which this may not be so. The first is when the diagnosis of phaeochromocytoma seems certain on clinical and biochemical grounds but the tumour is difficult to find because it is very small (or ectopic). The second is when the clinical and biochemical evidence is equivocal, making the diagnosis doubtful or even unlikely, but a phaeochromocytoma must be ruled out as a possible curable cause of the patient's hypertension.

Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

D J ALLISON, FRCR, consultant diagnostic radiologist
M J BROWN, MRCP, senior lecturer in clinical pharmacology
D H JONES, MRCP, lecturer in clinical pharmacology
J B TIMMIS, DMRD, FRCR, registrar in diagnostic radiology

Correspondence and requests for reprints to: Dr D J Allison, Department of Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS.

In both sets of circumstances the subsequent clinical management of the patient will be principally determined by the results of various diagnostic techniques that attempt to show whether or not a tumour exists, and if it does to pinpoint its location for the surgeon. With advances in diagnostic imaging methods several investigations may now be used in the search for a phaeochromocytoma, and these should be applied in the most effective sequence. We have analysed the results of diagnostic venous samplings in 31 patients with suspected phaeochromocytoma and evaluated the current position of this technique relative to other methods of identifying the presence of a tumour.

Methods

The study is based on investigations performed over seven years in 31 patients suspected of having a phaeochromocytoma on clinical and biochemical grounds (figure). The 16 men and 15 women were aged from 17 to 68 (average 46). Radiological investigations included intravenous urography, venous sampling, ultrasound scanning, computed tomography, and angiography. Ultrasound and computed tomography were only available to patients presenting in the last half of the series.

Techniques

INTRAVENOUS UROGRAPHY

All 31 patients underwent intravenous urography, 20 at this hospital and 11 at their referring hospital, and these 11 results were excluded from the present analysis to ensure uniformity of technique in the series. Urography in the 20 patients was performed with intravenous sodium and meglumine diatrizoate (Urografin 325), 2 ml/kg with immediate nephrotomography.

VENOUS SAMPLING

Venous samples were withdrawn through a preshaped polyurethane catheter introduced into the femoral vein under local anaesthesia using the Seldinger technique. Samples were obtained from the internal jugular veins, subclavian veins, brachiocephalic veins, thymic vein, superior intercostal vein, azygos vein, superior vena cava, right atrium, inferior vena cava, hepatic veins, renal veins, adrenal veins, common iliac veins, and internal and external iliac veins. A single arterial sample was also obtained by needle puncture of the femoral artery. The exact sampling sites were recorded on a map. The 10 ml blood samples were collected into chilled lithium heparin tubes; the plasma was separated at 4°C and assayed for adrenaline and noradrenaline by a radioenzymatic technique.[2] The hazards, limitations, and potential errors of venous sampling have been described.[3,4] The procedure is relatively non-invasive, and no morbidity was observed as a result of venous sampling alone in any of the patients in the present series. Samples were obtained from the adrenal veins with great care to avoid infarction of the glands.[3,5,6]

Some patients were already being treated with adrenergic antagonists for their hypertension, but this treatment was never started specifically for the venous sampling, and no untoward cardiovascular effects were recorded during any of the procedures.

ULTRASOUND

Ultrasonic scanning was performed in 11 patients using a diasonograph.

COMPUTED TOMOGRAPHY

Computed tomography, like ultrasound, was only available to patients in the latter part of the series, and was performed in 13 subjects.

ARTERIOGRAPHY

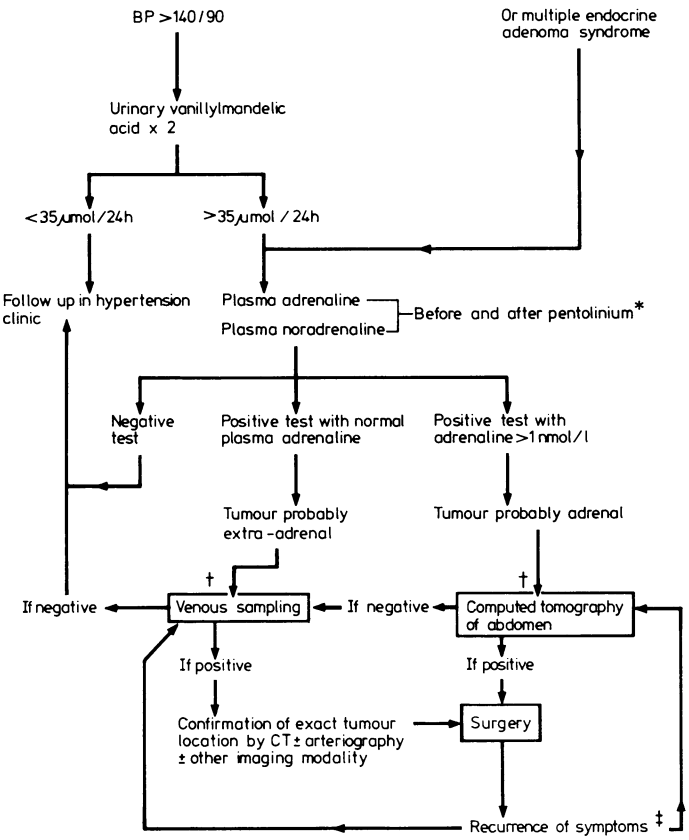
Arteriography was performed in 17 patients. Before computed tomography was available arteriography was performed as a diagnostic test to confirm the results of previous positive venous sampling. In the last part of the series arteriography was done only if the surgeon required preoperative information about the vascular supply to the tumour, or if other tests yielded conflicting or equivocal results.

Arteriography was performed only in patients receiving adrenergic blocking agents and was not associated with any morbidity. During the venous sampling and angiography a physician as well as a radiologist were present throughout the procedures.

Results

From the results of venous sampling and other tests 21 surgical explorations were undertaken in 20 of the original 31 patients. In one patient no tumour was found, and this case represents the false positive venous sampling result in the table. In the remaining 19 patients one or more phaeochromocytomas were found. In this group of 10 men and nine women three (16%) had bilateral adrenal tumours and four (21%) had ectopic tumours. One patient had two operations only one of which showed a tumour. The 12 patients who were thought not to have a phaeochromocytoma were followed up for an average of four years (range 14 months-five years) using repeated estimations of the vanillylmandelic acid and the pentolinium suppression test (figure).[7] For the purposes of this study they are regarded as not having tumours.

Using these operative and follow up data as criteria for assessing the relative accuracy of different tests, the results of the investigations were analysed and are given in the table. Venous sampling correctly identified all patients who were subsequently shown to have a phaeochromocytoma and, apart from one false positive result, correctly identified all those who were not. In six patients the sampling procedure was repeated because of clinical or biochemical suspicion that the tumour had recurred despite the removal of a phaeochromocytoma after the first venous sampling. In three patients the second sampling suggested the presence of further tumour, which was confirmed subsequently, and in two the result of the sampling was normal, and this remains correct to date (follow up: three years and four years respectively). In the sixth patient the procedure was repeated because the result of the first sampling was equivocal. The second sampling did not suggest the presence of a tumour, and the patient remains well to date (follow up: three years).



Suggested sequence of investigations for a patient with suspected phaeochromocytoma. The pentolinium test was used only in those patients investigated after 1980.
*Brown *et al*, 1981.[7]
†Isotopic methods[15] may be inserted at this point in the diagnostic sequence. Their role relative to computed tomography has yet to be determined.
‡Choice of next investigation determined by nature of symptoms and extent of previous surgery.

Discussion

The identification of the presence of a phaeochromocytoma by vena caval catheterisation with analysis of regional blood samples for noradrenaline was first described by Von Euler *et al* in 1955.[8] Since then advances in both radiological and assay techniques have considerably increased the accuracy of the method, and the data obtained in the present study show that selective venous sampling is a safe and reliable method of confirming or refuting the diagnosis of phaeochromocytoma when this is suspected. In the case of a positive result the sampling method accurately identifies the presence of the tumour, which is particularly useful in the case of multiple or ectopic growths.

During the seven years covered by this investigation computed tomography has been used widely[9–11] and has rapidly become established as the most accurate and least invasive technique available for detecting an adrenal phaeochromocytoma.[12 13] The

Results of various investigations in 31 patients with suspected phaeochromocytoma

Investigation	No performed	True positive		True negative		False positive		False negative		Correct result	
		No	%	No	%	No	%	No	%	No	%
Intravenous urogram	20	5	25	4	20	3	15	8	40	9	45
Ultrasound	11	6	55	2	18	0	0	3	27	8	73
Computed tomography	13	8	61	3	23	1	8	1	8	11	84
Venous sampling	37*	22	59	14	35	1	3	0	0	36	97
Arteriogram	17	11	65	4	24	1	6	1	6	15	88

*Six patients had two studies.

diagnostic accuracy of computed tomography is emphasised by its high success rate in the present study—a level achieved although the study was being done as computed tomography was being introduced and experience in its interpretation acquired.

As computed tomography is now unquestionably the investigation of first choice in the search for a phaeochromocytoma the question arises as to what part, if any, venous sampling has to play in the diagnosis of this tumour. We believe that sampling complements computed tomography and applies in three situations: firstly, when a patient presents with strong clinical and biochemical evidence of a phaeochromocytoma, yet computed tomography fails to find a tumour, venous sampling may show the presence of an ectopic tumour. Computed tomography or another imaging technique such as arteriography may then be effectively directed towards the specific region under suspicion (figure). The possibility of an ectopically sited tumour seems to be higher when the plasma adrenaline concentration is normal in the presence of a raised noradrenaline concentration, and in these circumstances venous sampling may be used as the first investigation. Secondly, venous sampling may be helpful if a patient's symptoms persist or recur after surgical removal of an adrenal phaeochromocytoma. The likelihood of a second ectopic tumour or of metastatic tumour occurring in these circumstances makes sampling the investigative procedure of first choice. Thirdly, venous sampling seems to be a very reliable means of refuting the diagnosis of phaeochromocytoma when the clinical and biochemical evidence is doubtful or conflicting. Thus where the evidence for a phaeochromocytoma is equivocal and computed tomography results are negative, a negative venous sampling result may be used to prevent further investigation and obviate a futile surgical exploration. If doubt persists the venous sampling procedure may be repeated.

The place of other imaging techniques in the diagnosis of phaeochromocytoma is now limited. Intravenous urography and ultrasound are often successful in identifying large tumours but are poor techniques for discovering small tumours. Neither technique may be used reliably to exclude a phaeochromocytoma —an important consideration when evaluating patients with equivocal clinical and biochemical findings. Adrenal phlebography carries the risk, albeit small, of adrenal gland infarction. This complication is undesirable whether the gland is the site of tumour or not, and we believe that there is no place for the procedure in the investigation of phaeochromocytoma.

Arteriography is still useful occasionally when the data from computed tomography are uncertain or when the surgeon desires information before the operation about the vascular supply to the tumour. The risk of inducing an adverse reaction by selective arteriography is small owing to the efficacy of modern adrenergic blocking agents, but the technique is clearly more invasive than either computed tomography or venous sampling, and its success rate in finding tumours is now lower. Advances in the chemistry of contrast media and improvements in imaging techniques such as digital vascular imaging will make arteriography safer and more accurate, however, and it will probably continue to be used in a small proportion of problem cases.

Radioisotope techniques for locating phaeochromocytomas have been the subject of much research, and some promising results are now available.[14 15] Isotopic methods should prove particularly useful in locating ectopic or metastatic phaeochromocytomas, and seem certain to be increasingly important in the investigation of these tumours.

The place of the new imaging modality, nuclear magnetic resonance, has yet to be evaluated.

In summary, we believe that in centres where facilities for computed tomography and plasma catecholamine assay exist the most accurate and least invasive sequence of investigation currently available to a patient suspected of harbouring a phaeochromocytoma is that given in the figure. Computed tomography occupies a central role in this sequence with venous sampling (and occasionally other techniques) being used only as complementary investigations when specific indications for their use exist.

We thank the physicians and surgeons at Hammersmith Hospital and referring hospitals who have helped in the investigation and treatment of the patients presented in this study.

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Does the daily consumption of two tablespoonfuls of unprocessed bran seriously interfere with absorption of calcium or iron, or both?

Probably not. The key word is seriously. In the short term bran can certainly cause a fall in the absorption of calcium, iron, and zinc, and some studies have shown a negative calcium balance. In the long term, however, adaptation to a low intake of calcium occurs, probably because of a fall in urinary loss. There is no evidence of calcium or iron deficiency in long term bran takers, but the data are limited.[1] In rural Africans, who have a much higher intake of fibre than would occur in a British diet plus two tablespoonfuls of bran, and also a lower intake of calcium, there is no evidence of increased metabolic bone disease: in fact, fracture of the femoral neck is uncommon.[2 3] It is conventional wisdom to advise caution in vulnerable groups such as the pregnant or lactating mother and the elderly, but I should be very surprised if bran caused mineral deficiency, even in these people, provided that a sensible dose is taken and a sensible mixed diet is eaten.—K W HEATON, reader in medicine, Bristol.

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