Ischemic Monomelic Neuropathy: Diagnosis, Pathophysiology, and Management

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INTRODUCTION

There is an approximate growth of 3% to 4% of patients undergoing dialysis every year as a result of an increased pool of chronic kidney disease (CKD) from various medical problems such as diabetes, hypertension, and cardiovascular diseases. Arteriovenous (AV) fistula use increased from 27.9% to 55% between 1998 and 2007 (Figure 1).[1] By December 2013, in 62.5% of prevalent dialysis patients an AV fistula was being used.[2] In 1966, Brescia *et al*. introduced the endogenous AV fistula, a revolutionary therapeutic modality for the management of renal patients. Most common complications of vascular access can be divided into hemodynamic and mechanical complications. Complications from hemodynamic alterations include venous hypertension, arterial steal syndrome, and high-output cardiac failure. Mechanical complications include pseudo-aneurysm, which may develop from a puncture hematoma, degeneration of the wall, or infection. A rare complication that can develop after hemodynamic alteration of vascular access is ischemic monomelic neuropathy (IMN).

CASE PRESENTATION

A 59-year-old African American man was admitted for creation of vascular access for dialysis. Past medical history included diabetes mellitus complicated by peripheral neuropathy and retinopathy, end-stage renal disease (ESRD) from diabetes and hypertension, a history of dialysis for about 7 years, multiple deep venous thromboses in the upper extremities at AV fistula sites, hypertension, hyperlipidemia, chronic pancreatitis, anemia, and previous smoking (half a pack per day for 20 years).

Physical examination showed a temperature of 98 °F, blood pressure 104/59 mm Hg, pulse 99 beats/min, respiratory rate of 16/min, and 98% saturation on room air. Extremities had bilateral edema 1+. The lower extremity pulses were difficult to determine because of the edema. The rest of the examination findings were normal. Laboratory values on admission were as follows: white blood cells 8.4, hemoglobin 10.4, platelets 274, and hematocrit 32. The basic metabolic panel included sodium 134 mEq, potassium 4.3, chloride 98, bicarbonate 20, blood urea nitrogen 33, and creatinine 4.0 mg/dl. Liver function tests include total protein is 8.8, albumin is 4.5, bilirubin 0.7, alkaline phosphate 269, AST 50, ALT 31. Coagulation tests showed an international normalized ratio (INR) of 1.2, prothrombin time (PT) 12.1 seconds, and activated partial thromboplastin time (aPTT) 45.9 seconds.

Hospital Course

The patient was started on heparin for bridging anticoagulation, as INR was subtherapeutic. He had a right femoral catheter for regular dialysis. After great saphenous vein mapping was performed, the patient underwent a left superficial femoral artery to vein loop graft without any perioperative complications. On postoperative day 0, the patient complained of pain at the incision site and weakness of left lower extremity. His pain was controlled with acetaminophen/oxycodone, and it was thought that his weakness could be from surgery or anesthetics or from his posture. On postoperative day 1, he complained of worsening weakness and numbness of left lower extremity.

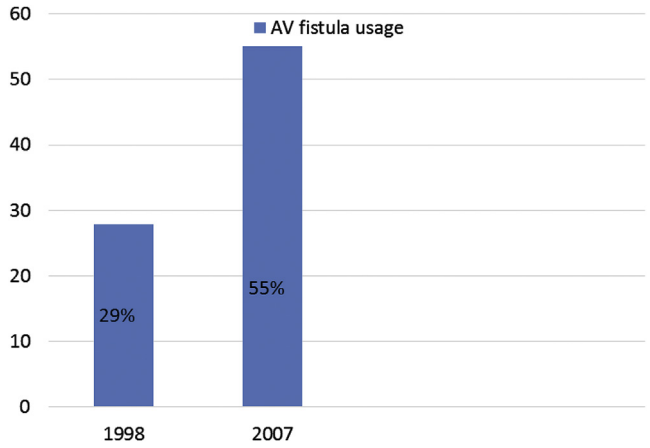

Figure 1. Arteriovenous (AV) fistula usage.

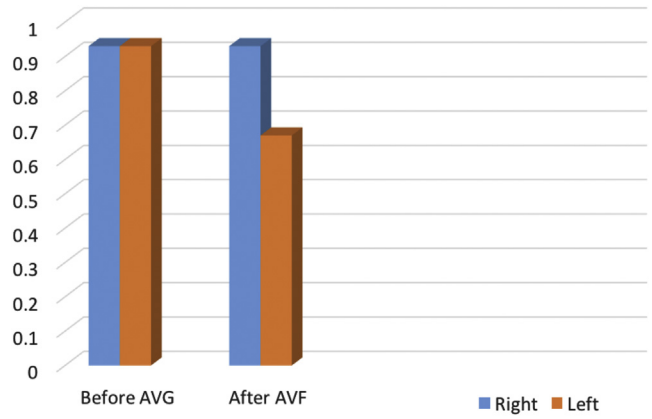

Figure 2. Ankle-brachial index (ABI) before and after graph placement. AVF, arterio-vascular fistula; AVG, arterio-vascular graft.

The neurology department was consulted at that time. On examination the patient had edema at the incision site, and the leg was warm to the touch. Neurological examination showed normal mental status, speech, language, and cranial nerves. The motor system showed normal bilateral upper extremity strength. The lower extremities showed left foot dorsiflexion of 1/5, left foot plantar flexion 3/5, and right dorsiflexion and plantar flexion of foot 5/5. Left hip flexion was 3/5 when the patient was lying on the bed and was 1/5 when he was sitting on the bed. The foot invertors were 0/5 and the foot evertors 0/5. Sensation to light touch, cold, pinprick, and temperature were decreased on the left from the lower third of the leg to the foot and were normal on the right side. Sensation to light touch and cold were normal on the right side. Coordination test results were normal. Pulses could not be determined because of chronic edema.

Ultrasound of the left thigh, computed tomography of the abdomen and pelvis, and magnetic resonance imaging of the spine did not explain the causes of the above-mentioned clinical findings. Ultrasound showed a patent AV graft and no hematoma. The ankle-brachial index (ABI) was 0.93 on the right and 0.67 on the left, and decreased on the left side following graft placement. The ABI before placing the AV graft was 0.93 in both legs (Figure 2). Current analog tracings were consistent with tibial obstructive disease on the left. The right leg was normal. Physical therapy was brought on board, as well as assistance with ambulation, and the patient was found to have a high stepping gait on the left. Vitamin D levels were normal. Foot drop and weakness after surgery without lumbar radiculopathy pointed to ischemic monomelic neuropathy (IMN), which was a diagnosis of exclusion.

After diagnosing IMN clinically, we evaluated the patient's risks and benefits of closing versus not closing the AV graft. He did not have any other site for creating another AV access for dialysis, and closing the AV graft would not completely resolve the problem. We planned to manage the foot drop by physical therapy and ankle–foot arthrosis. The patient's ambulatory status was somewhat impaired due to arthritis and general medical decline for some months prior to the vascular access surgery. He and his family agreed with conservative management and decided not to close AV graft. He was discharged with follow-up neurology consultation for electromyography to evaluate the extent of damage, and also followed up with vascular surgery for assessing the AV graft.

DISCUSSION

Our patient had neurological symptoms confined to the left lower extremity, weakness, and a foot drop complication. The differentials were IMN, lumbar plexopathy, nerve compression by hematoma or by edema, spinal cord pathology, and iatrogenic nerve injury.

Ultrasound, computed tomography of the abdomen and pelvis, and magnetic resonance imaging of the spine ruled out any of above differential diagnoses. The ABI were done before and after surgery and clearly showed decreased ABI on left after surgery, which was due to a physiological steal phenomenon. The patient did not have vascular ischemic symptoms. The recent vascular access surgery and neurological symptoms of foot drop, numbness, and weakness were suggestive of nerve damage at the level of the mid-thigh or leg or both. As there was no nerve compression, the most likely possibility was IMN.

Ischemic neuropathy of upper limb nerves after dialysis surgery was first reported by Bolton *et al.* in 1979.[3] The term "ischemic monomelic neuropathy" was introduced in 1983 by Wilbourn, a neurologist at the Cleveland Clinic, and was intended to distinguish isolated ischemia of the arterial supply from multiple nerves of a single extremity.[4] The term refers to the combination of ischemia and neuropathy in a single

limb ("*melos*" is Greek for "limb"). Wilbourn *et al*. defined IMN as a type of multiple axonal-loss mononeuropathy distally in a limb, resulting from an impaired blood supply after graft insertion. It is an underappreciated complication because of its variable manifestations in the postoperative period, and is difficult to diagnose with underlying comorbidities. It requires a high index of suspicion and multidisciplinary involvement to diagnose promptly and manage.

Most cases are in patients with underlying diabetes with peripheral complications. There are few cases seen in patients with severe vascular extensive calcific disease. This complication occurs with the steal phenomenon, which is a diversion of blood supply away from the peripheral. It is unusual to expect this complication presenting with neurological injury rather than vascular injury. This leads to both short- and long-term disability. Miles described IMN symptoms as being immediate in onset, with dominant neurologic signs and symptoms.[5] In general, sensory complaints are more prominent than motor.

Some authors consider IMN to be result of dialysis-associated steal syndrome (DASS), not involving muscles; thus it could be a condition on the spectrum of DASS rather than a different entity. In DASS, there will be peripheral muscle or skin ischemia as a typical feature. Both conditions have a common pathophysiology: that is, they occur as a result of ischemia. Recently, the Vascular Access Society has suggested using the phrase dialysis access–induced ischemic syndrome (DAIIS) instead of steal syndrome, which includes IMN in the spectrum.

A greater global awareness among the multidisciplinary team, which often includes internists, neurologists, nephrologists, vascular surgeons, interventional radiologists, nurses, and dialysis care technicians, is necessary to advocate for the early consideration of IMN.

Pathophysiology

The exact mechanism of IMN is poorly understood. IMN is a form of steal phenomenon, as the access surgery "steals" blood flow from distal nerve tissue, causing multiple axonal loss mononeuropathies distally in the limb. So far, we have seen cases in the upper extremities. Kelly *et al*. demonstrated, with electron microscopy, decreased perfusion of the vasa nervorum after acute large vessel ligation in their experiment model.[6]

In the upper extremities, the median nerve shows a greater susceptibility to ischemic injury, based on the finding of greater axonal loss in the median as compared with the ulnar nerves. Physiologically there is diversion of some amount of blood away from distal vessels to the fistula or graft; if it large enough to cause ischemia, then we might see this complication. If surgery is proximal, the chance of having this complication is great. Nerves are susceptible to ischemia owing to the lack of a collateral supply. The sensory fibers are more sensitive to ischemic insult than are the motor fibers.

Diagnosis

This condition is a clinical diagnosis. It should be associated with artery manipulation with underlying peripheral neuropathy and peripheral artery disease. It is a distinct diagnosis that occurs in the setting of mild to moderate ischemia.[7] The symptoms most commonly occur immediately postoperatively, and the nerve deficits are disproportional to any ischemic changes seen in other tissues of the affected limb.[7] The most commonly reported location is from the brachial artery manipulation. This is the first report of a case from the left femoral artery manipulation.

When the clinical neurologic examination results are equivocal, electro-diagnostic studies may facilitate diagnosis.[8] Electromyography and nerve conduction studies can be used to confirm the diagnosis. The electromyogram typically shows axonal loss, low amplitude or absent responses to the sensory and motor nerve stimulation, and relatively preserved conduction velocities. For our case, we were able to make the diagnosis clinically with the help of neurologists, and no decision was made to do repeat electromyography confirming IMN.

Incidence

Because diagnosis of IMN requires a multidisciplinary approach, it is assumed that there are underdiagnoses and underreporting. Lack of experience and equivocal symptoms may be the reasons for the paucity of reports of IMN, most of which were not published before the end of the 1990s. Two reports suggested incidences around 0.5% or 3%.[9]

Treatment

A patient complaining of neurological symptoms postoperatively after AV procedures should have a neurology consultation for early diagnosis and management. So far, treatment has been based on case reports and expert opinion. Treatment recommendations are derived from observational data. Theoretically, if we reduce the flow in the AV graft or shunt leads, it will cause increased perfusion in the extremities and will reduce the neuropathy. Most authors prefer hemodialysis access closure by ligation, banding, or angioplasty as an option to improve blood flow to the extremities.

It would make sense to close the fistula or graft so that blood supply back to the periphery may lead to recovery, but actual scenarios have shown inconclusive results. According to one study that involved 19 cases, 10 patients were not improved even after correction of hemodialysis access.[10] However, even if surgical correction of the shunt is performed within a short time, symptoms may be only slightly or even not at all improved. Despite attempts at earlier closure, several published reports suggest that even with this aggressive management, IMN symptoms may be permanent or only partially reversible.[11] As a practical matter, many patients may have few alternative sites or none (as in our patient) for future hemodialysis access construction.

The decision to close a functioning access requires careful deliberation. This complication can occur in other sites, given that the underlying risk factors are unchanged. As it is nerve injury, cases have shown poor prognoses despite access closure. Most patients will be left with residual neurologic impairment. Further treatment for IMN is mainly supportive and should include pain control. Anticonvulsants, antidepressants, and narcotics have been suggested for pain control.[12] Hand ischemia from arterial steal should be treated with a distal revascularization internal ligation procedure. If this fails or is not feasible, ligation of the AV fistula or graft should be considered. This is a grade D recommendation from a vascular surgery board. Despite our limited experience, there seems to be no doubt that any time delay plays a major role in the prognosis of IMN. Accordingly, immediate diagnosis means more time for adequate treatment.

CONCLUSION

In conclusion, IMN is not confined to the upper extremities. All health care practitioners taking care of ESRD patients undergoing vascular access procedures should be aware of this complication. Suspicion and recognition are very important. This complication is less associated with tissue ischemia. Every case of IMN should be carefully documented and, if possible, published so as to gain more experience with pathophysiology and treatment. Considering all the risks and benefits of vascular access closure or nonclosure, choosing wise management is crucial. We will see more cases in the future, as there are a growing number of ESRD patients requiring vascular access for dialysis. IMN is a difficult diagnosis, because of the inconsistency of the clinical signs and the occurrence in the immediately postoperative period.

DISCLOSURE

All the authors declared no competing interests.

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