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Review Article

Ischemic nephropathy

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ABSTRACT

Renovascular disease is an entity which leads to hypertension as well as to ischemic nephropathy if the gradual process continues unabated. It may be discovered incidentally in an asymptomatic individual during imaging studies and more frequently due to its associated aftermath like accelerated hypertension and on workup of unexplained chronic kidney disease. Various advanced diagnostic modalities aid in diagnosis of this entity with their merits and associated limitations. Strategies to manage include mainly medical management and revascularization as per recommendations and where indications exist.

1. Introduction

Hypertension may be considered as the level of blood pressure at which treatment instituted to lower it results in major reductions in clinical morbidities and mortalities. Amongst the various clinical entities responsible for secondary hypertension, renovascular disease holds significant position. Renovascular disease includes in its realm renal artery stenosis caused by atherosclerosis, arteritis, fibro muscular dysplasia, extrinsic compression of renal artery. Renovascular disease associated hypertension accounts for 5% of all hypertensive patients.[1]

Renal artery stenosis is conventionally ascribed to narrowing of the lumen of main renal artery by 50–70% with critical stenosis attributed to more than 70% narrowing. Various entities which lead to renal artery stenosis are outlined in Table 1. Renovascular hypertension arises due to coexistent renal artery stenosis with renin dependent hypertension in unilateral disease whereas hypervolemia associated hypertension in bilateral renal artery stenosis. When the progressive lesion leads to significant hemodynamic compromise, it leads to ischemic nephropathy.

Hence, ischemic nephropathy is a clinical entity arising from hemodynamically significant renal artery stenosis leading to significant decline in glomerular filtration rate with involvement of major functional renal parenchyma. It is also referred to as azotemic renal vascular occlusive disease, chronic ischemic renal disease.[2,3]

Fibro muscular dysplasia is a non-inflammatory lesion involving the arterial wall structure with multiple lesions affecting the distal part of renal artery. The affected individuals mainly pertain to younger age group with female preponderance. It mainly manifests in the tunica media of the artery which assumes clinical significance when it leads to critical narrowing of renal artery causing hypertension in a young female. It leads to renal artery stenosis, renovascular hypertension but ischemic nephropathy is not the frequent outcome of this disease as hypertension in young is usually

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Table 1 – Causes of renal artery stenosis.

1. Atherosclerosis
2. Fibro muscular dysplasia
3. Vasculitis (e.g.Takayasu's arteritis)
4. Radiation exposure
5. Extrinsic compression of renal artery

worked up aggressively, diagnosed effectively with available modalities and above all therapeutically gratifying by renal artery angioplasty. Similarly, Takayasu's arteritis is a vasculitis which involves the renal artery, clinically manifesting as accelerated hypertension usually in a young female presenting with visual complaints, cerebrovascular lesion, and renal insufficiency.

Atherovascular disease is the major cause of renal artery stenosis leading to ischemic nephropathy. It involves mainly the ostial segment of the renal artery which may be an extension of the aortic plaque in the descending aorta. The lesion may manifest unilaterally or in bilateral manner; similarly it can affect renal artery perfusing a solitary kidney. This review mainly deals with the atherovascular renal artery disease as the main prototype commonly leading to varied manifestations of ischemic nephropathy.

2. Prevalence

Renal artery stenosis is not synonymous with renovascular hypertension as evidenced by several autopsy series.[4,5] It was also found out that 49% of normotensive and 77% of hypertensive patients have evidence of moderate to severe stenosis.[4] The prevalence in form of elucidation of gross pathologic lesions in renal artery increases with age. In autopsy series, it is fairly less common below 60 years, 20% in age group 65–74 years and approximately 40% in >75 years age group. The prevalence is 10–40% in patients with coronary artery disease, aorto-iliac disease and >40% in patients with peripheral vascular disease. These pathologic al lesions assume relevance in terms with ischemic nephropathy when they are hemodynamically significant. The prevalence of ischemic nephropathy is not precisely available and is usually correlated with atherovascular lesions in renal artery with decline in glomerular filtration rate in the kidney with concomitant extrarenal atherosclerotic lesions. Atherovascular renal artery stenosis which gradually affects the functioning kidney(s) can lead to end stage kidney disease due to hemodynamic compromise in 5–20% cases of advanced renal failure in individuals in age group more than 50 years.[6]

3. Presentation

The usual presentation is an elderly individual with resistant/uncontrolled hypertension, exacerbation of previously controlled raised blood pressure with renal insufficiency, frequent episodes of symptoms suggestive of congestive heart failure (Table 2). The coexistent morbidities include diabetes mellitus, extrarenal atherosclerotic lesions viz. coronary artery disease, cerebrovascular disease, peripheral vascular disease with dyslipidemia and history of smoking. They are otherwise detected during routine coronary angiograms, during workup of acute rise of serum creatinine when initiated on angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARB). On routine coronary angiograms, the aortic phase of angiogram may reveal 5% patients with >75% stenosis. In these patients, the 4-year survival is 60% which is mainly on account of coronary artery disease whereas 90% 4-year survival rate if no renal artery stenosis is evident. These patients usually die from coronary artery disease before they reach end stage kidney disease or need maintenance hemodialysis. In a study it was found that if serum creatinine is 2 mg% at presentation, the 2-year survival rate is 40% with event rate of 1/3 died at the end of 2 years, 1/3 had recurrent admissions due to congestive heart failure, 30% had stroke. It is estimated that 27% patients develop ESRD within 6 years.[7]

Table 2 – Clinical clues in the diagnosis of renal artery stenosis.

1. Onset of hypertension before age 30 years or severe hypertension after age 55 years.
2. Accelerated, resistant, or malignant hypertension.
3. Development of new azotemia or worsening renal function after administration of ACEI/ARB.
4. Unexplained atrophic kidney or size discrepancy >1.5 cm between kidneys.
5. Sudden, unexplained pulmonary edema.
6. Unexplained renal dysfunction including patient starting renal replacement therapy.
7. Multivessel coronary artery disease or peripheral arterial disease.
8. Unexplained congestive heart failure.
9. Refractory angina.

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4. Pathogenesis

In the milieu of atherovascular risk factors, the typical lesion involves the ostia of renal vessels gradually compromising the renal blood flow which initiates autoregulatory mechanism in the kidney and development of collateral circulation derived from lumbar, suprarenal arteries which compensates for decreased renal flow. Further decrease in renal blood flow leads to steep decline in GFR when renal artery is narrowed by 70–80% (critical stenosis).[8,9]

In unilateral renal artery stenosis which is similar to Goldblatt two kidney one clip model, there is persistent activation of renin-angiotensin system (RAS) leading to increased Angiotensin II and aldosterone levels with resultant pressure natriuresis from the non stenotic kidney with no volume retention. The hypertension in this condition is thus renin-angiotensin system dependent. Whereas, in bilateral renal artery stenosis or single kidney with renal artery stenosis, the initial RAS activation leads to volume retention, eventually leading to decreased RAS activity and persistently elevated blood pressure. These patients do not have persistent RAS blockade and may not respond to antihypertensive effects of ACEI/ARB.[10]