

Atheroembolic Renal Disease

The term renovascular disease refers to vascular complications involving renal arteries and veins that affect the blood circulation leading to high blood pressure and damage to the kidneys. These include renal artery stenosis (luminal narrowing of an artery to the kidneys due to atherosclerosis, fibromuscular dysplasia, Takayasu's arteritis), renal artery thrombosis (formation of a clot in a renal artery that may occur due to infection, trauma, renal cell cancer, inflammatory disease, or fibromuscular dysplasia), renal artery aneurysm (bulging, weakened area in the wall of an artery to the kidney as a result of a congenital weakness or trauma to the arterial wall, fibromuscular dysplasia, or atherosclerosis), Renal vein thrombosis (formation of a clot in a renal vein due to trauma, nephrotic syndrome, pregnancy, steroid medications, or oral contraceptives), and atheroembolic renal disease (AERD).

AERD (also known as cholesterol atheroembolic renal disease, atheroembolism or cholesterol crystal embolization) is a multisystemic renovascular disease defined as renal failure occurring secondary to renal artery, arterioles, or glomerular capillary occlusion by atherosclerotic plaque rupture and embolization (releasing cholesterol crystals) distally from aorta and/or other major arteries into the small renal arteries.^[1] Kidney is commonly involved because of proximity of renal arteries to the abdominal aorta and its enormous blood supply. Embolization also affects other organs, such as the skin, gastrointestinal system, muscle, eyes, and brain.

Predisposing risk factors for AERD include atherosclerosis, smoking, hypertension, DM, and/or hypercholesterolemia, trauma, invasive vascular procedure involving the aorta such as aortic angiography, coronary angiography, cardiac catheterization, and cardiovascular surgery; may also occur spontaneously.^[2] Male patients older than 50 years are more commonly affected. AERD can also occur following thrombolytic therapy and/or anticoagulant therapy because it can interfere with the healing of ulcerated atheromatous plaques, however anticoagulant induced AERD is uncommon.^[3]

Because of the multiple organ involvement, clinical characteristics of AERD are extremely variable and may lead to renal, cutaneous, gastrointestinal, neurologic, and ophthalmic manifestations [Table 1].^[1,4,5] After an inciting event, most common clinical presentation is subacute kidney injury for several weeks or more (renal dysfunction occurs in staircase pattern). Less commonly acute kidney injury may be occurred within 1-2 weeks after an inciting event.

Following obstruction, eosinophilic and neutrophilic infiltration occurs and secrete various inflammatory and vasospastic mediators. Laboratory findings include

Table 1: Clinical and laboratory features of atheroembolic renal disease

System	Manifestation
General	Fever
	Weight loss
Renal	Myalgia
	Acute kidney injury
	Hematuria
	Nephritic range proteinuria
Cutaneous	Severe hypertension
	Livedo reticularis-purplish rash over the lower extremities and abdominal wall
	Digital mottling and nail pulp infarcts, Purple toes, Gangrene of toes
Nervous system	Fugax
	Headache
	Transient ischemic attack
	Cerebrovascular accidents
	Sudden onset paraparesis
	Mental confusion
Gastrointestinal	Mononeuropathy
	Anorexia
	Vomiting
	Nonspecific abdominal pain
	Gastrointestinal hemorrhage
	Intestinal ischemia
	Occult or frank blood loss
	Bowel infarction and perforation
Acute pancreatitis	
Ophthalmic	Abnormal liver enzymes
	Occlusion of retinal arteries leading to retinal infarction (Hollenhorst sign)

eosinophilia, C3 hypocomplementemia (commonly occur during the acute phase) reflecting immunologic activation at exposed atheroembolic surface, increased serum cholesterol, C-reactive protein, and ESR. The urinalysis is benign with hematuria, few red cells, or casts. Proteinuria is routinely not a prominent features; however, nephrotic-range proteinuria has been reported.^[6] In acute renal insufficiency, eosinophiluria may indicate AERD in addition to the other known causes.^[7]

Renal or skin biopsy seems to be a reliable definitive method for diagnosis (the procedure has some limitations as typical lesion, i.e. blockage usually is focal). However, a tissue biopsy is not necessary in patients with iatrogenic AERD presenting with the classical clinical features include

precipitating event (aortic or coronary angiography), subacute or acute kidney injury, typical skin findings such as blue toe syndrome and/or livedo reticularis and/or presence of retinal cholesterol crystal emboli (Hollenhorst plaques). Thus, like histology, fundoscopic examination should not be omitted that may confirm the diagnosis.

Patients with AERD have very poor overall prognosis with reported mortality of 64--81%.^[8] Mortality is usually due to multiorgan failure secondary to ischemia. The prognosis is depended on the severity of underlying disease, number of risk factors, and size of emboli.

There is no specific treatment for the existing vascular lesions. Treatment modality is supportive and all patients should be aggressively managed for secondary prevention of cardiovascular disease risk factors. In addition to the lipid lowering agents---statins, the treatment should include blood pressure control, glycemic control in diabetes patients, and cessation of smoking.

In the last issue of IJN^[9], Jansi *et al.* presented a biopsy proven retrospective case series of eight patients with AERD (male:female, 7:1, mean age >60 years) from a single center. Seven patients were older than 50 years and three patients did not have any predisposing factors for AERD. Seven patients (87.5%) were known hypertensives, three patients were diabetic (37.5%), four patients (50%) were chronic smokers. They performed simultaneously coronary angiogram in three patients and treated with thrombolytics. CAD and LV dysfunction was seen in three patients. All patients presented rapidly worsening of renal function or acute on CKD and three patients had flash pulmonary edema. Serum cholesterol was elevated in all the eight patients and high ESR was seen in 75% cases. Eosinophilia was present in three cases (37.5%); however, eosinophiluria was not measured in all cases. Overall prognosis was poor with mortality of 25% due to the underlying disease. Since this is a single center study of a single digit cases, it may not truly reflect disease characteristics. More studies are required to characterize the true epidemiological nature of the entity.

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