Severe bilateral renal artery stenosis after transluminal radiofrequency ablation of renal sympathetic nerve plexus

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Percutaneous renal sympathetic denervation is an evolving therapy for resistant hypertension. Evidence to date demonstrates a reduction of blood pressure in the short term to medium term. Reported complications relate to problems with vascular access vessels and dissection of the renal artery. Renal artery stenosis has not been described in the literature. We present a patient with hypertensive crisis, flash pulmonary edema, and deterioration of renal function, secondary to bilateral renal artery stenosis, 9 months after renal sympathetic radiofrequency ablation denervation. (J Vasc Surg 2015;62:222-5.)

Chronic hyperstimulation of renal sympathetic nerves has been postulated as a cause of resistant hypertension,[1] defined as elevated blood pressure persisting despite concurrent use of three or more antihypertensive agents of different classes (one of which is a diuretic) prescribed at optimal doses.[2] Renal sympathetic nerve fibers in the outer tunica media and tunica adventitia[3] have consequently been identified as a therapeutic target. Their destruction is thought to decrease the afferent sympathetic signals from the kidney to the brain as well as the efferent signals from the brain to the kidney, thus reducing sympathetic activation, vasoconstriction, and activation of the renin-angiotensin system.[4]

Initial approaches targeting sympathetic nerves involved nonselective surgical sympathectomy,[5] with significant associated adverse effects. Minimally invasive techniques of targeting the renal sympathetic nerves have been developed, including intraluminal denervation by radiofrequency ablation (RFA),[6,7] extracorporeal denervation by high-intensity focused ultrasound,[8] or computed tomography-guided or magnetic resonance-guided chemical denervation with agents like ethanol[9] or vincristine[10,11] in an effort to reduce associated surgical morbidity.

Several types of RFA devices are currently used for transluminal renal artery denervation (RDN). The two most common devices are the Symplicity Renal Denervation System (Medtronic Inc, Plainfield, Ind), and the EnlighHTN Renal Denervation System (St. Jude Medical Inc, St. Paul, Minn). These devices deliver controlled, low-power RF energy to the arterial walls where these nerves are located.

RFA uses high-frequency alternating current generating a thermal energy source. This heats tissue to a prespecified temperature, altering its protein structure. The volume of tissue destroyed depends on the temperature distribution of the RFA-treated lesion. RFA is an established therapy for percutaneous ablation of tumors,[4] treatment of cardiac arrhythmias,[5] and treatment of varicose veins.[6]

Current evidence demonstrates that patients undergoing RDN with RFA have an observed decrease in blood pressure.[6,12-16] Although renal artery stenosis has been described as a potential complication, it has not been reported to date. We report a patient with severe bilateral renal artery stenosis that occurred as a consequence of transluminal RDN using RFA.

CASE REPORT

A 51-year-old woman was referred to our institution with severe hypertension (blood pressure, 225/110 mm Hg despite seven antihypertensive agents), multiple episodes of flash pulmonary edema, and acute renal failure (serum creatinine, 3050 mg/dL; estimated glomerular filtration rate [eGFR], 21 mL/min). Renal function had steadily deteriorated during a 9-month period.

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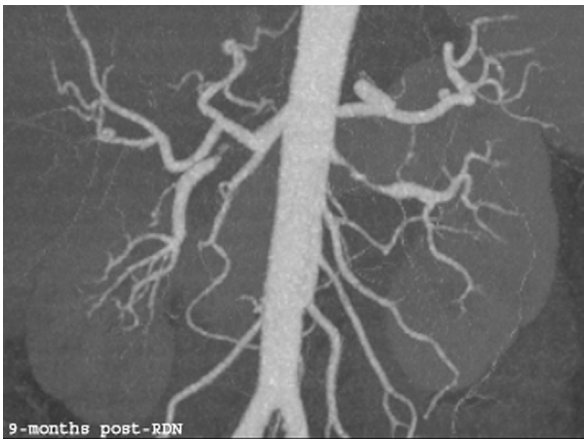

Fig 1. Post-transluminal renal denervation (*RDN*) and prestenting computed tomography angiography.

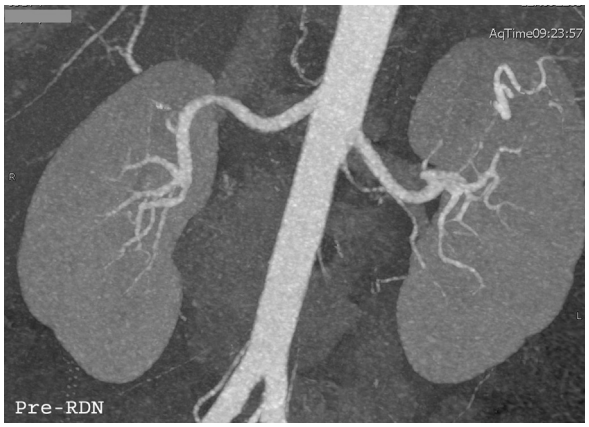

Fig 2. Pretransluminal renal denervation (*RDN*) computed tomography angiography.

Duplex ultrasound imaging showed peak systolic velocities of 523 cm/s in the right renal artery and 264 cm/s in the left renal artery. Magnetic resonance angiography and computed tomography angiography (Fig 1) confirmed new bilateral renal artery stenosis.

She had undergone bilateral RDN 9 months earlier at another institution for persistent essential hypertension (140/60 mm Hg on four antihypertensive agents) using the EnligHTN-I Trial (Safety and Efficacy Study of Renal Artery Ablation in Resistant Hypertension Patients) protocol.[16] Other treatable causes of hypertension had been excluded. Before RDN, she had normal renal function (creatinine, 611 mg/dL; eGFR, >60 mL/min) and computed tomography angiography demonstrated bilateral single renal arteries with no evidence of stenosis (Fig 2).

The patient subsequently underwent bilateral renal artery stenting. She received prehydration with sodium bicarbonate solution (100 mL of 8.4% sodium bicarbonate in 500 mL of 5% dextrose at 3 mL/kg/h for 1 hour preprocedure and at 1 mL/kg/h for 4 hours postprocedure) and *N*-acetylcysteine (600 mg at 12 and 24 hours before and after renal artery stenting) for prevention of contrast-induced nephropathy.

Access was obtained under local anesthetic and ultrasound-guided retrograde puncture of the right common femoral artery and secured with a 7F sheath. Heparin (5000 units) was administered before cannulation of the renal arteries with a 0.014-inch Command wire (Abbott Vascular, Abbott Park, Ill). A 6-mm × 24-mm Advanta V12 RX covered stent (Atrium Medical Corp, Hudson, NH) was used for the right renal artery stenosis, and two 6-mm × 21-mm Advanta V12 RX covered stents were used for the left (Fig 3). She received a loading dose of clopidogrel (300 mg) after stenting and was prescribed daily clopidogrel (75 mg) for 1 month and lifelong aspirin (100 mg).

Significant clinical improvement was noted over the following 48 hours. Blood pressure decreased to baseline 145/75 mm Hg on five antihypertensive agents, and renal function normalized (creatinine, 713 mg/dL; eGFR, >60 mL/min). Renal artery duplex imaging after stenting demonstrated significant improvement in peak systolic velocity (right renal artery, 225 cm/s; left renal artery, 171 cm/s). Subsequent follow-up with arterial duplex ultrasound imaging and a nuclear medicine renal scan demonstrated no evidence of restenosis.

DISCUSSION

Transluminal RDN is described as a treatment for hypertension in a number of studies, including several case series,[15] several nonrandomized comparative studies,[6,13,14,16] and one randomized control trial,[15] A nonrandomized cohort study, Symplicity-HTN-1 (Renal Denervation in Patients With Refractory Hypertension), described a reduction in blood pressure of 32/14 mm Hg at 24 months in 153 patients with essential hypertension.[15]

The Symplicity-HTN-2 (Renal Denervation in Patients With Uncontrolled Hypertension) trial[12] randomized 106 patients, of whom 52 underwent RDN plus maintenance of antihypertensive medications and 54 received antihypertensive medications alone. The study showed significant reduction in blood pressure in the RDN group (32/12 mm Hg) compared with controls at 6 months. The 12-month follow-up of RDN patients showed that blood pressure remained significantly lower than before treatment.[17] This study also permitted the control patients to undergo RDN at 6 months. The crossover group of 34 patients had a significant reduction in blood pressure after RDN. Symplicity-HTN-2 was limited by small size, short follow-up, and was not blinded. There was also inclusion of patients with white-coat hypertension, secondary hypertension, and inadequately prescribed medications or noncompliant patients.[18]

Symplicity-HTN-3 (Renal Denervation in Patients With Uncontrolled Hypertension) is a new, large-scale, multinational, multicenter randomized controlled trial that has a more stringent screening process to confirm true resistant hypertension in the RDN and control arms of the study.[19] In addition, the control arm in the Symplicity-HTN-3 study will have more intensive assessment of drug adherence monitoring.

Reported vascular complications from RDN include access vessel injury and two patients with renal artery dissection.[17] Renal artery stenosis has not been described.