HK J Paediatr (new series) 2005;**10**:109-114

Case Reports

Hypertensive Encephalopathy in a Chinese Girl Secondary to Juxtaglomerular Cell Tumour of the Kidney

KL ***NG,*** PLS ***IP***

Abstract Hypertension owing to a neoplasm of juxtaglomerular cell origin, commonly called Juxtaglomerular cell tumour (JGCT), had been reported with increasing frequency since the initial description in 1967. The hypertensive effects, usually poorly responsive to antihypertensive medications, are often incapacitating. We describe a JGCT which caused hypertensive encephalopathy in an 11-year-old Chinese girl. This tumour appears to be benign and makes comprehensive investigations for this treatable cause of hypertension worthwhile.

Key words Hypertensive encephalopathy; Juxtaglomerular cell tumour; Renin; Surgery

Introduction

Juxtaglomerular cell tumour of the kidney was first described in 1967 by Robertson and one year later Kihara reported an identical case following surgical removal of a tumour-containing kidney. The name Robertson-Kihara syndrome has been used to refer to Juxtaglomerular cell tumours (JGCT). This mesenchymal neoplasm appears to be benign and usually occurs in young patients. We report a JGCT which caused hypertensive encephalopathy in an 11-year-old Chinese girl (OL).

Case Report

OL was an 11-year-old girl, admitted for sudden onset of impaired consciousness. She had a history of headache for one month, associated with vomiting and blurred vision. One week prior to the admission, she was also noted to have polydipsia and polyuria. Her past health was otherwise good with no history of taking drugs. There was no family history of renal or cardiovascular diseases.

On admission, she was confused with Glasgow Coma Scale of 11/15. Blood pressure was 230/160 mmHg with no significant differential between upper and lower limbs. She had grade IV hypertensive retinopathy but no cardiopulmonary or focal neurological abnormalities.

Examination of the abdomen was normal. Genital examination revealed a normal female external genitalia.

Urine analysis was negative and creatinine clearance was 105 ml/min/1.73mP^{2P}SA. Other laboratory studies, including plasma renin activity obtained before anti-hypertensive therapy, were shown in Table 1.

Echocardiogram showed normal cardiac anatomy with no evidence of co-arctation of the aorta.

CT abdomen identified normal adrenal glands and a small 1 cm intra-renal lesion in the mid-pole of the left kidney (Figure 1).

MRI also showed normal adrenal glands and a 1 cm x 1 cm solid mass in the left kidney, which demonstrated contrast enhancement. MRA revealed no evidence of stenosis along both main renal arteries (Figure 2).

Renal arteriogram did not demonstrate any evidence of renal artery stenosis. The lesion was avascular. Selective

Department of Paediatrics & Adolescent Medicine, United Christian Hospital, 130 Hip Wo Street, Kwun Tong, Kowloon, Hong Kong, China

KL **NG** （吳國樑） *MBBS, FHKCPaed, FHKAM(Paed)*
PLS **IP** （葉麗嫦） *MBBS, FHKCPaed, FHKAM(Paed)*

Correspondence to: Dr KL **NG**

Received March 10, 2004

Table 1 Laboratory Investigations before antihypertensive therapy

Test	Result	Age-adjusted reference range	Units
Hb	17.1	(11.5-15.0)	g/dL
RBC	5.84	(4.0-5.4)	x 10^{12}/L
WBC	8.1	(4.0-10.0)	x 10^{9}/L
PLT	298	(150-400)	x 10^{9}/L
ESR	5	(0-10)	mm/hr
Sodium	142	(134-149)	mmol/L
Potassium	2.3	(3.2-5.2)	mmol/L
Urea	4.8	(3.0-8.0)	mmol/L
Creatinine	52	(50-120)	umol/L
Calcium	2.31	(2.10-2.60)	mmol/L
Phosphate	1.06	(0.70-1.40)	mmol/L
Magnesium	0.8	(0.6-1.1)	mmol/L
pH	7.54	(7.35-7.45)	
pCO_2	40	(35-45)	mmHg
pO_2	92	(75-100)	mmHg
HCO_3	32.8	(21-28)	mmol/L
BE	8.6	(-3-3)	mmol/L
TSH	1.01	(0.3-4.0)	mIU/L
Renin (recumbent)	13.2	(0.51-2.64)	ng/ml/hr
Aldosterone (recumbent)	2989	(<444)	pmol/L
Adrenaline (24-hr urine)	12	(0-15)	nmol/mmol creatinine
Noradrenaline (24-hr urine)	22	(0-60)	nmol/mmol creatinine
VMA (24-hr urine)	0.7	(0-4.3)	umol/mmol creatinine

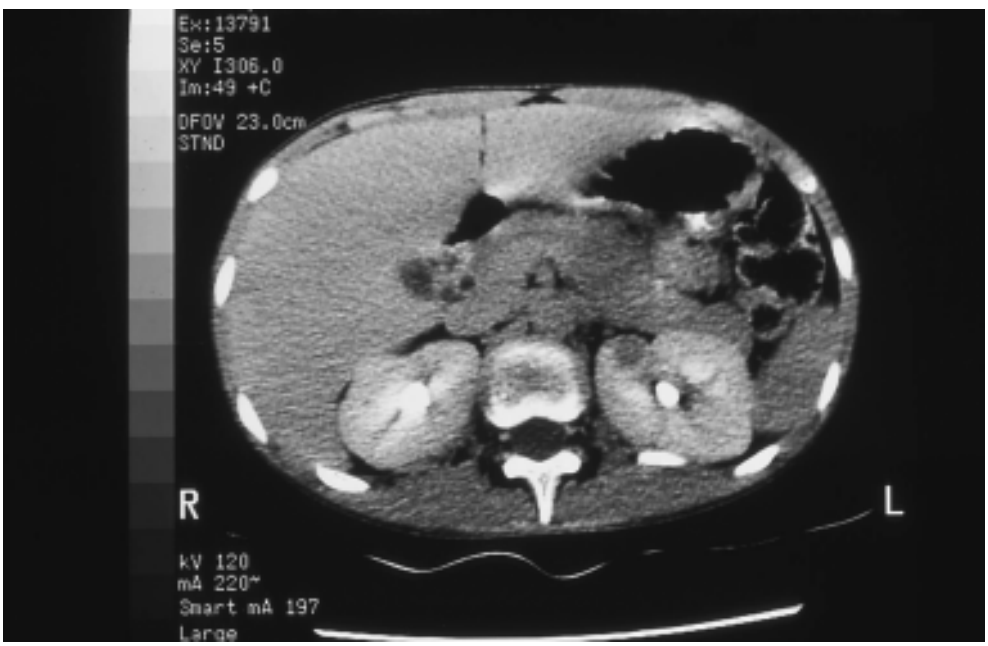

Figure 1 CT abdomen demonstrated a small 1 cm intra-renal lesion in the mid-pole of the left kidney.

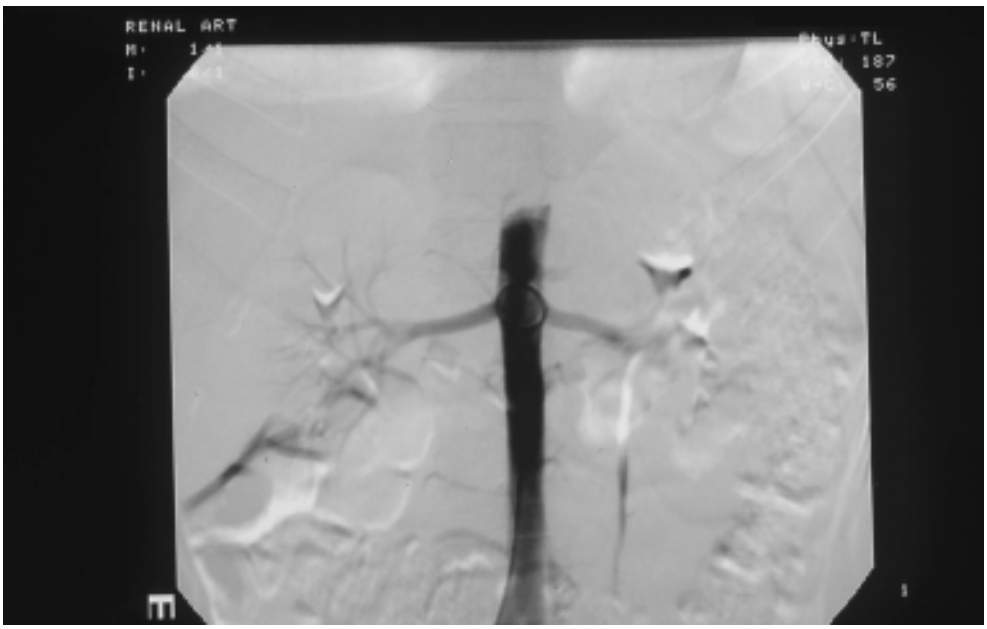

Figure 2 MRA showed no evidence of stenosis along both main renal arteries.

and segmental sampling of the renal veins was not performed because the lesion was already detected by radiological means.

In view of encephalopathy, fluid was restricted and mannitol was given intravenously to decrease the intracranial pressure. Hypokalaemia was corrected with potassium supplement. Hypertension was treated with a number of antihypertensive medications (labetolol, hydralazine, nifedipine and captopril) with the best control being achieved with a combination of nifedipine and captopril. The blood pressure immediately prior to surgery was 130/80 mmHg.

The patient underwent an uneventful laparotomy with excision of the tumour. Immediately after the operation, the blood pressure was 128/75 mmHg. She was maintained on anti-hypertensive drugs for 1 month. Her headache and visual symptoms resolved. Her blood pressure was normal during a follow up period of 12 months without any medications. Recumbent plasma renin activity and aldosterone level were normal 12 months postoperatively (2.25 ng/ml/hr and 230 pmol/L respectively). Haemoglobin level also returned to normal level.

Intraoperative and Pathological Findings

Within the mid-pole of the left kidney, there was an 1 cm x 1 cm tumour which was confined to the renal cortex. Microscopic examination showed that the tumour was well circumscribed and compressed onto the adjacent renal tissue forming a pseudocapsule. The tumour formed a haemangiopericytic pattern. Tumour cells were mainly polyhedral with eosinophilic granular cytoplasm. There was no mitotic figure, cellular atypia, necrosis or haemorrhage seen (Figure 3). Electron microscopy showed the presence of many electron dense granules in the tumour cells (Figure 4). A crystalline pattern was evident in these granules. The features were consistent with JGCT.

Discussion

Juxtaglomerular cell tumour, a term coined in 1968 by Kihara, was first recognised in 1967 by Robertson, who described a renin-secreting renal cortical tumour causing severe hypertension. This form of hypertension is referred to as "primary reninism", a term first proposed by Conn.[1]

Since the initial recognition of this tumour, there were about 70 cases reported in the literature including no more than 13 Chinese cases.[2] Teenagers constitute the largest single population with JGCT. The female-to-male ratio is 1.8:1.[3]

The typical presentation of a patient with JGCT includes the triad **of hypertension, hypokalaemia and elevated**

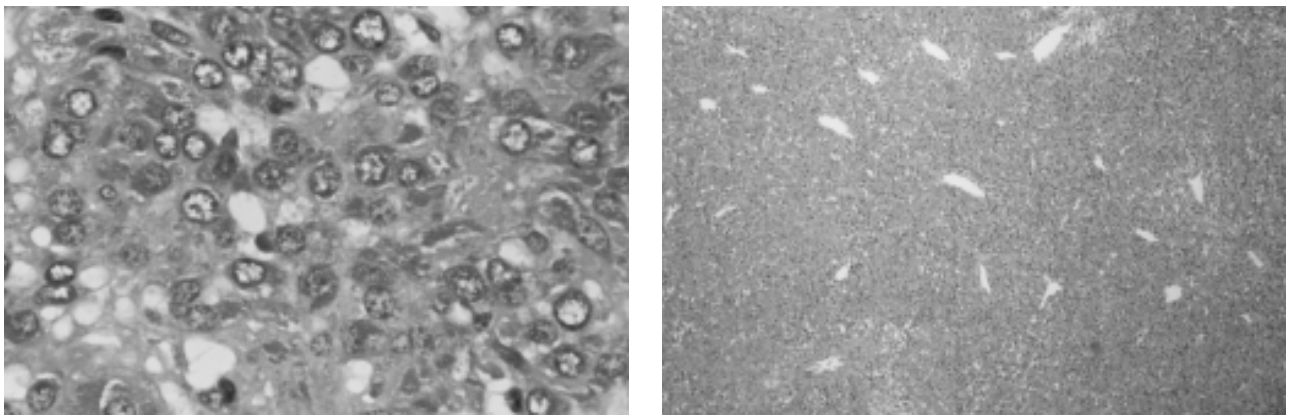

Figure 3 Histology of the tumour with a haemangiopericytic pattern.

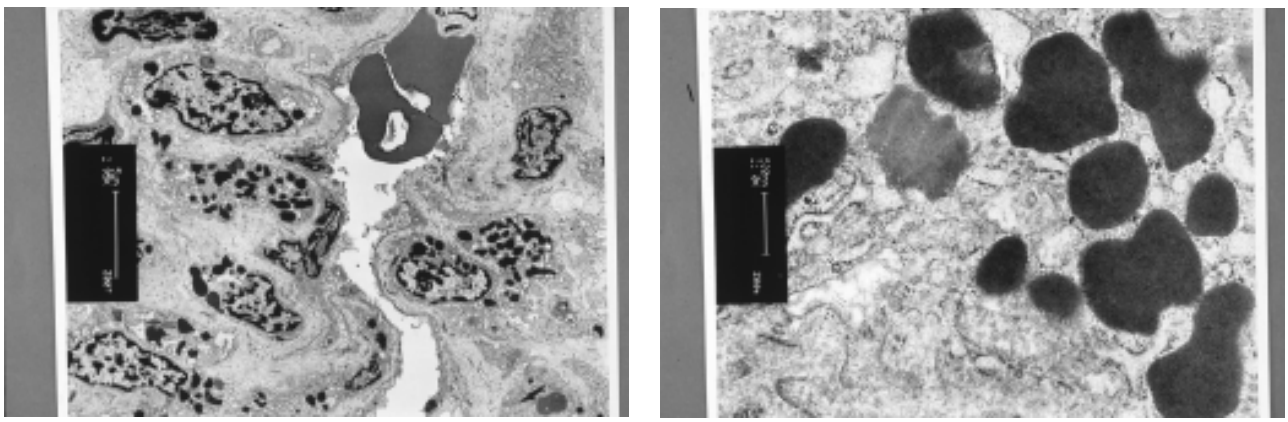

Figure 4 Electron microscopy showed electron dense granules inside the tumour.

plasma renin. Hypertension is usually severe with a mean diastolic pressure of 150 mmHg.[4] Hypertensive retinopathy (up to grade IV) also appears to be common. Comparison of children and adolescents with the adult population showed that the features of JGCT were similar in the two groups except for the average duration of symptoms prior to the diagnosis (2.6 years for the paediatric group vs 6.0 years for the adult group). This is probably because of the practice of more immediate and extensive investigation of hypertension in youth[5] as in our case. Clinical symptoms may be related to hypertension or hypokalaemia and headache is the most frequent presenting symptom. Similar to all forms of hypertension caused by activation of the renin-angiotensin system, angiotensin converting enzyme inhibitors (ACEi) are usually effective in controlling the blood pressure. Calcium channel blockers have also been reported as effective and safe medications for treating this model of pure renin hypertension with the additional advantage of suppressing renin secretion, although the mechanism involved is not understood.[5]

JGCTs tend to be small, solitary and confined to the kidney. They are well circumscribed, cortically located and encapsulated. Histologically, the tumour is composed of polyhedral cells, proliferating solidly or uniformly. Confirmation of the diagnosis depends on the detection of renin secretion or identification of the secretion granules by electron microscopy.[6] The most important and constant routine laboratory finding is hypokalaemia due to secondary hyperaldosteronism associated with an excess of renin. These tumours may release more prorenin because of abnormal processing or storage in the tumoural cells.[7] When patients with JGCT were subjected to acute blockade of the renin-angiotensin system by ACEi, some of them failed to demonstrate the expected rise in plasma renin activity showing an abnormal and autonomous hormonal production. Moreover the tumoural renin secretion may or

may not be regulated by orthostatism.[7] Responses to beta-blockers and vasodilators are also variable. Thus, pharmacological testing is not likely to elicit the diagnosis. There is also no correlation between tumour size and plasma renin activity.[8]

Plasma aldosterone is usually elevated but a normal aldosterone level has been reported which may be due to hypokalaemia of long duration resulting in direct inhibition on aldosterone secretion.[3] Erythrocytosis in our patient may be secondary to an associated elevated serum erythopoietin as reported by Remynse.[9]

Several methods have been suggested for the localisation of these tumours. The first is the demonstration of an elevated plasma renin activity in the renal vein of the affected kidney during selective renin measurement. In most cases, renin lateralization may be difficult and the renin concentration is only slightly elevated on the affected side. In one study by Haab et al, renal vein sampling was only positive in 64% of cases.[10] This may result from the tumour being located at the surface of the kidney and thus most of the venous blood is collected by the pericapsular veins and not drained into the main renal vein. Another possibility is that high levels of angiotensin II found in the arterioles of the tumour affect the vascularization of the tumour.[7] Moreover, antihypertensive treatment with propanolol or captopril may lead to difficulties in the interpretation of renin levels in the renal veins. Frusemide given several days before renin sampling, upright posture as well as segmental renal vein sampling can improve the sensitivity.[10] In our patient, renal vein sampling was not performed as the tumour was large in contrast to those which cannot be visualised by imaging study. The second method of tumour localisation is radiographic visualisation of the tumour. Renal arteriography may reveal a hypovascular cortically located tumour. However, these tumours are usually small, poorly visualised, and located at the surface of the kidney which make their visualisation difficult on angiography. Arteriography is still useful to rule out renal artery stenosis and to demonstrate other vascular tumours, such as renal cell carcinomas which also secrete renin. Besides, arteriography would also provide a renal vascular topography in cases when partial nephrectomy or local excision is to be performed.

Ultrasonography is not sensitive for the diagnosis because of the small size and an echotexture which is similar to the renal cortex. Abdominal CT is helpful to exclude pheochromocytoma. However, in patients with suspected pheochromocytoma, intravenous contrast material may not be used because of the fear of hypertensive crisis. Lack of intravenous contrast limits the CT evaluation of small renal tumours.

Recently, MRI and MRA have proven to be useful as the initial diagnostic test for assessment of adrenal glands (to exclude pheochromocytoma), renal arteries (to exclude renal artery stenosis) and kidneys (to exclude parenchymal lesions) (Figure 5).[11]

The differential diagnoses include renal artery stenosis and other renin secreting tumours, such as, renal cell carcinoma and Wilm's tumour. Wilm's tumours have a peak incidence in children around 2 years old and are large tumours. Renal cell carcinoma in contrast to JGCT is hypervascular and rare in children.

Treatment of JGCT includes total nephrectomy, partial nephrectomy or tumour resection. Perioperatve echography may be necessary to rule out some intraparenchymal tumours. In one study, hypertension recurrence rate is about 12.5% which is the result of hypertension-induced vascular damage. Nephron-sparing surgery is also justified as the tumours are benign with no malignant transformation or local recurrence.[12] The normalisation of plasma renin activity and aldosterone post-operation in our case were indicative of complete tumour resection. In one series by Haab et al with a mean follow-up of 98 months (range 24 to 204), no tumour recurrence was documented.[10] The long term prognosis for this disease is therefore excellent and makes comprehensive investigation for this readily treatable cause of hypertension worthwhile.

References

1. Conn JW, Cohen EL, Lucas CP, et al. Primary reninism. Hypertension, hyperreninemia, and secondary aldosteronism due to renin-producing juxtaglomerular cell tumors. Arch Intern Med 1972;130:682-96.
2. Ren G, Yu X, Li Y, Shi S, Wang L, Ye H. Juxtaglomerular cell tumor of the kidney: a clinicopathological analysis of five cases. Chin Med J (Engl) 2003;116:1789-92.
3. Dennis RL, McDougal WS, Glick AD, MacDonell RC Jr. Juxtaglomerular cell tumor of the kidney. J Urol 1985;134:334-8.
4. Squires JP, Ulbright TM, DeSchryver-Kecskemeti K, Engleman W. Juxtaglomerular cell tumor of the kidney. Cancer 1984;53: 516-23.
5. McVicar M, Carman C, Chandra M, Abbi RJ, Teichberg S, Kahn E. Hypertension secondary to renin-secreting juxtaglomerular cell tumor: case report and review of 38 cases. Pediatr Nephrol 1993;7:404-12.
6. Hasegawa A, Iwasaki T. Rhomboid secretion granules in a juxtaglomerular cell tumour of the kidney. Br J Urol 1997;79: 296-7.

7. Corvol P, Pinet F, Galen FX, et al. Seven lessons from seven renin secreting tumors. Kidney Int Suppl 1988;25: S38-44.
8. Brown JJ, Fraser R, Lever AF, et al. Hypertension and secondary hyperaldosteronism associated with a renin-secreting renal juxtaglomerular-cell tumour. Lancet 1973;2:1228-32.
9. Remynse LC, Begun FP, Jacobs SC, Lawson RK. Juxtaglomerular cell tumor with elevation of serum erythropoietin. J Urol 1989;142:1560-2.
10. Haab F, Duclos JM, Guyenne T, Plouin PF, Corvol P. Renin secreting tumors: diagnosis, conservative surgical approach and long-term results. J Urol 1995;153:1781-4.
11. Agrawal R, Jafri SZ, Gibson DP, Bis KG, Ali-Reza. Juxtaglomerular cell tumor: MR findings. J Comput Assist Tomogr 1995;19:140-2.
12. Mete UK, Niranjan J, Kusum J, Rajesh LS, Goswami AK, Sharma SK. Reninoma treated with nephron-sparing surgery. Urology 2003;61:1259.

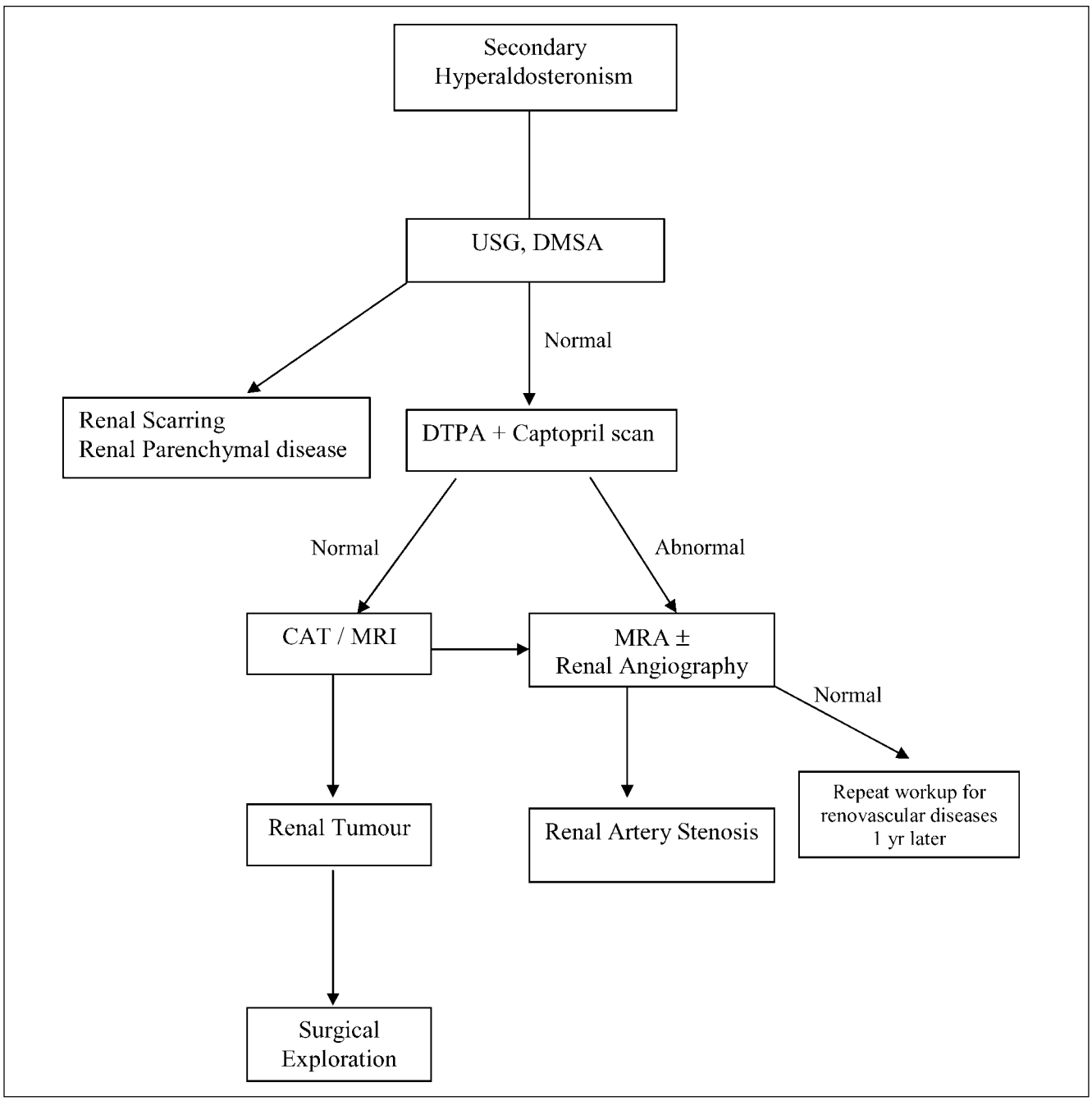

Figure 5 Outlines the logistic approach to the diagnosis of JGCT.