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Clinical Reasoning:

A 51-year-old woman with acute foot drop

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SECTION 1

A 51-year-old woman presented with sudden onset of weakness in her right leg and paresthesiae in the dorsum of her right foot. The symptoms began abruptly 2 hours earlier during her daily work as a housekeeper when she suddenly noticed a “double tap” sound on each step of her right foot. She denied any history of trauma to the lumbar spine or to the affected lower extremity. She had no habits such as crossing her legs, kneeling, or squatting.

The patient’s medical history was significant only for hyperlipidemia, smoking, and depression. No family members were reported to have neurologic disease.

Neurologic examination showed weakness of ankle dorsiflexion (Medical Research Council [MRC] grade 3/5) and great toe extension (MRC grade 3/5) in the right lower extremity. Foot eversion

was affected as well; however, inversion seemed to be preserved. Ankle and toe plantar flexion, knee flexion, as well as hip abduction, extension, and internal rotation, were normal. The Achilles tendon and patellar reflexes were elicited symmetrically (2+) on both sides. Close inspection did not reveal any area of local swelling or tenderness. Sensory examination demonstrated decreased sensation to pinprick on the dorsum of the right foot and the patient reported a vague discomfort in the lateral part of the right lower leg. She was able to walk unaided; however, she could not stand on the heel of her right foot.

Questions for consideration:

1. What is the differential diagnosis?
2. What is the most probable anatomic location of the lesion responsible for these symptoms?

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SECTION 2

In cases of foot drop, the clinician initially contemplates neurologic dysfunction at each level of the motor system from the corticospinal tract to the spinal nerve roots, the lumbosacral plexus, the peripheral nerves, the neuromuscular junction, and the muscles. The presence of focal muscle weakness in a nonpyramidal distribution without evidence of corticospinal tract impairment (e.g., increased tendon reflexes, positive Babinski sign) argues against central involvement. Several authors have described rare central causes of foot drop, such as lesions affecting the paracentral lobule¹ (e.g., parasagittal meningiomas, metastases, stroke). Likewise, disorders of the neuromuscular junction or the muscles are usually excluded because they generally manifest with diffuse weakness affecting bulbar, proximal, or distal muscles.

Therefore, foot drop is commonly attributed to lower motor neuron pathology and L5 radiculopathy is often suspected in the context of herniated nucleus pulposus or foraminal stenosis. The second most common cause is fibular (peroneal) neuropathy, particularly at the region of the knee. Preferential injury of fibular nerve fibers can also occur in the sciatic nerve, where the fibular division is separately encased from tibial fibers or at the lumbosacral plexus causing a clinical picture indistinguishable from true fibular neuropathy. The fibular division of the sciatic nerve is considered susceptible to injury because it comprises a smaller number of larger fascicles compared to the tibial division and supportive connective tissue is relatively sparse.

Clinical examination is to a degree an exercise of logical deduction where muscles belonging to the

same myotome but receiving innervation from different peripheral nerves are sequentially examined. In this setting, a diagnostic clue favoring fibular neuropathy is the preservation of ankle inversion. Specifically, ankle inversion is carried out by the posterior tibialis muscle that receives L5-S1 innervation from the tibial nerve. Moreover, ankle and toe dorsiflexion, as well as ankle eversion, are performed by fibular innervated muscles that likewise are partially supplied from the L5 root. Therefore, when ankle inversion is intact, this strongly suggests fibular neuropathy. Furthermore, in cases of L5 radiculopathy, toe extension tends to be more severely affected than ankle dorsiflexion because the extensor hallucis longus muscle receives the major bulk of its innervation from the L5 root. At this point, the exact site where fibular nerve fibers are damaged cannot be identified.

The fibular nerve is extremely vulnerable due to its superficial course particularly at the fibular neck, where the nerve is covered only by subcutaneous fat and skin.² Fibular neuropathy may result from penetrating trauma, operative injury, entrapment, habitual leg crossing or prolonged squatting, immobilization, and marked weight loss. Additionally, it is associated with conditions such as diabetes mellitus, alcohol abuse, malnutrition, polyarteritis nodosa and other systemic vasculitides, anorexia nervosa, bariatric surgery, and hereditary neuropathy with liability to pressure palsy. A subset of cases is due to compression from intraneural or extraneural masses such as ganglia, Schwannomas, neurofibromas, and osteochondromas.

Question for consideration:

1. What investigations would you recommend?

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SECTION 3

Neurophysiologic examination was performed on the third day. Motor nerve conduction study of the right fibular nerve showed a reduction of compound muscle action potential (CMAP) amplitude stimulating at the fibular neck (figure, A). Distal CMAP amplitude of the right fibular nerve was relatively lower compared to the left side. Additionally, the sensory nerve action potential (SNAP) amplitude of the right superficial fibular nerve was decreased (2 μ V, reference value >7 μ V). Motor tibial and sural sensory studies were normal.

Needle EMG of the right tibialis anterior and the right extensor digitorum brevis revealed spontaneous activity in the form of positive sharp waves and fibrillation potentials (+2). Motor unit action potential (MUAP) morphology was not indicative of denervation; however, motor unit recruitment was reduced. Examination of the right tibialis posterior and medial gastrocnemius was normal.

Questions for consideration:

1. How would you interpret the results of the electrophysiologic studies?
2. Would you recommend any further testing?

The above findings indicate conduction block (CB) of the right fibular nerve at the fibular neck. According to the consensus criteria of the American Association of Electrodiagnostic Medicine, CB is defined as a reduction of CMAP amplitude in

proximal vs distal stimulation exceeding 50% with minimal temporal dispersion (i.e., increase of CMAP duration by 30% or less).³ CB is considered the result of focal demyelination leading to failure of impulse propagation along the affected region.⁴

The distribution of sensory disturbances and the results of electrodiagnostic testing confirm that both the superficial and the deep branch of the common fibular nerve are involved. In addition, the reduction of the superficial fibular nerve SNAP amplitude on the affected side shows that apart from the localized demyelination documented from the motor study, axonal loss is also present. Accordingly, right fibular nerve distal CMAP amplitude is relatively reduced and denervation potentials are observed on the EMG. The latter are usually detected 2–3 weeks after nerve injury; hence axonal damage most likely was already present prior to the appearance of symptoms.

Our patient demonstrated reduced recruitment of normal-appearing MUAPs, a finding associated with subacute axonal and pure demyelinating lesions. Conversely, in chronic neuropathic disease, reinnervation of damaged muscle tissue from sprouting of surviving axons presents as polyphasic MUAPs with increased duration and amplitude. Normal tibial and sural studies, as well as the lack of denervation in nonfibular innervated muscles, rule out a coexisting lumbosacral plexopathy or L5 radiculopathy.

Considering there was no history of trauma or compression at the fibular neck, other disorders that are

Figure Electrodiagnostic testing, imaging, and intraoperative photograph

(A) Right fibular motor conduction study to the extensor digitorum brevis. Stimulation at the neck of the fibula produces a low-amplitude CMAP indicative of conduction block. (B) MRI sagittal T2-weighted image shows a high signal intensity lesion in the region of the proximal tibiofibular joint located along the anatomical course of the deep and superficial peroneal nerves (arrow). (C) Intraoperative photograph shows dilation of the proximal portion of the deep fibular nerve extending to the distal common peroneal nerve and the superficial fibular nerve. The articular branch is noted stemming from the proximal deep fibular nerve.

associated with mononeuropathies should be excluded. Complete blood count, erythrocyte sedimentation rate, fasting blood glucose levels, and hepatic and renal function tests were normal. Testing for antinuclear antibodies, antineutrophil cytoplasmic antibodies, antibodies against double-stranded DNA, anti-Sm antibody, Ro antigen, La antigen, and rheumatoid factor was negative. Serum protein electrophoresis and thyroid function were also normal. Serum antiganglioside antibodies (anti-GM1) were not detected.

On follow-up after 1 month, the clinical picture remained unchanged. An MRI of the right knee was performed. A lobulated cystic mass of longitudinal diameter approximately 2.5 cm, occupying the space between the proximal tibia and the fibular neck, was revealed (figure, B). It was located along the anatomical course of the deep and superficial fibular nerves. The lesion showed low to intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images. On T1-weighted images after gadolinium administration, the mass demonstrated a cystic appearance due to peripheral enhancement. These features were consistent with an intraneural ganglion cyst.

Surgical decompression was performed. An incision posterior to the fibular neck dissected the underlying fascia. Proximal enlargement of the deep fibular nerve (DFN) was revealed extending to the bifurcation of the common fibular nerve and the superficial fibular nerve (figure, C). An articular branch that emerged from the proximal DFN towards the proximal tibiofibular joint was recognized. The epineurium was incised and the content of the ganglion cyst consisting of jelly-like mucous material was removed. The articular branch was transected and ligated. Postoperatively the patient displayed significant improvement and several weeks afterwards only minor weakness of foot dorsiflexion remained. After 1 year, her condition remains stable without recurrence of symptoms.

DISCUSSION Intraneural ganglia are benign fluid-containing cystic masses most commonly found in the fibular nerve near the superior tibiofibular joint.^{5,6} However, they may arise in other sites, causing compression of peripheral nerves such as the median nerve at the carpal tunnel or the ulnar nerve at Guyon's canal.⁷ Patients usually seek medical attention due to weakness or sensory symptoms in the distribution of the affected nerve. A palpable mass is often noted in the region occasionally accompanied by local pain. A positive Tinel sign is usually present. Our case featured acute onset of symptoms during physical activity, which is rarely described in previous reports.⁸

There are 2 leading pathogenetic theories. The degenerative theory advocates that connective tissue

degradation of the epineurium or the perineurium is the key process leading to cyst formation. Alternatively, the articular theory posits that fibular ganglia formation is the result of cystic fluid migration from the superior tibiofibular joint through the articular branch.⁹ The inciting event is the development of a capsular defect in the knee or the superior tibiofibular joint as a result of trauma or other disorders that is followed by cystic enlargement of the articular branch. Fibers of the DFN closest to the junction with the articular branch are initially affected. At latter stages, proximal expansion may lead to involvement of the superficial peroneal nerve or even the sciatic nerve. Further support to the articular theory is the identification of a pathologic articular branch stemming from a nearby joint in cases of intraneural ganglia located in other nerves, such as the tibial and the median nerve.

Consequently, the persistent pathologic communication between the superior tibiofibular joint and the fibular nerve needs to be addressed in order to avoid postoperative recurrences. Previous studies have shown that ligation of the articular branch is a crucial determinant of outcome.¹⁰

Clinicians should retain a high index of suspicion for intraneural ganglion cysts in atypical cases of fibular neuropathy, even if local pain or swelling in the region of the knee are absent. Long-term success of surgical treatment relies to a great extent on performing careful ligation of the pathologic articular branch, thereby eliminating the underlying pathogenetic mechanism.

AUTHOR CONTRIBUTIONS

Dr. Rallis: outline of original manuscript, elaboration of clinical localization, differential diagnosis, revision of final draft. Dr. Skafida: electrodiagnostic testing, literature search, analysis of case discussion. Dr. Alexopoulos, Dr. Petsanas: design and implementation of surgical approach. Dr. Foteinos: interpretation of imaging studies. Dr. Katsoulakou: diagnostic evaluation, clinical follow-up. Dr. Koutra: review of neurophysiologic study, supervision of clinical care.

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