The approach to clinical conundrums by an expert clinician is revealed through presentation of an actual patient's case in an approach typical of morning report. Similar to patient care, sequential pieces of information are provided to the clinician who is unfamiliar with the case. The focus is on the thought processes of both the clinical team caring for the patient and the discussant.

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Nerves of Steal

A 60 year-old woman with advanced kidney disease presented with one month of progressively worsening, sharp burning pain and decreased sensation in her left hand. Cold air exacerbated the pain. She noted decreasing ability to utilize her left fingers, a weakened grip and that the muscles in her hand looked smaller.

Localized sensory and motor symptoms in a discrete region of a single limb suggest neuropathy. The lack of symptoms in the face or ipsilateral lower extremity would dissuade a clinician from considering central etiologies; the presence of neuropathic pain is uncommon for cortical lesions. The involvement of motor and sensory nerves indicates peripheral nerve involvement.

The general approach to patients with peripheral neuropathy begins with identifying the neuropathy as a mononeuropathy (involving a single nerve), a polyneuropathy (symmetric involvement of multiple nerves) or a mononeuropathy multiplex (asymmetric involvement of multiple nerves). The patient, in this case, described subacute neuropathic pain, sensory loss, and weakness in her left hand in a distribution consistent with mononeuropathy or mononeuropathy multiplex.

This patient could have carpal tunnel syndrome given its prevalence in patients with advanced renal disease. The differential diagnosis is broad, however, and includes ulnar mononeuropathy, nerve ischemia due to vasculitis or vasculopathy, lower cervical radiculopathy (though the patient does not describe neck or radicular pain), lower brachial plexopathy, and complex regional pain syndrome.

The patient was diagnosed with advanced kidney disease one year ago when biopsy revealed focal segmental glomerulosclerosis secondary to lithium. Since her diagnosis, two grafts were placed in the left upper arm in anticipation of dialysis: the first, placed seven months prior to this admission, failed to mature; the second, placed one month prior to this admission, was complicated by bleeding at the fistula site and was not yet mature. Prior to this admission she had not required hemodialysis. Her past history included hypertension, dyslipidemia, hypothyroidism, secondary hyperparathyroidism, a remote history of cervical cancer (stage unknown, recent PAP smear negative), microcytosis and schizoaffective disorder. Her medications were furosemide, amlodipine, lisinopril, atenolol, ator-

vastatin, pantoprazole, olanzapine, levothyroxine, iron, darbepoetin, sevelamer, multivitamin and docusate.

Given the history of procedures in the left arm one should consider ischemic injury to the left median nerve. Other local complications could include compressive lesions such as an abscess or hematoma or direct nerve injury from the procedure. Carpal tunnel syndrome remains high on the differential due to its prevalence and because renal failure and hypothyroidism increase the risk of carpal tunnel syndrome.

A careful physical examination would localize the nerve or nerves involved. Examination findings that would be consistent with carpal tunnel syndrome include sensory loss in the distribution of the left median nerve, weakness of muscles innervated by the median nerve, including the abductor pollicus brevis and opponens muscles, and a Tinels and Phalens sign of the left wrist. A proximal median neuropathy resulting from ischemia or compression might also involve median-innervated forearm muscle such as the pronator teres (forearm pronation) and flexor carpi radialis (hand flexion and abduction) muscles. Complex regional pain syndrome can be seen after a traumatic injury or surgery and is typified by severe neuropathic pain in a limb, often in combination with trophic changes in the affected extremity. A cervical radiculopathy would affect muscles supplied by the injured nerve root. For example, a C8 radiculopathy would affect all of the intrinsic hand muscles, the wrist and finger extensors, and the triceps brachii. A lower brachial plexopathy would present similarly to a lower cervical radiculopathy on clinical examination; electrodiagnostic evaluation would be necessary to distinguish these two disorders.

The patient appeared fatigued and her left hand was wrapped in blankets. Her vital signs were stable. There was no thyroid enlargement or lymphadenopathy. There was marked thenar, hypothenar and forearm atrophy on the left. Strength testing of her left hand demonstrated a grip strength of 2/5, finger extension and interosseous strength of 1/5, left wrist flexion and extension of 3/5; left biceps and triceps were 5/5. Sensation was mildly decreased to light touch, temperature, pain and proprioception throughout the left hand. Strength and sensation were intact in the right upper and bilateral lower extremities. Reflexes were 2+ throughout. The left radial pulse was diminished compared to the left ulnar that was 1+. The left hand was dry and cool. Laboratory evaluation revealed an elevated white blood cell count of 15,300/mm³, a hematocrit of 33 percent, mean corpuscular volume of 73 fL, and a normal platelet count. Electrolytes were consistent with advanced renal disease. The thyroid stimulating hormone level was normal.

The patient's examination reveals an injury to the sensory and motor components of the left ulnar, median, and distal radial nerves. The volar forearm wasting suggests proximal median motor nerve injury in the forearm. Because the triceps is spared, the weakness of finger and wrist extension implies distal radial motor nerve injury. The interosseous weakness is consistent with injury to the ulnar motor nerve. Weakness of grip and wrist flexion is less specific and it may be explained by injury to either the median or ulnar motor nerves. The diffuse sensory loss over the palmar and dorsal aspect of the left hand is consistent with neuropathic injury to the left median, ulnar, and radial sensory nerves. The preserved deep tendon reflexes are controlled by the musculocutaneous nerve (the biceps reflex) and branches arising from the proximal radial nerve (the triceps and brachioradialis reflexes), both of which are proximal to the apparent level of neuropathic insult.

Carpal tunnel syndrome is excluded since abnormalities extend beyond the median nerve distribution. The presentation is consistent with a mononeuropathy multiplex. Axonal etiologies of mononeuropathy multiplex—including vasculitis, ischemia, neoplastic infiltration, and infectious etiologies such as Lyme disease—are more common than demyelinating causes. Vasculitic neuropathy commonly involves the lower extremities and may have systemic symptoms, not present in this case. Neoplasm or other compressive lesions such as hematoma could explain these findings. Abscess must be considered given the leukocytosis. A lower brachial plexopathy, technically a mononeuropathy multiplex involving the proximal arm at the level of the brachial plexus, is also in the differential diagnosis. Another axonal disorder to consider would be neuralgic amyotrophy, an idiopathic form of acute brachial plexopathy associated with pain that is a complication of surgery that typically presents within a few hours to weeks of the procedure.
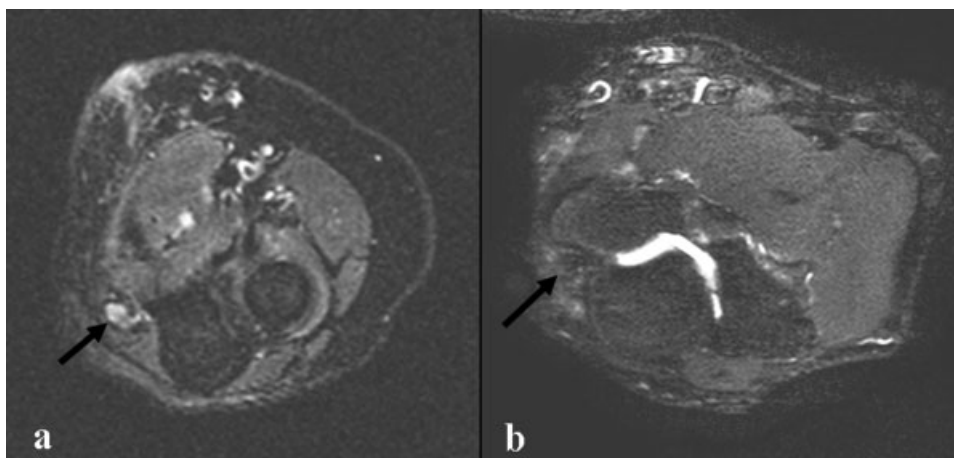
FIGURE 1. MR Neurogram (Axial STIR) (a) of the elbow demonstrating abnormal increased size and increased signal of the ulnar nerve (arrow). (b) in a normal patient demonstrating normal signal and normal size of the ulnar nerve (arrow).

Demyelinating causes of mononeuropathy multiplex are less likely and include a variant of chronic inflammatory demyelinating polyneuropathy (Lewis-Sumner syndrome) and hereditary neuropathy with liability to pressure palsies. Both processes are typically indolent and usually not painful, though the latter may present with fulminant numbness and weakness.

Nerve conduction and needle electromyography of the arm and cervical paraspinal muscles would differentiate axonal degeneration from demyelination. It would identify the affected nerves and any nerve root involvement. Given the concern for abscess or hematoma, MR neurography focused on the surgical site would also be important.

Electromyography and nerve conduction velocities demonstrated severe axonal loss of the left median, ulnar and distal radial sensory nerves consistent with acute denervation. A magnetic resonance neurogram following the course of these nerves revealed enlarged ulnar and median nerves with abnormal signal, but no compressive lesion (Fig. 1).

The electrodiagnostic testing is consistent with severe acute axonal injury to the left ulnar, median and radial nerves. This supports a diagnosis of mononeuropathy multiplex with axonal injury. Demyelinating causes are excluded at this point.

The MR neurogram demonstrates nonspecific nerve enlargement, which may be seen in ischemia, neoplastic processes (primary or metastatic),

demyelinating disease, or, rarely, amyloidosis. Neoplastic involvement is unlikely in this case given the absence of a compressive mass lesion and the long segmental involvement of both the median and ulnar nerves. Compression from an abscess or hematoma is excluded. Neuralgic amyotrophy does not typically cause nerve enlargement.

Ischemia is the most likely diagnosis. Laboratory evaluation for vasculitis would be reasonable. Vasculitides that could present in this fashion include: polyarteritis nodosa, mixed connective tissue disease, Wegner's granulomatosis, Churg-Strauss angiitis, Sjogren's, hepatitis C with serum cryoglobulinemia and possibly rheumatoid arthritis. Given the history of fistula placement in the affected limb, vascular sufficiency must be assessed.

Anti-nuclear antibodies and anti-neutrophilic cytoplasmic antibodies were negative, and a C- reactive protein was 5.9 mg/L (normal range, 0 to 10 mg/L). The erythrocyte sedimentation rate was 32mm/hr (normal range, 0 to 20) and serologies for hepatitis B and C were negative. There was no evidence of serum cryoglobulins.

A modestly elevated sedimentation rate and normal C-reactive protein argue against a diagnosis of vasculitis. The negative ANA, ANCA, hepatitis serologies and cryoglobulin tests render unlikely the diagnoses of polyarteritis nodosa, Wegner's granulomatosis, Churg-Strauss angiitis, or hepatitis related cryoglobulinemia. Eosinophilia (present in Churg-Strauss), ENA (positive in mixed
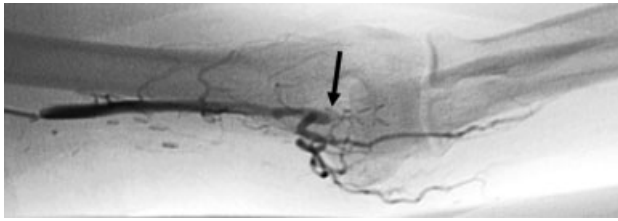
FIGURE 2. Angiogram of the left upper extremity with injection of the brachial artery. Pcclusion of the brachial artery is present (arrow), with filling of several small collateral vessels

FIGURE 3. Post-embolization angiogram demonstrating improved collateral flow to the distal arterial vasculature.

connective tissue disease), anti-SSA and SSB (positive in Sjogren's) and a rheumatoid factor would round out this evaluation for vasculitis. A left radial sensory nerve biopsy could also be of value in diagnosing vasculitic neuropathy in this patient.

Given the evidence against vasculitis, the possibility of ischemia due to vascular insufficiency is concerning. Two ischemic complications of hemodialysis are known to cause distal multiple mononeuropathies. The first, ischemic monomelic neuropathy syndrome is seen almost exclusively in diabetics. It is characterized by the development of acute pain, weakness of the forearm and hand muscles, and sensory loss within minutes or hours of AV graft placement. Transient occlusion of the blood supply to the nerves of the forearm and hand induces nerve ischemia, but does not cause necrosis of other tissues. The nerve conduction findings in this patient are consistent with ischemic monomelic neuropathy syndrome. The delayed onset of her symptoms, however, makes this diagnosis unlikely.

The second ischemic complication of hemodialysis, and the likelier diagnosis, is vascular steal syndrome. This has a similar clinical and electrodiagnostic presentation to ischemic monomelic neuropathy syndrome, but has a latency period after surgery of days to months. Vascular steal occurs when a reversal of blood flow into the fistula "steals" flow from the palmar arch arteries and induces ischemia of the vasa nervorum. Vascular studies should be obtained urgently when this diagnosis is considered.

Evaluation of the arteriovenous graft and vascular surgery consultation were sought. Digital photoplethysmography revealed diminished waveforms in all fingers of the left hand. Arterial Doppler evaluation of the left upper extremity confirmed low-velocity flow in the radial and ulnar arteries and failed to confirm flow in the
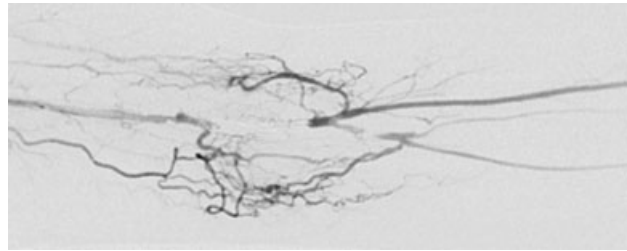
brachial artery distal to the arteriovenous fistula. The patient underwent an angiogram of the left axillary and brachial arteries. There was normal flow until the level of the arteriovenous fistula but minimal flow distal to the fistula (Fig. 2).

The diminished waveforms on digital photoplethysmography are consistent with poor perfusion distally. The angiogram suggests that the multiple mononeuropathies are a consequence of ischemia from impaired blood flow.

Consulting the vascular surgeons in this setting is essential because restoring adequate blood flow to the affected nerves can prevent further loss of function. Prognosis is dependent on many factors, including the severity of the functional loss and the duration of the symptoms prior to the restoration of blood flow. The patient's severe weakness and substantial muscle atrophy, manifestations of axonal degeneration, imply a poorer prognosis for recovery of function.

Embolization of the arteriovenous fistula was performed by interventional radiology. Post embolization angiograms demonstrated improved peripheral arterial flow (Fig. 3). One day later, the patient's finger flexion and extension improved. She reported mildly decreased dysesthesias and on examination her fingers were warmer to the touch. One month after discharge, her strength continued to be impaired, though improved and she still experienced pain.

COMMENTARY

Hospitalists must be equipped to recognize urgent and potentially reversible causes of neuropathy. The hospitalist should maintain a high index of suspicion for ischemia (either due to vasculitis or vascular compromise), traumatic nerve injury, nerve compression or entrapment, lymphoma or

TABLE 1
Differential Diagnosis of Mononeuropathy Multiplex

Diagnosis	Associated features	Specific evaluation
Axonal neuropathies		
Ischemia (including vascular steal)	Poor arterial pulses, history of vascular surgery	Digital photoplethysmography, Doppler, angiography
Nerve compression and trauma	History of traumatic injury, mass, infection/abscess	MR neurography
Lymphoma or metastatic infiltration	History of known cancer, weight loss	PET, whole body CT, bone marrow biopsy
Vasculitis	Waxing and waning symptoms, association with connective tissue diseases, painful	CRP, ESR, Hepatitis C, cryoglobulins, ANA, ANCA, antibodies to SSA/SSB, ENA, eosinophil count, serum complement, SPEP/UPEP, RF, nerve biopsy
Neurosarcoidosis	Hilar lymphadenopathy, chronic cough	Chest CT, ACE, nerve biopsy
Lyme	Tick bite, erythema chronicum migrans	Lyme serology
Leprosy	Resident of southeast Asia, skin lesions	Skin smear for acid fast bacilli (mycobacterium), nerve biopsy
Demyelinating neuropathies		
Lewis-Sumner syndrome (i.e. asymmetric CIDP)	Relapsing remitting or chronic progressive course, areflexia	Lumbar puncture (increased spinal fluid protein common)
Hereditary neuropathy with liability to pressure palsy	Family history, recurrent episodes of entrapment/compression neuropathies	Genetic testing (deletion in the gene for peripheral myelin protein-22)
Multifocal motor neuropathy with conduction block	Multifocal weakness in the distal arms/legs without sensory symptoms	Only motor abnormalities on nerve conduction including conduction block

metastatic infiltration, hepatitis C with cryoglobulinemia, Guillain-Barre syndrome and toxic exposures. Table 1 highlights important causes of mononeuropathy multiplex and summarizes associated findings and indicated diagnostic tests for specific evaluation.

Another challenge for hospitalists is efficient evaluation of neuropathy. A systematic framework for creating a differential diagnosis and familiarity with available diagnostic tests is crucial. Hospitalists should be aware of three broad categories of neuropathy: mononeuropathy, polyneuropathy and mononeuropathy multiplex. Electrodiagnostic testing is essential to confirm the involved nerves and distinguishes axonal from demyelinating etiologies. Ultrasound, MR neurogram and, when indicated, nerve biopsy may be useful. Table 2 reviews these diagnostic tools as well as their indications and limitations.

Ischemic steal syndrome should be considered when neuropathy develops in a limb subsequent to arterio-venous access procedures. Any vascular network, including the vertebral, carotid and coronary arteries, is at risk for steal. A feature common to all steal syndromes is the diversion of blood away from its original destination toward a lower pressure alternative. In some cases, this leads to a reversal of arterial flow and ischemia. Ischemic complications from AV access occur in 1-9% of patients.[1] Symptoms of steal can be mild, such as

self-limited dialysis induced pain, coldness and numbness, or severe, including severe pain, sensory and motor loss.[2] If vascular compromise is sufficient, gangrene can ensue. Sensory deficits usually precede motor loss and the radial pulse is commonly absent or diminished. Other findings can include pallor of the fingers, muscle atrophy, resorption of the nail bed, and gangrene or ulcerations of the fingers. Risk factors for steal include atherosclerotic disease, female gender, age greater than 60 years, diabetes mellitus, previous surgery on the same arm, and use of the brachial artery as a donor.[3] Symptoms of ischemic steal typically present within the first month after surgery, but can also be delayed; there is one report of a patient presenting one year postoperatively.[4]

Imaging studies such as doppler and angiography can be helpful in diagnosing ischemic steal syndrome. Fistulagrams may reveal a reversal of blood flow in the distal arm and hand, but these are reserved for cases with suspected proximal obstructive arterial disease.[5] Vascular imaging studies can be misleading, however, as many patients will have physiologic but asymptomatic reversal of flow. Thus, a functional assessment such as digital plethysmography is recommended, especially in cases where clinical symptoms are vague. Digital pressures less than 60mmHg demonstrated 100% sensitivity and 87% specificity in one case control study of 40 patients.[6] Treatment of ischemic steal

TABLE 2
Diagnostic Modalities for Evaluation of Peripheral Nerves

Test	Indications	Limitations
Electrodiagnostic Testing[7]	● Any peripheral neuropathy, muscle or neuromuscular junction disorder *Detects severity, chronicity, axonal v. demyelinating, diffuse v. focal, asymmetric v. symmetric*	● Concomitant disease can reduce accuracy
Electromyography (EMG) ● Monopolar/concentric needle electrode inserted into the muscle belly ● Measures action potential at rest vs. during voluntary activation	EMG Differentiates axonal v. muscle damage; sensitive for even mild axon degeneration; localizes lesions.	EMG ● Patient discomfort ● Evaluates only motor fibers ● Does not detect demyelination ● Might not be positive in first 21 days of symptoms
Nerve Conduction Studies (NCS) *Sensory* ● Recording electrode placed over sensory nerve ● Sensory nerve stimulated distally ● Measures stimulus at proximal site *Motor* ● Recording electrode placed over muscle belly ● Motor nerve stimulated proximally ● Measures stimulus at muscle *Specialized NCS tests*	NCS High sensitivity to differentiate axon loss from demyelination; localizes lesions. *Sensory* – localizes lesion to proximal vs. distal or to dorsal root ganglion *Motor* – amount of axonal loss *Specialized testing* – can identify radiculopathy, peripheral neuropathy, myasthenia gravis	NCS ● Certain sensory responses lost with aging ● Less sensitive for mild axonal loss
Ultrasound[8] ● Performed with typical ultrasound equipment ● Clinician must localize lesion for technician and explicitly guide test process ● Normal nerves appear tubular with linear echoes on a longitudinal scan; honeycomb on transverse scan	● Suspected nerve entrapment ● Evidence strongest for evaluation of median and ulnar nerves and Morton's neuroma *Detects lesions, nerve thickening, decreased echogenicity*	● Doesn't show pathologic changes within nerves ● Difficult to visualize deep nerves or nerves surrounded by fat ● Small field of view unless reconstructed ● Results operator dependent ● Less accurate than MRI for tumors
MRI[9,10] **"MR neurography"** ● Standard MRI equipment ● Optimizes nerve resolution compared with surrounding tissues	● Concern regarding entrapment, trauma or mass lesions ● To narrow differential when clinical and electrodiagnostic studies are inconclusive ● When carpal tunnel syndrome does not respond to conservative management *Detects mass lesions compressing nerves, nerve enlargement and abnormal signal (neuritis, infiltration), increased signal in denervated muscle groups (once strength is ≤3 of 5). These changes can be seen as early at 4 days post trauma compared to 2–3 weeks on EMG.*	● Expense ● Time (15–60 minutes depending on scan requested)
Nerve Biopsy[11] ● Biopsy a nerve in the region of sensory loss or of a sensory nerve demonstrating electrophysiological abnormalities (decrease risk of adverse effects and to increase the likelihood of diagnosis ● Concomitant muscle biopsy increases likelihood of diagnosing vasculitis or sarcoidosis ● Commonly targeted nerves include: LE – sural, superficial peroneal, UE – superficial radial	● Rarely necessary ● Use as last resort when evaluation not definitive ● Greatest yield in multifocal neuropathies, or suspected amyloidotic polyneuropathy, vasculitis, sarcoidosis, lepromatous neuropathy, or rare hereditary disease where no genetic testing exists *Detects inflammation, amyloid deposits, tumor infiltration*	● Painful, often for months ● Risk of bleeding and infection

syndrome is aimed at decreasing flow through the access shunt.

In conclusion, this case highlights the importance of timely and systematic evaluation of peripheral neuropathy in the hospital setting. Neuropathy with rapid progression and high potential for permanent damage necessitates early neurologic, or in this case, vascular consultation. Hospitalists should be facile in evaluating peripheral neuropathies and recognizing the appropriate indications for diagnostic tests and procedures.

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