Renal artery aneurysm associated with Leber hereditary optic neuropathy

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ABSTRACT

Leber hereditary optic neuropathy is an inherited, rare, mitochondrial metabolic disease that leads to progressive vision loss due to the accumulation of reactive oxygen species. The disorder has been associated with microangiopathy and macroangiopathy. We present a novel case of saccular left renal artery aneurysm in a 27-year-old man with known Leber hereditary optic neuropathy. The lesion was asymptomatic and grew from 1.8 to 2.0 cm during the course of 1 year. We successfully performed an endovascular left renal artery aneurysm repair. (J Vasc Surg Cases and Innovative Techniques 2018;4:5-7.)

Leber hereditary optic neuropathy (LHON) is a rare disease of progressive central vision loss. The disease prevalence is variable, depending on the population, and it is estimated that the prevalence is 1:45,000 in Europe.1 LHON is caused by various mutations of mitochondrial DNA, leading to the dysfunction of complex I of the respiratory chain.2,3 It is thought that oxidative stress causes microangiopathic damage to retinal arteries.4 Although vision loss is the defining characteristic of LHON, damage to other organ systems is seen. Common extrapthalmic features include peripheral neuropathy, ataxia, myopathy, dystonia, and cardiac conduction defects. LHON is inherited maternally with variable penetrance, affecting males more than females.3-5 It has been suggested that LHON is a multiorgan disease and may present with various vascular manifestations. Macroangiopathic consequences are seen, including arterial hypertension and aortic disease.6 Furthermore, mitochondrial metabolic disorders such as LHON are associated with vascular manifestations such as aneurysm formation, dissection, and vascular malformations. In addition, patients with mitochondrial metabolic disorders appear to be predisposed to accelerated cardiovascular disease in the absence of classic risk factors.3,5,6 We present a novel association of renal artery aneurysm in a patient with LHON. The patient underwent successful endovascular repair. He provided written consent for publication of his clinical case.

CASE REPORT

The patient was a 27-year-old man with known LHON that was diagnosed at the age of 8 years, when he first experienced gradual vision loss. Genetic testing confirmed the diagnosis with mutation 11778, and the degree of heteroplasmy was unknown. The patient affirmed that both of his brothers also carry the diagnosis of LHON, and his identical twin had a history of aortic coarctation with surgical repair as a child. The patient’s vision remained stable over time. As a young adult, he developed migraine variants that were attributed to his disease. These manifested as transient vision loss. Workup for these symptoms included magnetic resonance angiography of his head and neck, which revealed no abnormality. He also underwent bilateral carotid duplex ultrasound examination, which had normal findings.

At the age of 25 years, the patient presented to the emergency department with right-sided abdominal pain after he fell down a flight of stairs. He had no external signs of trauma or flank pain. Abdominal computed tomography was performed to evaluate his pain. He had no traumatic injury, but a 1.8-cm saccular aneurysm in the proximal left renal artery was incidentally discovered (Fig 1). He exhibited evidence of atherosclerosis scattered throughout the abdominal aorta and iliac vessels. In addition, a 7-mm thrombosed pseudoaneurysm arising from the right common iliac artery was noted. Computed tomography angiography (CTA) of the chest, abdomen, and pelvis was performed, which revealed no further abnormalities. The patient was prescribed aspirin and antihypertensive and lipid-lowering agents because of evidence of arterial hypertension and CTA-identified atherosclerotic arterial disease. He consumed alcohol biweekly and was exposed passively to cigarette smoke. His creatinine level was normal. His imaging and laboratory workup excluded additional renal disorders such as nephrolithiasis, renal cysts, rhabdomyolysis, and tubular dysfunction, and thus kidney biopsy was not undertaken. Operative repair of the left renal artery aneurysm (LRAA) was deferred, given that it did not meet conventional size criteria for repair, and it was asymptomatic.
On 1-year follow-up CTA imaging, the LRAA progressed in size to 2.0 cm, which approached the size of his abdominal aorta. He remained asymptomatic. Because of the lesion’s growth and morphology, the patient was counseled to undergo repair. Findings on preoperative echocardiography were normal. We performed endovascular renal artery aneurysm repair through percutaneous common femoral arterial access. Abdominal aortography was performed, followed by selective catheterization of the left renal artery main branch. The aneurysm was excluded by use of two covered stents (GORE VIABAHN Endoprosthesis; Gore Medical, Flagstaff, Ariz), 6 mm and 7 mm in size (Fig 2). An 8F Angio-Seal device (Terumo Interventional Systems, Somerset, NJ) was used for arterial closure. The patient tolerated the procedure well and was discharged home the next day. He was prescribed aspirin and clopidogrel for a month, with plans to continue aspirin for life. On 1-month clinical follow-up, he was asymptomatic and without complications. His blood pressure remains controlled on one medication, and his creatinine level is normal. Given this patient’s lack of classic risk factors for arterial disease, we suspect that his hypertension is due to decreased arterial elasticity caused by LHON, and arterial duplex ultrasound is scheduled both to evaluate his repair and to detect abnormalities in arterial elasticity. The 1-month postoperative CTA imaging showed exclusion of the renal artery aneurysm without endoleak while maintaining arterial flow to the kidney (Fig 3). He will return for arterial duplex ultrasound examination to assess the repair 6 months after his postoperative CTA.

**DISCUSSION**

We present a novel association of LHON with a renal artery aneurysm. The indications for repair were the saccular morphology and progressive growth during 1 year to meet the conventional size criterion of 2 cm. The natural history of renal artery aneurysms in LHON is unknown, and rupture risk is undefined. Case reports suggest that mitochondrial arteriopathies behave aggressively with spontaneous arterial rupture after minimal tissue manipulation, which is related to extremely friable arterial tissue. This concern for catastrophic, uncontrollable bleeding during open repair was the primary reason for selecting endovascular repair for this patient with LHON. In addition, the patient preferred endovascular repair. His repair was successful, and he continues to lead a normal, active life. The LRAA is completely excluded on postoperative CTA. Surveillance of the patient’s endovascular LRAA repair will be conducted by alternating duplex ultrasound and CTA, with intervals...
between examinations lengthened once repair stability is demonstrated.

LHON is a multifactorial disease spectrum characterized by complex interactions between genetic and environmental factors. Heteroplasmy is a significant genetic factor that determines the clinical manifestations of LHON. Individual cells may harbor varying amounts of mutant mitochondrial DNA, which may lead to varying degrees of metabolic injury within a single patient. Although the metabolic injury of LHON appears to primarily target the optic nerve, it may also concentrate in other nervous or vascular tissue. Reports of aortic stiffening and microvascular ectasia have been directly linked to LHON. In addition, other mitochondrial disorders that are similar in pathophysiology to LHON have been associated with vascular findings, such as carotid artery occlusive disease and dissection, Leriche syndrome, and aortic rupture. With regard to environmental factors, reports link exogenous toxins or environmental stress with a worsening of the LHON syndrome. These include systemic illness, nutritional deficiencies, medications, trauma, and industrial toxins that stress mitochondrial metabolism. Tobacco and alcohol cause the accumulation of reactive oxygen species and can trigger the conversion of subclinical LHON mutations to overt disease. A large, multicenter study found that tobacco smoking was significantly associated with vision loss in LHON carriers in a dose-response relationship. Therefore, these patients should refrain from tobacco and alcohol consumption.

This case illustrates that LHON can present with significant vascular disease, including renal artery aneurysms. Clinicians should strongly consider vascular imaging for LHON patients who present with signs or symptoms concerning for vascular manifestations. In addition, these patients should be counseled about their increased cardiovascular risk even if they lack classic risk factors, and physicians should regularly take preventive measures to reduce cardiovascular risk in patients with LHON.

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