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Resistant Hypertension in a Patient with "Incidental" Renal Artery Stenosis

Dr. Pyara Masiha Topno (MD. Medicine)
Dr. Thakurmani (MD. Medicine)
Central Hospital Dhanbad

Renal artery stenosis is considered to be one of the more frequent causes of secondary arterial hypertension. Through its progression renal artery stenosis can cause renal insufficiency, uncontrolled hypertension, and increased cardiovascular morbidity.
Renal Artery Stenosis is general term that refers to any vascular lesion causing narrowing of the renal artery thereby impairing blood flow to the kidney. This disease encompasses a broad range of pathophysiologies, the two most common being fibromuscular dysplasia (FMD) and atherosclerotic vascular disease. It is associated with three major clinical syndromes: ischemic nephropathy, hypertension, and destabilizing cardiac syndromes. However, a diagnosis of RAS may also result from an incidental finding in an otherwise asymptomatic patient.

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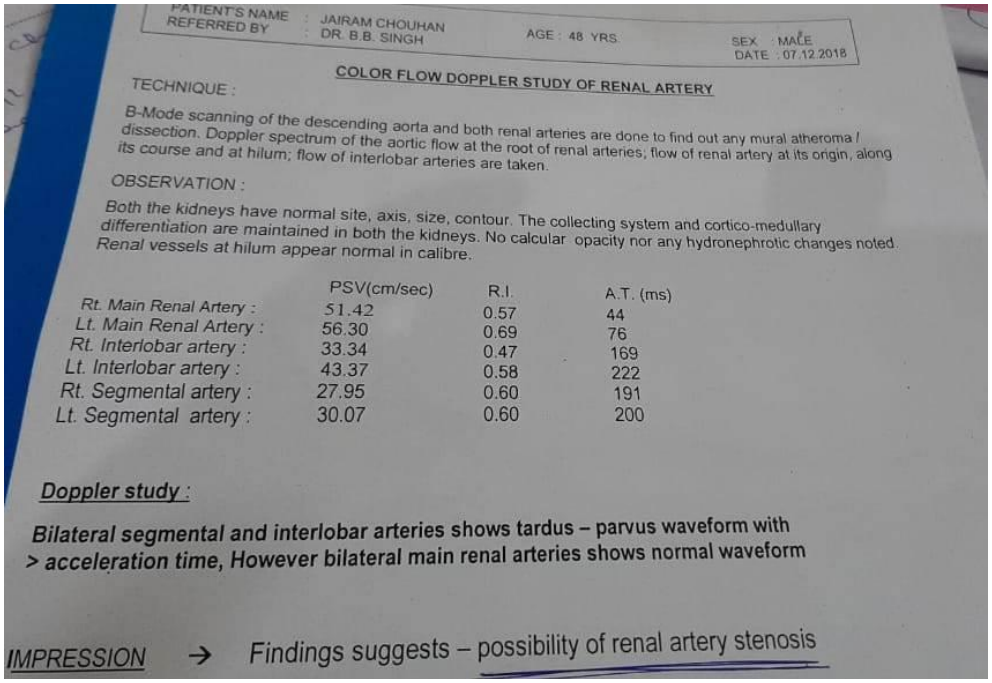
I. Case Study

Patient 48 years old male was admitted in Central Hospital dhanbad with complains of headache , giddiness and vomiting since ten days . There was no previous history of hypertension, diabetes mellitus or any other illness. He was employee of coal mines .On examination patient was conscious well oriented to time place and person , with no focal neurological deficit. Pulse was 88/minute regular fair volume , blood pressure was 210/110 mm of Hg. There was clear chest with bronchovesicular breath sound, Heart sound was normal , there was no murmur .There was no Organomegaly or any bruit during per abdomen examination. Lab investigation suggests Hb 13 gm/gl TLC 11,000/cmm,blood urea 19 mg/dl, serum creatinine 0.9 mg/dl , serum bilirubin 0.7 mg/dl. His USG Abdomen shows early fatty change in liver with Benign Prostate Hypertrophy Grade 1. His CT Scan Brain reports shows bilateral periventricular lacunar infarcts . His X-ray cervical spine shows degerative changes of spine. His ECG was normal. Patient received 60 mg Nifedepine, 10 mg Torsemide , and Arkamine six hourly to achieve blood pressure with in normal range. After that patient under went for Doppler studies which revealed there was narrowing of renal vessels.



PATIENT'S NAME : JAIRAM CHOUHAN
REFERRED BY : DR. B.B. SINGH
AGE : 48 YRS.
SEX : MALE
DATE : 07.12.2018

COLOR FLOW DOPPLER STUDY OF RENAL ARTERY

TECHNIQUE :

B-Mode scanning of the descending aorta and both renal arteries are done to find out any mural atheroma / dissection. Doppler spectrum of the aortic flow at the root of renal arteries; flow of renal artery at its origin, along its course and at hilum; flow of interlobar arteries are taken.

OBSERVATION :

Both the kidneys have normal site, axis, size, contour. The collecting system and cortico-medullary differentiation are maintained in both the kidneys. No calcular opacity nor any hydronephrotic changes noted. Renal vessels at hilum appear normal in calibre.

	PSV(cm/sec)	R.I.	A.T. (ms)
Rt. Main Renal Artery :	51.42	0.57	44
Lt. Main Renal Artery :	56.30	0.69	76
Rt. Interlobar artery :	33.34	0.47	169
Lt. Interlobar artery :	43.37	0.58	222
Rt. Segmental artery :	27.95	0.60	191
Lt. Segmental artery :	30.07	0.60	200

Doppler study :

Bilateral segmental and interlobar arteries shows tardus – parvus waveform with > acceleration time, However bilateral main renal arteries shows normal waveform

IMPRESSION → Findings suggests – possibility of renal artery stenosis

The prevalence of renal artery stenosis is probably less than 1% of patients with mild hypertension but can increase to as high as 10 % to 40% in patients with acute (even if superimposed on a preexisting elevation in blood pressure), severe, or refractory hypertension. Several studies report the prevalence of unilateral stenosis (compared with bilateral stenosis) approximately from 53 % to 80%.

Studies suggest that ischemic nephropathy may of 5% to 22% of advanced renal disease in all patients older than 50 years. Patients with fibromuscular dysplasia have involvement of the renal arteries in proximately 75% to 80% of cases. Roughly two-thirds of patients have involvement of multiple renal arteries. Fibromuscular dysplasia is more common in females than in males.

II. Discussion

Renal artery stenosis (RAS) is the narrowing of one or both renal arteries. "Renal" means "kidney" and "stenosis" means "narrowing." The renal arteries are blood vessels that carry blood to the kidneys from the aorta—the main blood vessel that carries blood from the heart to arteries throughout the body. This disease encompasses a broad range of pathophysiologies, the two most common being fibromuscular dysplasia (FMD) and atherosclerotic renal artery disease. RAS is associated with three major clinical syndromes: ischemic nephropathy, hypertension, and destabilizing cardiac syndromes. There are two major causes of unilateral renal artery stenosis (RAS):

- Atherosclerosis (60% to 90%): RAS is primarily caused by a buildup of fatty substances and cholesterol (atherosclerosis) in the renal arteries. These substances harden as they accumulate in the arterial walls. This not only narrows the arteries, but it also decreases overall blood flow .Atherosclerosis primarily affects patients (men over the age of 45 years) and usually involves the aortic orifice or the proximal 2 cm of the main renal artery. This disorder is particularly common in patients who have atherosclerosis, however, can also occur as a relatively isolated renal lesion. Any of the multiple renal arteries (occurring in 14% to 28%) may be affected. Risk factors for atherosclerosis include dyslipidemia, cigarette smoking, viral infection, immune injury, and increased homocysteine levels.
- Fibromuscular dysplasia (10% to 30%): In contrast to atherosclerosis, fibromuscular dysplasia most often affects women younger than the age of 50 years and typically involves the middle and distal main renal artery or the intrarenal branches.

Other less common causes (less than 10%) include thromboembolic disease, arterial dissection, infrarenal aortic aneurysm, vasculitis (Takayasu arteritis, Buerger disease, polyarteritis nodosa, post radiation), neurofibromatosis type 1, retroperitoneal fibrosis. Other risk factors for renal artery stenosis are similar to those of other forms of atherosclerosis. These include:

- A diet high in fat, sodium, and sugar
- Diabetes
- High cholesterol
- family history of heart disease
- sedentary lifestyle, or a lack of exercise
- Obesity

Smoking

Renal Artery Stenosis is a common cause of secondary hypertension. Though likely an oversimplification of a more complex pathophysiology, the mechanism leading to the development of renovascular hypertension is typically classified as either renin-dependent or primarily a result of volume overload. This theory dates back to the 1930s, when Goldblatt et al performed a series of studies examining the impact of unilateral and bilateral RAS (BRAS) on blood pressure. By clamping renal arteries in dogs, Goldblatt et al demonstrated a systemic pressor effect. They postulated that this effect was due to a substance produced by the kidneys causing vasoconstriction. The substance was ultimately isolated and identified as the proteolytic enzyme now known as renin. Renin is an early effector in the larger renin angiotensin aldosterone neurohormonal cascade. When ischemia occurs downstream of a stenotic renal artery, renin is released from juxtaglomerular cells. Renin then cleaves angiotensinogen to form angiotensin I, which must be further processed to angiotensin II by angiotensin-converting enzyme (ACE) produced in the lung endothelium and vasculature. Angiotensin II is the active enzyme and has multiple downstream effects. Angiotensin-II-mediated vasoconstriction causes hypertension, leading to pressure diuresis of the unaffected kidney. Glomerular filtration rate (GFR) is increased via vasoconstriction of the efferent arteriole. Antidiuretic hormone is released from the posterior pituitary gland, causing water conservation, further contributing to pressure diuresis. Release of aldosterone from the adrenal glands enhances exchange of sodium in the nephron-promoting volume retention. In addition, angiotensin increases sympathetic tone. The mechanism behind BRAS or unilateral RAS with a solitary kidney is due to extracellular fluid overload secondary to decreased diuresis rather than a renin-mediated mechanism. Ischemic nephropathy can be defined as an obstruction causing decreased perfusion

leading to renal ischemia and subsequent excretory dysfunction. The cause of ischemic nephropathy has not been fully elucidated. However, several interrelated mechanisms have been proposed explaining how a hemodynamically significant lesion ultimately results in interstitial fibrosis. By one pathway, recurrent local ischemia causes tubulointerstitial injury and microvascular damage.

RAS may either cause or exacerbate cardiac destabilizing syndromes, including unstable angina (UA) and congestive heart failure characterized by flash pulmonary edema. RAS precipitates these conditions through three general mechanisms: volume overload, peripheral arterial vasoconstriction, and direct effects of angiotensin on the myocardium. Flash pulmonary edema can be described as a specific presentation of acute decompensated heart failure characterized by rapid fluid accumulation within the lungs. Flash pulmonary edema can occur secondary to several conditions, all of which result from an acute increase in end diastolic left ventricular pressure. Flash pulmonary edema does occur in unilateral RAS, but tends to occur more often in patients with BRAS. In BRAS, the mechanism can be explained by impaired natriuresis and thus, a propensity for volume overload. This phenomenon was first reported by Pickering et al in 1988 in a case series of eleven hypertensive patients with BRAS and recurrent pulmonary edema.UA is defined as pain due to cardiac ischemia that is new in onset or is increasing in frequency or intensity. The prototypical cause of UA is atherosclerosis and plaque rupture. RAS, however, may contribute to UA via an acute angiotensin-mediated increase in afterload. Increased left ventricular workload leads to increased oxygen demand, resulting in myocardial ischemia.

EPIDIMIOLOGY

The prevalence of renal artery stenosis is probably less than 1% of patients with mild hypertension but can increase to as high as 10 % to 40% in patients with acute (even if superimposed on a preexisting elevation in blood pressure), severe, or refractory hypertension. Several studies report the prevalence of unilateral stenosis (compared with bilateral stenosis) approximately from 53 % to 80%.

Studies suggest that ischemic nephropathy may of 5% to 22% of advanced renal disease in all patients older than 50 years. Patients with fibromuscular dysplasia have involvement of the renal arteries in proximately 75% to 80% of cases. Roughly two-thirds of patients have involvement of multiple renal arteries. Fibromuscular dysplasia is more common in females than in males. Although hemodynamically significant renal-artery stenosis may result in refractory hypertension and end-stage kidney failure, these outcomes are uncommon in patients with atherosclerotic renal-artery stenosis that is treated medically .

Symptoms

Renal artery stenosis often doesn't cause any signs or symptoms until it's advanced. The condition may be discovered incidentally during testing for something else. There are certain situations which gives a clue regarding underlying cause.

- High blood pressure that begins suddenly or worsens without explanation
- High blood pressure that begins before age 30 or after age 50

As renal artery stenosis progresses, other signs and symptoms may include:

- High blood pressure that's hard to control
- A whooshing sound as blood flows through a narrowed vessel (bruit), which is hear by a clinician through a stethoscope placed over kidneys .
- Elevated protein levels in the urine or other signs of abnormal kidney function
- Worsening kidney function during treatment for high blood pressure
- Fluid overload and swelling in body's tissues
- Treatment-resistant heart failure

EVALUATION

The presence of chronic kidney disease, advanced age, and other atherosclerotic risk factors is associated with an increased prevalence of atherosclerotic renal-artery stenosis; however, these characteristics are also common in patients with essential hypertension. The classic clinical clues that suggest the diagnosis of renal-artery stenosis include the onset of stage 2 hypertension (blood pressure >160/100 mm Hg) after 50 years of age or in the absence of a family history of hypertension, hypertension associated with renal insufficiency (especially if renal function worsens after the administration of an agent that blocks the renin–angiotensin–aldosterone system), hypertension with repeated hospital admissions for heart failure, and drug-resistant hypertension (defined as blood pressure above the goal despite treatment with at least three drugs of different classes at optimal doses).

Once renal-artery stenosis is suspected, confirmation of the diagnosis is typically made by means of imaging , since biochemical tests such as the measurement of plasma renin concentrations lack specificity.

Doppler ultrasonography is an excellent tool because it is noninvasive and has no apparent side effects. Doppler measurement of renal-artery velocity provides a functional assessment of the severity of stenosis; higher velocity correlates with a greater pressure differential across the stenosis . However, duplex imaging is limited by abdominal obesity or bowel gas, is technically demanding, and is not available at all centers.

1 Alternative methods include MRA and computed tomographic angiography (CTA) with the use of high-resolution multislice detector devices. These techniques can provide elegant images of the renal arteries and the abdominal aorta and can show images in multiple planes to enhance clarity . However, equipment, technique, and reconstruction of the images may affect image quality, as can patient-related factors, including the presence of calcium, the presence of stents, and the ability to hold one's breath during imaging. In patients with chronic kidney disease, the use of MRA and CTA is limited by toxicity of the contrast medium: nephrogenic systemic fibrosis is associated with gadolinium, and nephropathy is associated with iodinated contrast dye. In experienced centers, high-quality digital-subtraction angiography with or without selective renal angiography may be performed with the use of small-diameter high-quality digital-subtraction angiography with or without selective renal angiography may be performed with the use of small-diameter catheters and minimal amounts of contrast material in order to reduce the risk of vascular complications and contrast nephropathy .

TREATMENT

Treatment for RAS depends on a combination of medications and lifestyle changes. Certain medical procedures may also be necessary.

Medications

One of the first ways to treat this condition is with medications. These medications to help relax blood vessels so they don't narrow. Options include:

- Angiotensin II receptor blockers (ARBs)
- Calcium channel blockers
- Angiotensin converting enzyme (ACE) inhibitors

Alpha-beta-blockers and beta-blockers can also help by decreasing blood vessel dilation. Patients may also be asked to take other medications, such as lipid lowering agents and aspirin. All patients with ARAS should receive anti-platelet agents as they reduce morbidity and mortality in cardiovascular disease. Dyslipidemia is often present in patients with ARAS, although the severity does not predict the progression of ARAS . There are no studies specifically reporting the use of statins in ARAS, although their benefit in improving cardiovascular outcome in high-risk patients is well-established. Reports indicate that aggressive lipid reduction may lead to regression of atherosclerotic disease, also in the renal arteries . In addition to lowering lipids, statins are anti-inflammatory and stabilize atherosclerotic plaques.

Many patients with renovascular disease is candidate for ACE inhibitor and/or angiotensin receptor blockade (ARB). Clinical data suggest that survival of patients with RVH is better when ACE inhibitors are part of therapy than when they are not . ARBs can be used safely in patients at risk of ARAS. No patient developed oliguric renal failure and Cr levels returned to baseline after stopping the drug . However, concurrent diuretic therapy should be initially avoided. In low doses and without diuretics, captopril has never been reported to induce functional acute renal failure . The drug should be stopped, however, if there is >20% rise in Cr levels and such patients should be considered for revascularisation. . In bilateral disease or stenosis of a single kidney, specific caution is recommended with ACE inhibitors, as renal function can be compromised due to dilatory drug effect on the efferent arterioles. This can reduce the capillary pressure within the glomerulus to below the critical perfusion pressure and acute renal failure can occur 1 to 14 days after the initiation of treatment with ACE inhibitors.

In bilateral disease or stenosis Calcium-channel blockers, which maintain renal perfusion by reducing afferent arteriolar tone and beta-blockers by lowering renin, are also established options for patients with renovascular disease .

For a small number of people, an intervention such as angioplasty, often with stenting or surgery, may be recommended. With angioplasty, a catheter is inserted into body through a blood vessel and guided to the narrowed or blocked renal artery. A balloon on catheter is then inflated to open up the inside of artery. A stent can be placed to keep the area open.Surgery to bypass

The narrowed or blocked portion of artery and /or remove a non functioning kidney may be needed for some patients. But this procedure is not often done.

Percutaneous transluminal renal angioplasty(PTRA)

PTRA with or without stenting is a widely accepted treatment for RAS. In most series, about 30% of the patients show an improvement in renal function after PTRA with or without stenting, with the remainder equally divided between no improvement and deterioration.

Unfortunately, details about methods of measuring BP, length of follow-up, and medication dosage and class vary widely between studies, as has been reviewed . Leertouwer et al. reported that after angioplasty, BP control improved in up to 49% of patients . Several studies indicate that hypertension is only rarely cured in patients with ARAS, while improvement occurs in <10% to 75% of patients. Little or no change in either BP control or medication requirements has been reported in 30% (range 0% to 54%) of the treated patients . Overall, BP changes commonly approach a reduction of 25/10 mm Hg .

STENTING

Endovascular stents have been recommended for failed PTRA (unsatisfactory results or complications) and for treatment of restenotic lesions.

The success and patency rates were significantly higher with stenting than with PTRA alone. However, renal function and BP were stable or unchanged in both groups at 6-month follow-up, with no significant difference between the PTRA and stent groups. . There are also data suggesting that angioplasty and stenting are associated with a reduction in cardiovascular mortality

III. Conclusion And Recommendation

A diagnosis of renal-artery stenosis should be considered in any patient with a history of severe or resistant hypertension, hypertension that is associated with renal insufficiency, or disease in other vascular beds. Initial examination should include measurement of kidney function and a lipid profile. An anatomical diagnosis may be made with the use of duplex ultrasonography; if high-quality duplex imaging is not available, then CTA or MRA may be appropriate. In patients with atherosclerotic renal-artery stenosis, such as the patient in the vignette, intensive medical therapy, including tight control of blood pressure with a regimen that includes a blocker of the renin–angiotensin–aldosterone system, is appropriate. Levels of serum creatinine and potassium should be closely monitored when such treatment is initiated and if the dose is increased. Administration of an antiplatelet agent and a statin and treatment of diabetes and chronic kidney disease, if present, with treatment aimed at currently recommended targets are also recommended. The role of revascularization in the treatment of atherosclerotic renal-artery stenosis is controversial. Since available data from randomized trials have not shown a benefit of revascularization over medical therapy, revascularization should be reserved for patients in whom aggressive medical therapy has failed and for patients who are participating in clinical trials.

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