

Dynamic phases of peroneal and tibial intraneural ganglia formation: a new dimension added to the unifying articular theory

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Object. The pathogenesis of intraneural ganglia has been a controversial issue for longer than a century. Recently the authors identified a stereotypical pattern of occurrence of peroneal and tibial intraneural ganglia, and based on an understanding of their pathogenesis provided a unifying articular explanation. Atypical features, which occasionally are observed, have offered an opportunity to verify further and expand on the authors' proposed theory.

Methods. Three unusual cases are presented to exemplify the dynamic features of peroneal and tibial intraneural ganglia formation.

Results. Two patients with a predominant deep peroneal nerve deficit shared essential anatomical findings common to peroneal intraneural ganglia: namely, 1) joint connections to the anterior portion of the superior tibiofibular joint, and 2) dissection of the cyst along the articular branch of the peroneal nerve and proximally. Magnetic resonance (MR) images obtained in these patients demonstrated some unusual findings, including the presence of a cyst within the tibial and sural nerves in the popliteal fossa region, and spontaneous regression of the cysts, which was observed on serial images obtained weeks apart. The authors identified a clinical outlier, a case that could not be understood within the context of their previously reported theory of intraneural ganglion cyst formation. Described 32 years ago, this patient had a tibial neuropathy and was found at surgery to have tibial, peroneal, and sciatic intraneural cysts without a joint connection. The authors' hypothesis about this case, based on their unified theory, was twofold: 1) the lesion was a primary tibial intraneural ganglion with proximal extension followed by sciatic cross-over and distal descent; and 2) a joint connection to the posterior aspect of the superior tibiofibular joint with a remnant cyst within the articular branch would be present, a finding that would help explain the formation of different cysts by a single mechanism. The authors proved their hypothesis by careful inspection of a recently obtained postoperative MR image.

Conclusions. These three cases together with data obtained from a retrospective review of the authors' clinical material and findings reported in the literature provide firm evidence for mechanisms underlying intraneural ganglia formation. Thus, expansion of the authors' unified articular theory permits understanding and elucidation of unusual presentations of intraneural cysts. Whereas an articular connection and fluid following the path of least resistance was pivotal, the authors now incorporate dynamic aspects of cyst formation due to pressure fluxes. These basic principles explain patterns of ascent, cross-over, and descent down terminal nerve branches based on articular connections, paths of diminished resistance to fluid flow within recognized anatomical compartments, and the effects of fluctuating pressure gradients.

KEY WORDS • articular theory • cyst regression • fluid dynamics • ganglion cyst • intraneural ganglion • peroneal nerve • sciatic nerve • tibial nerve

UNTIL recently, descriptions of intraneural ganglia have centered on their static appearances. The unifying articular or "synovial" theory³³ we initially proposed was based on critical analyses of clinical, operative, and imaging observations as well as on assessments of reported cases. Using this theory, we sought to explain the most common form of intraneural cyst—that affecting the

peroneal nerve.³² More recently, the theory was validated with respect to the tibial nerve^{31,35} and corroborated by other authors as well.²⁷ In short, we have shown that intraneural ganglia have characteristic, stereotypical appearances.^{34,35} For example, peroneal and tibial intraneural ganglia arise from the anterior^{8,32} and posterior^{31,35} aspects of the superior tibiofibular joint, respectively, and extend intraepineurally via their own articular branches into the parent nerve, sometimes as far proximal as the buttock!^{13,42}

These observations, made at a single point in time and based on individual MR images and/or operative views,

Abbreviations used in this paper: EMG = electromyogram; MR = magnetic resonance.

provide us with important information. Admittedly, the observations are static representations, essentially a snapshot of a dynamic process. Therefore, we must take other factors into consideration, specifically intraarticular pressure and/or pressure gradients leading to dynamic fluxes over time. These could explain fluctuating clinical symptoms and signs^{1,9,25,32} as well as the broad spectrum of operative and imaging findings encountered.

We present three cases with multiple, apparently distinct intraneural ganglia in the popliteal fossa affecting the peroneal, tibial, sciatic, and sural nerves. These atypical features offer a unique opportunity to elucidate the pathogenesis of these cysts. Our purpose is to provide evidence demonstrating that if a peroneal or tibial intraneural ganglion arising from the superior tibiofibular joint extends proximally enough and has access to the common epineurial sheath of the sciatic nerve, it may cross over within the sciatic nerve and descend down all its terminal branches (that is, the peroneal, tibial, and sural nerves). Such a dynamic mechanism would support and extend our previously described unified articular theory of intraneural ganglion formation.

Summary of Cases

Case 1

After heavy lifting in a squat position, this 41-year-old man noted severe left shin and lateral malleolar pain extending to his big toe. Two weeks later he noted a partial footdrop, and 1 month later he noted numbness in his big toe. Because the man had a previous history of low back pain and had undergone L5–S1 instrumented posterior fusion 10 years earlier, epidurography with a transforaminal injection was performed. The following day the patient noted exacerbation of pain as well as complete footdrop, which persisted. He then underwent electromyography and MR imaging of his knee. The EMG showed complex changes in the man's peroneal neuropathy as well as L-5 radiculopathy. Interpretation of the MR images made at another institution documented a "fluid collection" around the sciatic nerve (Figs. 1A and 2A), which was deemed to be of indeterminate significance. The MR imaging report did not, however, identify the cyst as a primary peroneal intraneural ganglion (Fig. 2B) arising from the superior tibiofibular joint (Fig. 3) and having a secondary extension into the sciatic nerve (the proximal extent of which could not be seen) with a cyst involving the tibial and sural nerves as well (Figs. 1 and 2). Although the more typical cyst architecture was seen within the peroneal nerve at the fibular neck with a classic "signet ring" sign, the more proximal portions of the peroneal, tibial, and sural nerves as well as the distal sciatic nerves exhibited unusual features. These new MR images demonstrated concentric cystic expansion within the distal sciatic and proximal peroneal, tibial, and even sural nerves (Figs. 1 and 2). The maximal width of the lesion was 2.5 cm.

Examination disclosed complete deep peroneal nerve loss with essentially preserved peronei muscle function. Asymmetric toe flexion was also seen. Other tibial nerve-innervated muscles functioned normally. Sensation was diminished, more in the deep than in the superficial peroneal nerve distributions, but was normal on the plantar

aspect of the foot. A Tinel sign was elicited from the tibial nerve in the distal thigh and from the peroneal nerve over the fibular neck, where a mass could be palpated.

There was electrophysiological evidence of a predominant deep peroneal nerve lesion. There were 3+ fibrillation potentials in the tibialis anterior and peroneus tertius muscles and 1+ fibrillation potentials in the peroneus longus muscle. Electromyography of the medial gastrocnemius, posterior tibialis, and biceps femoris muscles yielded normal findings. Peroneal motor nerve conduction was absent. Tibial motor and sural sensory conduction were normal.

To our surprise, a repeated MR imaging study performed at our institution 3 weeks later showed near-complete resolution of the intraneural cyst. Only a small cyst could be seen to extend from the superior tibiofibular joint along the articular branch to the level of the sciatic nerve bifurcation (Fig. 4). There was marked abnormality of the peroneal nerve sheath extending to the sciatic nerve. It appeared thickened and showed signal enhancement on MR images. About 18 cm proximal to the knee joint, the sciatic nerve appeared normal. The tibial nerve distal to the bifurcation appeared slightly hyperintense over a distance of 2 cm. In addition, a small intramuscular, extraneural cyst was now seen (data not shown). Denervation changes in the anterior compartment were indicated by the appearance of hyperintensity and fatty changes in the muscles. Meniscal degeneration was present as was fragmentation of the tibial tubercle consistent with prior Osgood–Schlatter disease. Last, moderate degenerative changes were evident in the superior tibiofibular joint and mild changes in the knee joint.

At surgery, the abnormal-appearing medial component of the peroneal nerve was visualized. There seemed to be a nonexpanded cyst wall (Fig. 5). An enlarged articular branch connection to the superior tibiofibular joint was also seen. Cyst fluid was seen in the joint. The joint was resected, as was a portion of the articular branch. Histological analysis confirmed the diagnosis of intraneural cyst.

Postoperatively, the patient showed signs of recovering active dorsiflexion after a period of 4 months. Magnetic resonance images obtained at that time showed no persistence of cyst within the peroneal nerve or within the superior tibiofibular joint (Fig. 6). The man discontinued wearing his ankle foot orthosis 6 months after surgery and regained Medical Research Council Grade 4 foot dorsiflexion at 8 months and Grade 5- function at 1 year postoperatively.

Case 2

This 17-year-old boy injured his ankle skateboarding. Immediately thereafter he noted footdrop and complained of ankle pain and paresthesias of the dorsal foot. A diagnosis of ankle sprain and peroneal nerve palsy was made. On examination, the boy was found to have a complete lesion of the deep peroneal nerve with normal eversion but diminished sensation in the superficial peroneal nerve distribution. An EMG demonstrated marked changes in muscles supplied by the deep peroneal nerve with sparing of the short head of the biceps and marked slowing in peroneal nerve motor conduction velocity across the fibular neck. A superficial peroneal nerve sensory action potential was unobtainable. Magnetic resonance imaging performed 1 month after the injury revealed a multilocular cyst at the pe-

Peroneal and tibial intraneural ganglia formation

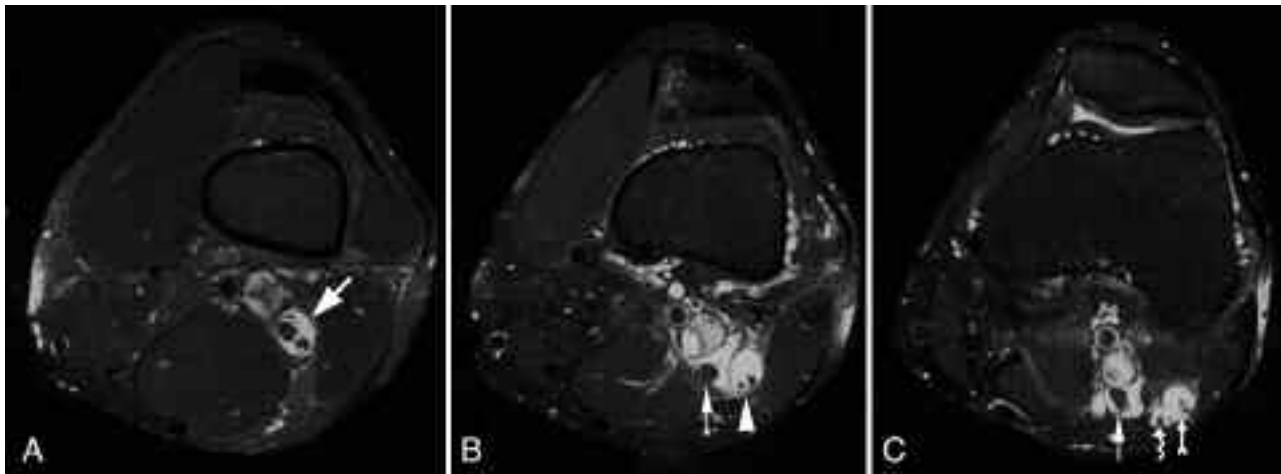


FIG. 1. Case 1. Initial axial MR images obtained at another institution. A: A T2-weighted fast spin echo (FSE) image with fat suppression showing the sciatic nerve with the tibial and peroneal divisions within the common epineurial sheath (arrow), which is surrounded by bright cyst fluid. B: A T2-weighted FSE image with fat suppression obtained distal to the site shown in panel A. Two separate epineurial sheaths, one containing the tibial nerve (arrow) and the second containing the peroneal and lateral sural cutaneous nerves (arrowhead), are demonstrated. Note that the nerves are located posteriorly within the cyst fluid in their individual sheaths. C: A T2-weighted FSE image with fat suppression obtained distal to the site shown in panel B. The tibial (straight arrow), lateral sural cutaneous (curved arrow), and peroneal (arrow with forked tail) nerves can be seen within three individual epineurial sheaths, each surrounded by cyst fluid. Reprinted from Spinner et al, *Neurosurg Focus* 22(6):E17, 2007.

ripheral posterior lateral knee region, which was believed to be a ganglion and an incidental finding (Fig. 7). A review of these films at our institution revealed a peroneal intraneural ganglion cyst arising from the superior tibiofibular joint, which extended proximally to the level of the sciatic nerve. In addition there was an intraneural cyst within the tibial and sural nerves at the level of the popliteal fossa. A surgical exploration was undertaken 6 weeks after the injury. A peroneal intraneural cyst was identified and decompressed but not resected. No joint connection was identified. Within weeks after the surgery, the patient recov-

ered Grade 2 toe extension and ankle dorsiflexion. Stability was maintained by use of an ankle foot orthosis.

The patient was referred for further evaluation 3 months after the initial injury. An additional EMG revealed a severe left common peroneal neuropathy below the branch leading to the short head of the biceps femoris muscle, which predominantly affected the deep peroneal nerve. An MR image demonstrated the peroneal intraneural ganglion cyst extending from the superior tibiofibular joint only to the level of the common peroneal nerve, approximately 1 cm superior to the fibular head. The maximal width of the

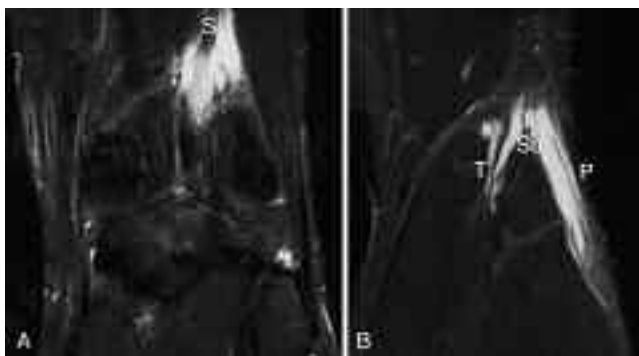


FIG. 2. Case 1. Initial coronal MR images obtained at another institution. A: A T2-weighted FSE image with fat suppression demonstrating the enlarged sciatic nerve (S) with surrounding cyst fluid. B: A T2-weighted FSE image with fat suppression showing the individual terminal branches of the sciatic nerve—the tibial (T), lateral sural cutaneous (Su), and peroneal (P) nerves—each in separate epineurial sheaths with the nerves in the center surrounded by cyst fluid. Available imaging did not include the most proximal extent of the cyst. The peroneal nerve has a multilaminar appearance. The joint connection to the peroneal intraneural ganglion is seen in Fig. 3.

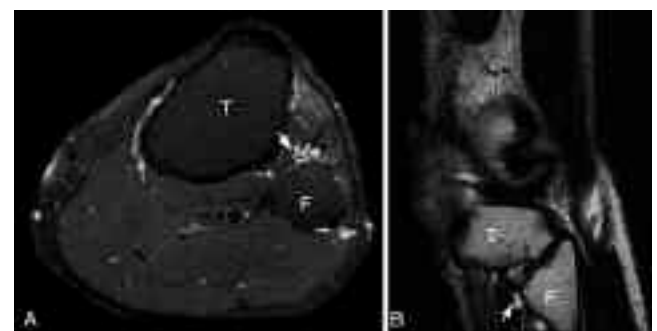


FIG. 3. Case 1. Initial MR images obtained at another institution. A: An axial T2-weighted FSE image with fat suppression demonstrating the more classic MR imaging appearance of a peroneal intraneural cyst involving the articular branch of the peroneal nerve with cyst extension along the transverse limb of the nerve (large arrow). Note the cyst located proximally within the common peroneal nerve (asterisk), which displays a signet ring sign depicting the nerve displaced by the cyst as well as a separate outer epineurial partial ring (thin arrow). B: A sagittal T2-weighted image showing the cyst connection to the anterior portion of the superior tibiofibular joint (arrow) and extension along the ascending portion of the articular nerve branch. F = fibula; T = tibia.

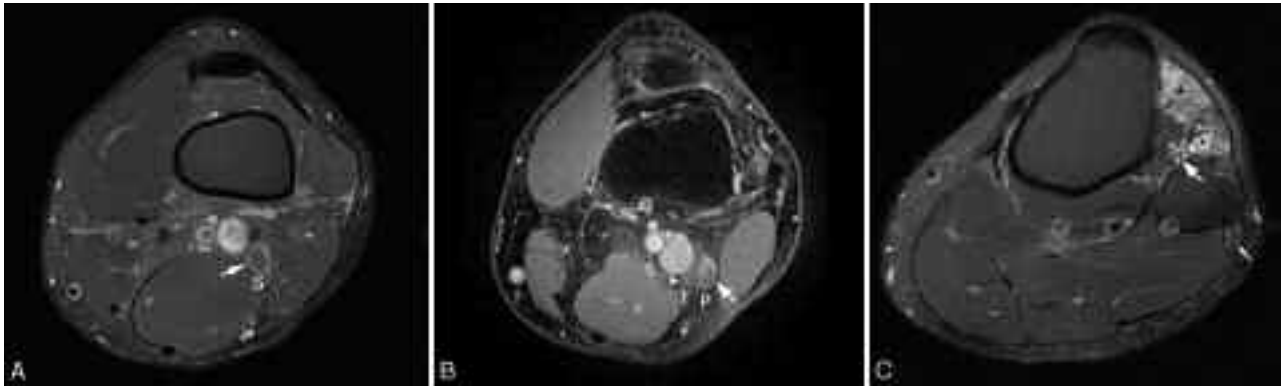


FIG. 4. Case 1. Axial T2-weighted MR images obtained at our institution 3 weeks after the images shown in Figs. 1 to 3, revealing spontaneous regression of the intraneural cysts. A: An FSE image with fat suppression showing a hyperintense ring of outer epineurial cyst (wedding ring sign) surrounding both divisions of the distal sciatic (S) nerve (*arrow*). B: An image obtained using the vastly undersampled isotropic projection reconstruction technique at the level of the distal thigh (just distal to the site shown in panel A, depicting a thickened, hyperintense rim (wedding ring sign) surrounding the peroneal (P) division of the distal sciatic nerve (*arrow*) with a trace of remaining cyst (*arrowhead*) within the tibial (T) division immediately adjacent. Both nerves are slightly enlarged and edematous. C: An FSE image with fat suppression showing an intraneural cyst within the transverse limb of the articular branch (*asterisk*) of the peroneal nerve. The common peroneal nerve (*thin arrow*) has a small residual circumferential cyst. Its connection to the superior tibiofibular joint can be seen (*thick arrow* indicates a tail sign). Note denervation changes in the anterior compartment musculature (*plus sign*).

cyst was 4 mm (Fig. 8A). There was no cyst within the distal sciatic, tibial, or sural nerves. In addition, the cyst now extended anteriorly from the superior tibiofibular joint along a capsular vein (Fig. 8B). There was an increased T2 signal within the anterior compartment consistent with denervation. There were moderate degenerative changes in the superior tibiofibular and knee joints and evidence of an acute ankle sprain with mild injury to the anterior inferior tibiofibular ligament.

Given the persistence of the cyst, surgery was recommended but deferred for 4 weeks so that the patient could attend his high school prom. By the time of the procedure, enlargement of the lesion and an essentially complete deep peroneal nerve lesion were noted. During surgery, we identified an intraneural cyst measuring 2.5 cm within the distal common peroneal nerve. The articular branch was also enlarged, and the cyst was traced to the superior tibiofibular joint. The superior tibiofibular joint was resected, and

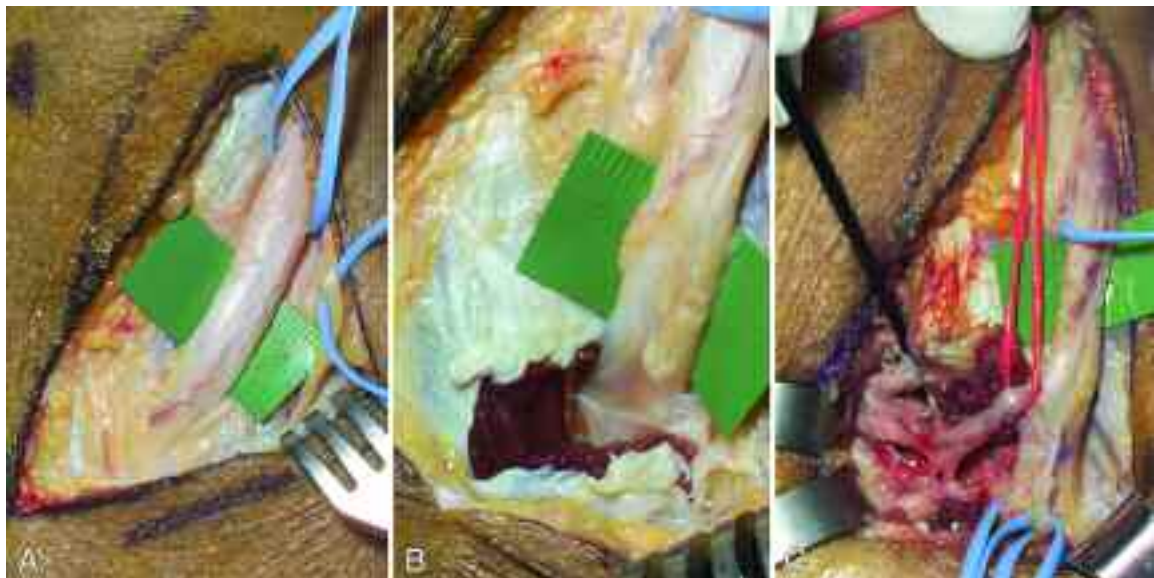


FIG. 5. Case 1. Intraoperative photographs. A: The abnormal-appearing medial component of the common peroneal nerve (over the *green background*) with a nonexpanded cyst wall. B: This unexpanded cyst wall extending to involve the most medial segment of the common peroneal nerve (over the *green background*) and, more distally, its articular branch portion at the entrance into the fibular tunnel. C: The slightly enlarged articular branch (in the *red vasooloop*), which is traced to the superior tibiofibular joint. Cyst was seen in the joint.

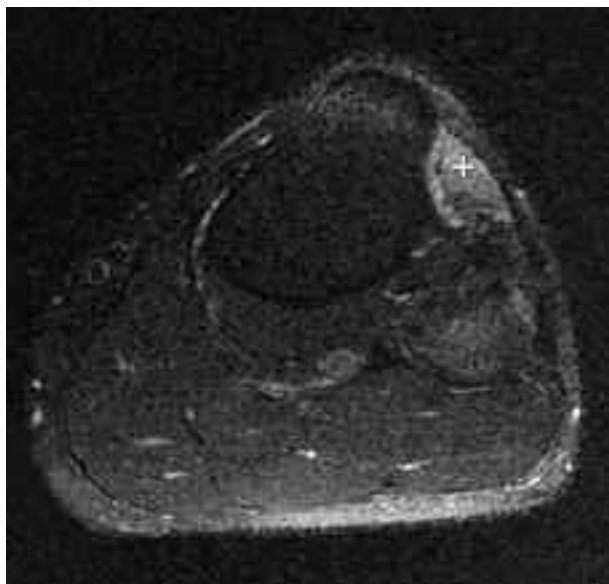


FIG. 6. Case 1. Postoperative axial T2-weighted FSE MR image with fat suppression demonstrating resection of the superior tibiofibular joint and no residual cyst. Note denervation in the anterior compartment muscles (*plus sign*).

the articular branch and capsular vein were ligated. The large cyst was then decompressed through a limited longitudinal incision. The cyst wall was not resected (Fig. 9), and the distal sciatic, tibial, and sural nerves were not exposed. The histological features of the lesion confirmed an intraneural cyst with adventitial extension (Fig. 10). An MR image demonstrated no cyst persistence at 3 months postoperatively (Fig. 11). The patient regained Grade 4+ ankle dorsiflexion and toe extension at 6 months and Grade 5- function at 1 year postoperatively.

Case 3

This patient was previously reported by other clinicians 32 years ago¹⁵ and was identified from our extensive literature review as being a clinical outlier. The patient was described as having intraneural ganglia involving several nerves without a joint connection; the pathogenesis of this anomaly was obscure.

The patient presented with left tibial neuropathy, which was localized to the popliteal fossa based on clinical and electrodiagnostic findings. No advanced imaging studies were available at that time. During surgery, he was found to harbor an extensive cyst within the sciatic nerve, which extended into the tibial nerve 9 inches distal to the knee and peroneal nerve (Fig. 12). The surgeon was able to remove the cyst while sparing the fascicles. Within 2 years postoperatively, the patient noted some mild neurological recovery.

The operative findings in this case could not be explained by our unifying theory as initially proposed. Based on our understanding of cyst pathogenesis and the patient's symptoms and findings, we predicted that modern MR imaging would visualize a residual joint connection to the posterior aspect of the superior tibiofibular joint due to the predominant tibial neuropathy. Demonstration of this joint connection would help explain both the cyst's unusual extension and the patient's present clinical status.

Despite marginal image quality due to technical parameters, the postoperative MR imaging examination did succeed in demonstrating a small cyst remnant arising from the posterior aspect of the superior tibiofibular joint (Fig. 13A). In addition, a short segment of cyst extending along the expected course of the articular branch of the tibial nerve was also identified (Fig. 13A). The cyst remnant arising from the joint represented an intraneural cyst within the articular branch of the tibial nerve, an appearance identical to that seen in other joint connections in tibial intraneural

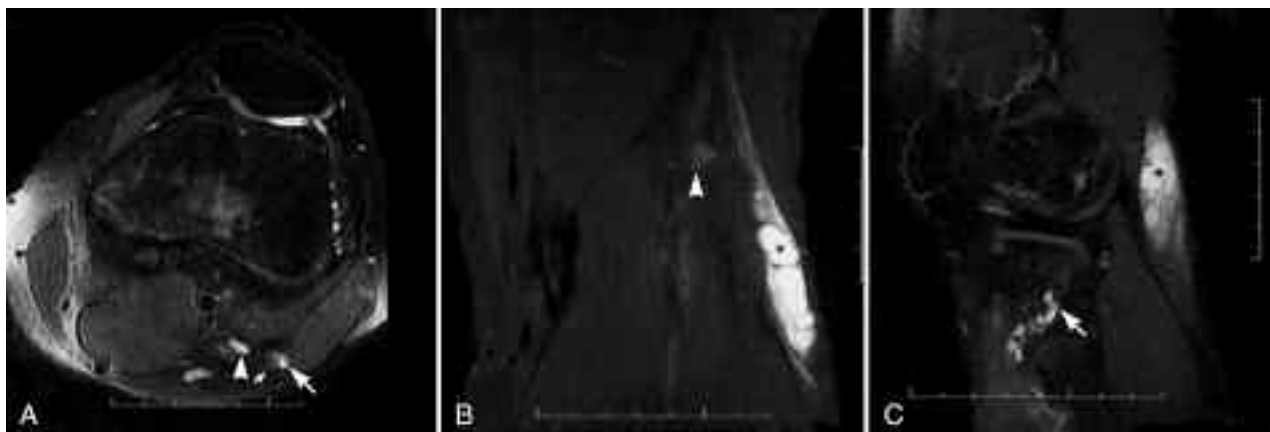


FIG. 7. Case 2. Initial MR images obtained at another institution. A: Axial T2-weighted FSE image with fat suppression obtained at just about the knee joint level, showing an intraneural cyst within the outer epineurium of the common peroneal nerve that is producing the signet ring sign (*large arrow*) and is surrounded by a thin circumferential cystic ring (*wedding ring [small arrow]*). There is also a cyst present within the outer epineurium of the tibial nerve (*arrowhead*). B: Coronal T2-weighted FSE image with fat suppression demonstrating the cyst extending along the course of the peroneal nerve (*asterisk*). Note an outer epineurial cyst associated with the tibial nerve, which is enlarged and hyperintense (*arrowhead*). The path of the cyst travels upward from the superior tibiofibular joint along the peroneal nerve and downward along the tibial nerve. C: Sagittal T2-weighted FSE image with fat suppression showing the multilocular cyst arising from the anterior superior tibiofibular joint (*arrow*) and extending along the course of the articular branch of the peroneal nerve. The larger, more proximal cyst extension into the common peroneal nerve (*asterisk*) is also visible.

ganglia arising from the superior tibiofibular joint.^{31,35} Magnetic resonance imaging showed prominent popliteus muscle and posterior compartment atrophy as well as mild atrophy of anterior compartment musculature (Fig. 13B), findings indicating preferential involvement of the tibial as opposed to the peroneal nerve. Severe degenerative joint disease at the knee and superior tibiofibular joint were also seen after the operation, similar to that seen in our other cases. Thirty-five years later, the patient stated that he still had moderate deficits in his tibial nerve and mild deficits in his peroneal nerve, symptoms that had remained unchanged for over three decades.

Discussion

Our unified theory, applied with some modification, explains the extensive cyst formation seen in the three cases described. All shared the cardinal imaging and operative features of peroneal and tibial intraneural ganglia—a cyst extending from a degenerate superior tibiofibular joint along an articular branch via an intraepineurial dissection following the path of least resistance. In Case 1 there was also evidence of coexistent extraneural extension of the cyst into muscle and in Case 2 into vascular adventitia—patterns we have seen previously^{33,36} that confirm the origin of these cysts in a pathological joint capsule. Our cases also exhibited two other unusual features: atypical cyst extension and cyst regression. Although seemingly trivial, these observations needed to be explained.

The explanation for the pathological anatomy we observed is rather simple and is based on understanding the anatomical constraints of a large nerve, specifically the layers of the epineurium. Terminology has varied,^{21,38,41} but our

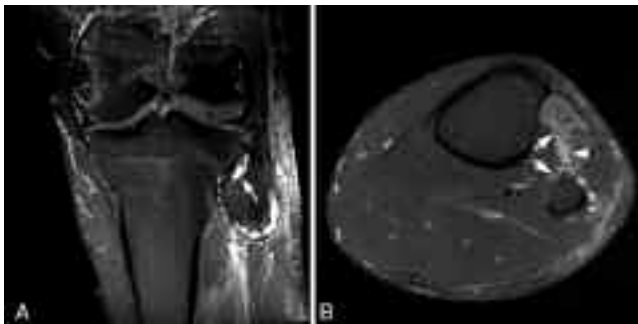


FIG. 8. Case 2. Magnetic resonance images obtained at our institution approximately 6 weeks after the MR images shown in Fig. 7 and 5 weeks after cyst decompression was performed at another hospital. A: Maximum intensity projection of a coronal T2-weighted FSE data set with fat suppression demonstrating the U sign of a typical peroneal intraneural cyst (arrow with dashed tail) with extension along the articular branch. A connection to the superior tibiofibular joint is also seen on this image (arrow). This image also shows the maximal proximal extent of the intraneural cyst, which is significantly smaller than that seen in Fig. 7. B: Maximum intensity projection of a T2-weighted axial FSE data set with fat suppression showing the path of the peroneal intraneural cyst along the transverse limb to the common peroneal nerve (asterisk) with anterior cystic adventitial extension (arrowhead) along the course of a small vein (arrows). The adventitial portion arises from the junction of the transverse and ascending limbs of the intraneural cyst. Note denervation changes in the anterior compartment musculature.

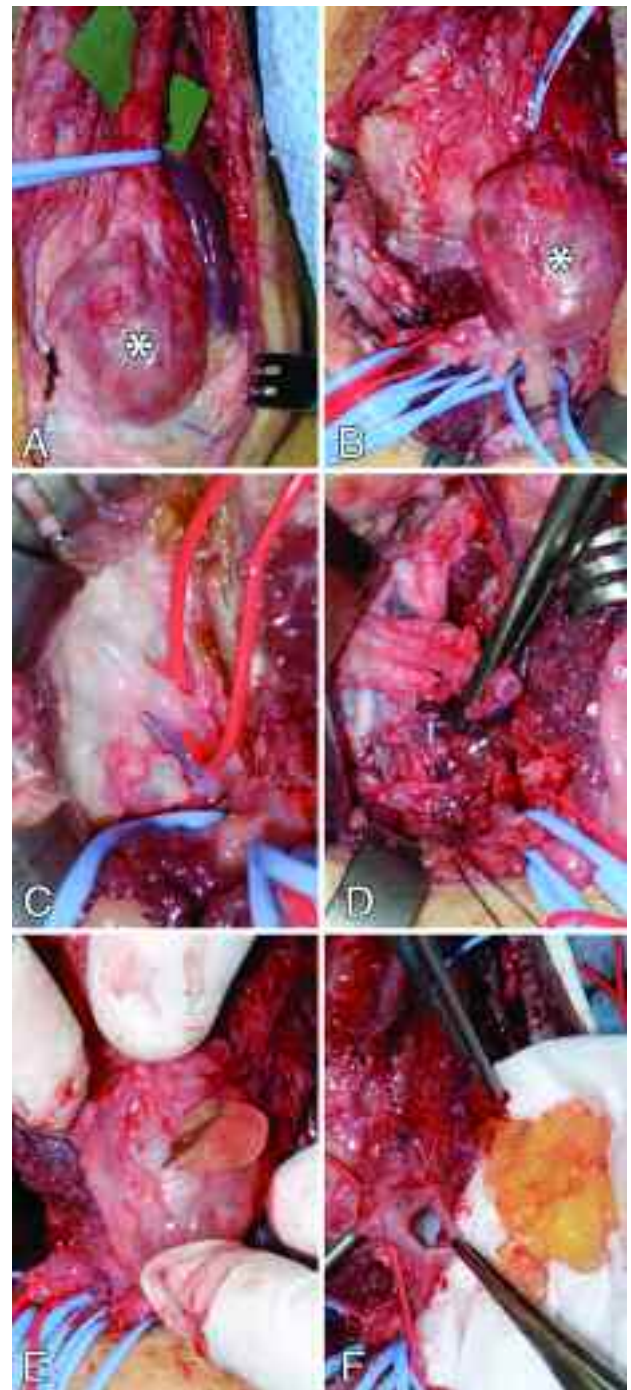


FIG. 9. Case 2. Intraoperative photographs obtained 4 weeks after MR images were obtained at our facility. A: The common peroneal nerve (against a green background). A large cystic expansion (asterisk) within the common peroneal nerve is noted just proximal to the fibular tunnel. B: The large peroneal intraneural cyst (asterisk) is mobilized; a more distal dissection allows identification and protection of the terminal branches of the common peroneal nerve in vasoloops. The red vasolooop encircles the articular branch. C: The cystic articular branch in the red vasolooop is directly adjacent to a cystic adventitial (venous) extension near the superior tibiofibular joint. D: The hollow cystic articular branch and vein have been divided and ligated. The superior tibiofibular joint is then resected (not shown). E: A small longitudinal incision is made in the peroneal intraneural cyst. F: A large amount of cyst is evacuated.

Peroneal and tibial intraneural ganglia formation

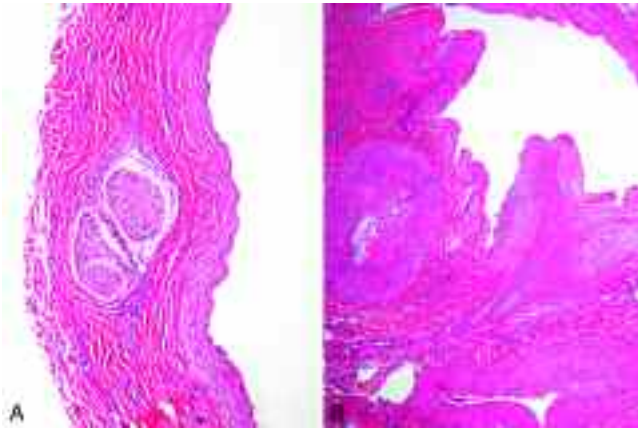


FIG. 10. Case 2. Photomicrographs. A: An intraneural ganglion cyst (on the *right side*) is involving the articular branch, represented by two small fascicles of myelinated nerve. The cyst resides within the epineurium. B: Perivascular adventitial extension of a ganglion cyst (shown in the *upper portion* of the panel), which also has an intraneural component (A). Note the muscular artery (*left*) and vein (*inferior*). H & E, original magnification $\times 160$ (A) and $\times 64$ (B).

use of terms is illustrated in Fig. 14. The epineurial (adventitial) sheath is a delicate, continuous fibrous tissue layer that encircles the outer (epifascicular) epineurium, a fibrofatty layer that in turn surrounds the inner (interfascicular) epineurium, which fills the space between fascicles. The latter are surrounded by a multilaminated perineurium, the basis of the nerve–blood barrier.

The outer epineurium is the common denominator that permits us to explain the pathological anatomy in our cases. By considering pressure fluxes and the continuous layer of the outer epineurium, we can explain bidirectional flow and the apparently separate albeit connected cysts involv-

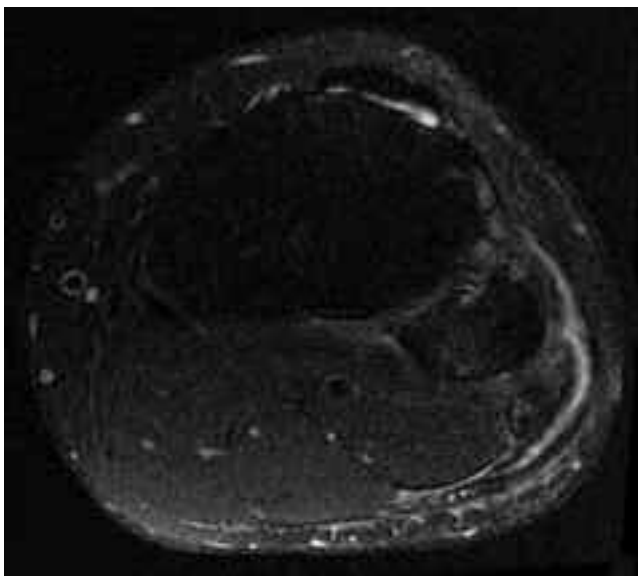


FIG. 11. Case 2. Postoperative axial T2-weighted FSE MR image with fat suppression showing resection of the proximal tibiofibular joint with no residual cyst. Note that postoperative changes appear superficially in lateral subcutaneous tissues

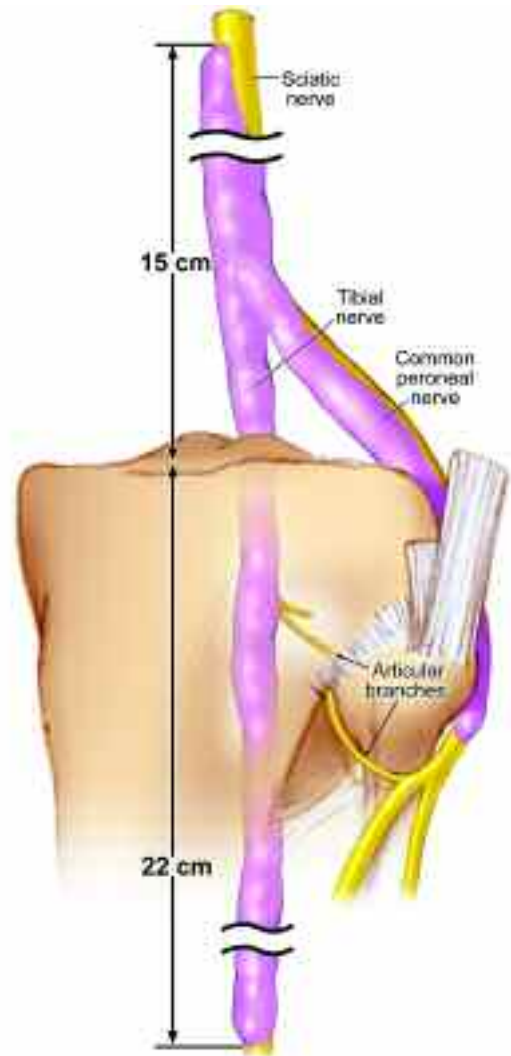


FIG. 12. Case 3. Artistic rendering of operative findings described in a report 32 years ago (Jacobs et al.). There is an intraneural cyst involving the sciatic, tibial, and peroneal nerves without a joint connection. No explanation for this pathological anatomy was made at the time.

ing multiple nerves. In dye studies, injection of the outer epineurium allows observation of primary ascent, sciatic cross-over, and terminal branch descent in an experimental model and a barrier between the outer and inner epineuria.^{37,41} We invoke these anatomically relevant data to draw a clinical corollary. We have identified three sequential phases of peroneal and tibial intraneural ganglia cyst formation (Fig. 15) that represent a dynamic chain of events and confirm our understanding of the pathogenesis of these cysts.

Three Sequential Phases

Phase I—Primary Ascent. Primary ascent may occur in one or more layers of the epineurium. In outer epineurial (epifascicular) cysts, this initial phase consists of eccentric cyst dissection from the superior tibiofibular joint, up the articular branch of the primarily affected nerve (either the

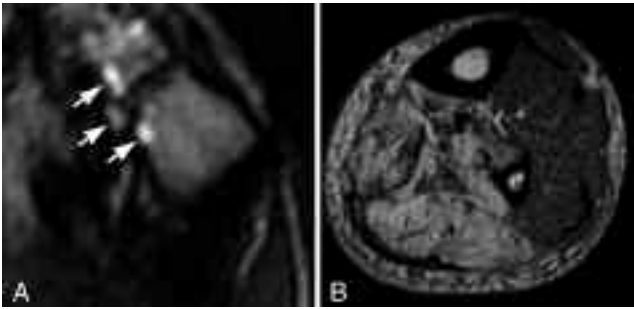


FIG. 13. Case 3. Magnetic resonance images providing proof of a remnant joint connection in this previously reported case. A: Coronal T2-weighted FSE MR image with fat suppression showing the residual cyst (*arrows*) arising from the posterior aspect of the superior tibiofibular joint. The image is suboptimal because of compromised spatial resolution, which is related to the large field of view and the poor signal-to-noise ratio. B: Axial T1-weighted FSE MR image through the midsection of the lower leg demonstrating profound fatty atrophy of the tibial nerve-innervated muscles in the posterior and deep compartments. Note complete popliteus muscle atrophy.

peroneal or tibial), to the level of the division of the sciatic nerve, typically located in the distal thigh. Phase I incorporates our previous published Stages 0 to 4.^{33,35} Depending on pressure fluxes, the cyst may either descend down the affected nerve or regress, presumably along the same intraepineurial path it ascended. In contrast, inner epineurial (interfascicular) cysts, rather than those within the outer epineurium, can continue their primary ascent between fascicles solely within the peroneal or tibial division of the sciatic nerve.

Phase II—Sciatic Nerve Cross-Over. Cysts having access to the outer epineurium can cross over when they extend to the level of the sciatic nerve bifurcation. At that point, the peroneal and tibial nerves form the sciatic nerve, their two epineurial sheaths coalescing to form a common connective tissue sheath surrounding their individual outer epineuria. At this point the cyst may partially or completely surround the sciatic nerve, encircling the neural elements—in essence, filling a potential space with cyst fluid (producing a “wedding ring” sign²⁹). Thus transit of the cyst from the peroneal to the tibial division, or vice versa, is facilitated. A linear streak could be seen in several cases and was also produced in our anatomical study;³⁷ a jet of injected ink was seen to ascend primarily within the outer epineurium of the division of the sciatic nerve even more proximal than the level of intrasciatic nerve cyst cross-over. In contrast, given the anatomical boundaries of the inner epineurium, a cyst contained within it cannot cross over unless there is a fenestration in the epineurium.

Phase III—Terminal Branch Descent. If cross-over occurs within the sciatic nerve, descent down the individual outer epineuria of the terminal branches may ensue. The process and degree of descent and circumferential filling depends on pressure gradients. Cyst fluid can pass into the peroneal or tibial nerves as well as sural nerve branches. Several cyst segments are thereby derived from one intraneural cyst and its joint connection. In some cases, Phase III may be seen without MR imaging evidence of Phase II, as this phase may not be captured in a timely fashion on MR images.

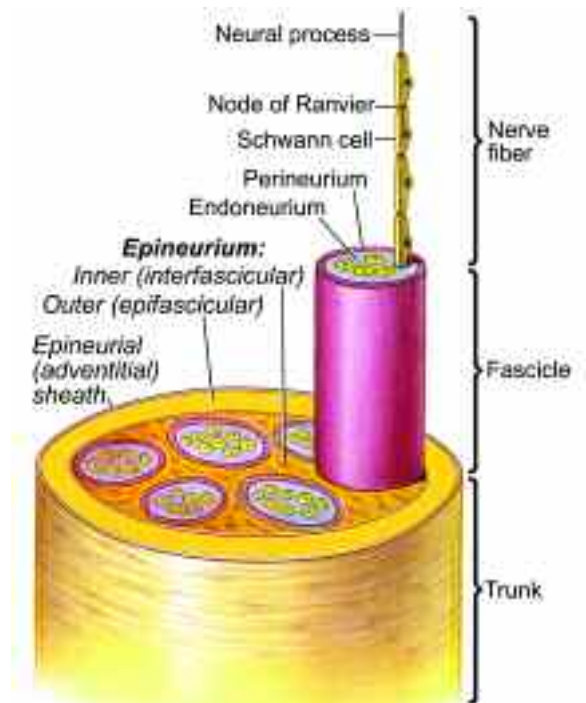


FIG. 14. Drawing showing the layers of a major peripheral nerve with attention to those of the epineurium.

Physiologically, however, Phase III will not occur without Phase II.

Pressure, Fluxes, and Dynamic Appearances

It has become apparent to us that the size, shape, and extent of a cyst vary depending on fluid pressures. Intra-articular pressures are increased with exercise, joint motion, and in the setting of degenerative joint disease. These factors contribute to intraneural cyst propagation. The frequently seen multilobular appearances of some cysts suggest pulsatility. Multilaminar flow (as seen in Fig. 2) also highlights the pulsatility occurring along different cleavage planes within the epineurium, the fluid following different paths of least resistance. Similarly, a small cyst neck at the articular branch connection becomes expansive more proximally. Such is the case in the common peroneal nerve proximal to the fibular tunnel^{32,33} and in the tibial nerve within the popliteal fossa.³⁵ With increased intraarticular pressure and perhaps associated inflammatory change, cyst fluid may extend from the proximal leg to as high as the buttock.^{13,42} Opposing pressures could be generated by numerous factors, including gravity, muscular contraction, external compression of the thigh, or even cyst or joint capsule rupture. The relationship of pressure to cyst formation is commonly seen in popliteal cysts (Baker cysts), which are known to be associated with intraarticular pathological conditions of the knee. Patients typically note a fluctuating course and variation in cyst size dependent largely on worsening of knee effusions.^{16,43}

To date, relatively few cases of intraneural ganglia with sciatic involvement have been described.^{13,15,17,18,42} We be-

Peroneal and tibial intraneural ganglia formation

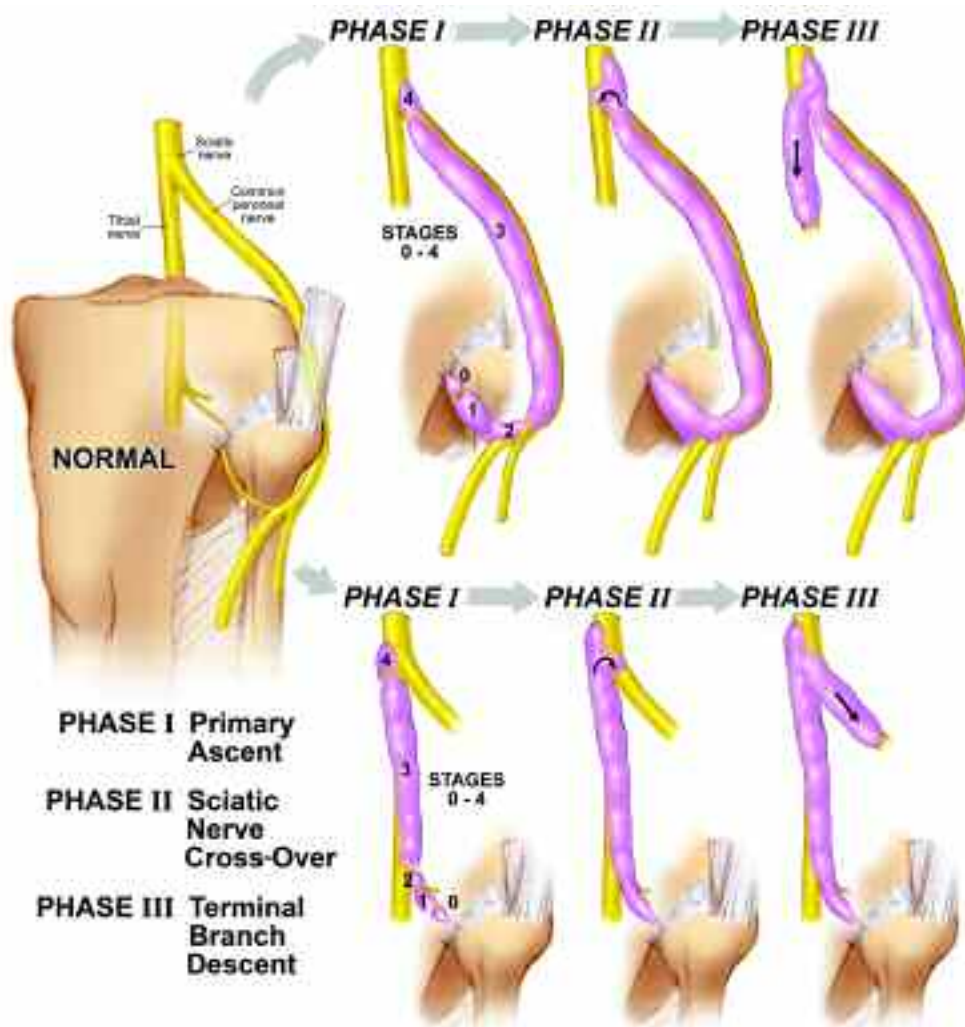


FIG. 15. Drawing showing the dynamic phases of peroneal and tibial intraneural ganglia formation. Phase I represents the primary ascent of the intraneural ganglia derived from the superior tibiofibular joint up the peroneal or tibial nerve. Stages 0 through 4 of Phase I summarize the proximal extension from the superior tibiofibular joint based on our previous descriptions. Phase II represents the cross-over within the single epineurial sheath of the sciatic nerve. A linear streak could be seen in several cases and was also produced in our anatomical study (Spinner et al, *Clin Anat* 2007). A jet of injected ink was seen to ascend primarily within the affected division of the sciatic nerve even more proximal than the level of intrasciatic nerve cyst cross-over. Phase III represents the descent down the terminal branches of the sciatic nerve.

believe that these form as a result of an increase in intra-articular pressure. Although joint connections were not described in these reported cases, we believe that they were present but unrecognized. Indeed, we proved this retrospectively in one such case³⁵ by demonstrating a joint connection in a “sciatic intraneural ganglion,” which the original authors failed to identify.¹⁷ This particular case actually represented an example of a tibial intraneural ganglion cyst extending from the posterior portion of the superior tibiofibular joint into the sciatic nerve to the mid-thigh level. It is not surprising that the farther a cyst appears to be located from a joint, the less often a connection is identified. In our experience, inability to identify a joint connection is due to the following: 1) technical limitations of resolution on MR images, 2) a radiologist’s or surgeon’s inexperience or lack of familiarity with the entity, or 3) inadequate visualization of the joint of origin. This is well illustrated in cases of per-

oneal or tibial intraneural ganglia as well.^{12,19,40} In one published instance, a case of a peroneal intraneural ganglion that extended to the buttock,⁴² rapid cyst recurrence was noted near the superior tibiofibular joint. These findings suggest to us that a joint connection exists in the other reported cases of tibial and peroneal ganglia extending into the sciatic nerves. Thus, the term “sciatic intraneural ganglion”^{17,18} is a misnomer in that it brings to mind de novo formation within the nerve rather than proximal extension of a joint-related cyst.

The presence of pressure fluxes in cysts contained within differing anatomical barriers not only can be used to explain their primary ascent but also the potential for cross-over within the sciatic nerve and descent in terminal branches. The findings of multiple cysts were readily apparent in Cases 1 and 3 but were more subtle in Case 2. Although the primary intraneural lesion is typically symp-

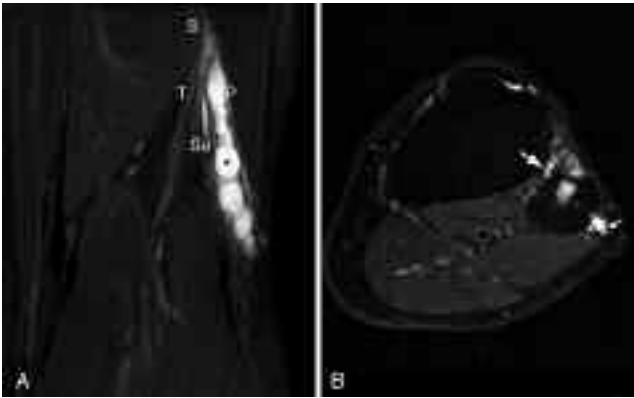


FIG. 16. One patient that we previously reported on (Spinner et al, *J Neurosurg* 99:330–343, 2003) presented with a deep peroneal nerve lesion and mild symptoms of a tibial sensory neuropathy. Although a lengthy peroneal intraneural ganglion derived from the superior tibiofibular cyst was noted initially (Phase I), the subtle evidence of extension into the sciatic nerve (Phase II) and descent into the terminal branches (Phase III) was only noted retrospectively. Nevertheless, surgery addressing the superior tibiofibular joint, the articular branch, and the peroneal cyst led to full recovery of neurological function and the postoperative MR images documented elimination of all intraneural cysts (not shown). A: Coronal FSE T2-weighted MR image with fat suppression demonstrating the primary cyst (*asterisk*) within the peroneal nerve (P), which extends upward to the sciatic confluence (S) with an outer epineurial descent of the cyst into the sural nerve (Su) toward the knee and the tibial nerve (T) just distal to its origin. B: Axial FSE T2-weighted MR image with fat suppression obtained at the level of the superior tibiofibular joint showing the cyst arising from the anterior portion of the joint (*large arrow*). The cyst was also noted intraneurally within two components of the outer epineurium of the common peroneal nerve (*asterisk* [signet ring sign] and *thin arrow* [wedding ring sign]) and intraosseously within the fibular head.

tomatic, other intraneural lesions may be subclinical. With proximal primary ascent into either the common peroneal or tibial nerve, the cyst tends to be eccentrically located. On MR images this typically results in the signet ring sign.³⁴ When a cyst has access to the outer epineurium within the sciatic nerve, the MR imaging appearance is completely different, resulting in a wedding ring sign pattern due to cyst encirclement of the nerve, when it is fully expressed. This pattern is maintained in the descent phase in varying degrees within the proximal tibial, peroneal, and sural nerves.

The clinical manifestations of pressure fluxes described herein are not isolated findings. The potential for cyst regression/enlargement and proximal extension with cyst cross-over and descent is underappreciated. This is likely due to failure to undertake serial imaging over time, incomplete imaging of the proximal extent of cyst involvement (as in the cases illustrated in Figs. 2 and 16), or simply to a lack of recognition of the process. We were gratified to identify these previously unrecognized, atypical clinical and imaging patterns in several of our patients as well as in published cases. We can cite several examples.

In one case in our previously published series,³³ we did not recognize an apparent discrepancy between the clinical and MR imaging findings. The patient had fluctuating symptoms. An intraneural cyst extended into only a portion of the articular branch of the peroneal nerve but none-

theless caused deep peroneal nerve dysfunction. An MR image showed denervation atrophy of all the anterior compartment muscles, thus substantiating deep peroneal nerve involvement. Retrospectively, we believe that this represents a case wherein the more proximal cyst extension regressed—given that it was not visible on imaging or at surgery—but left distal disease in place. Although a small nerve emanating from the articular branch does innervate the tibialis anterior muscle, simply its involvement by cyst would not explain the full clinical picture or the MR imaging findings. Similar intermittent fluctuating symptoms and findings, documented on serial examinations in Cases 1 and 2 in this paper, have been described by others as occurring in patients with intraneural ganglia;^{1,9,25,32} these dynamic changes in intraneural cysts are directly analogous to those seen in other types of cysts, ranging from common ganglion cysts to extraneural ganglia at the superior tibiofibular joint or spinoglenoid notch,^{7,23} spinal facet-related cysts,^{4–6,11,14,20,22,39} and rare adventitial cysts.^{3,24,26,28}

Nevertheless, other examples of proximal extension of a cyst into the sciatic nerve² or of distal descent of a cyst into its terminal branches⁴⁰ have gone unrecognized on MR images (Fig. 16). Additional subtle MR imaging findings that can be used to help identify and characterize these dynamic features are further elaborated on in a separate publication; we show that cyst extension into the sciatic nerve is underreported and underrecognized.²⁹

With pressure fluxes, we also need to consider the phenomenon of distal descent. In Case 3 considerable cyst descent was demonstrated within the tibial nerve component; the cyst traveled 9 inches below knee level—in other words, distal to the level of the superior tibiofibular joint. Whether an intraneural cyst that is primarily connected to the joint and undergoing ascent (Phase I) has a greater propensity to cyst descent (Phase III) than secondarily involved nerve(s) (for example, our published Case 3¹⁵) is unknown. Can a common peroneal nerve cyst that is derived from the superior tibiofibular joint and in the process of resolution or retreat extend down the deep peroneal or superficial peroneal nerves distal to the superior tibiofibular joint? We do not know if this is possible but believe it is plausible. To our knowledge, there is only one report of distal descent of a cyst into the deep peroneal nerve.¹⁰ Our review of the single MR image published in that report suggests that the joint-related lesion was an intramuscular rather than an intraneural cyst.

The fact that fluid dynamics underlie the formation of the cysts under discussion has certain treatment implications. That cysts can regress spontaneously lends support to the opinion that surgical approaches limited to the source of the problem—that is, the joint synovium, the capsular rent, and/or the articular branch connection—are preferable to attempts at radical resection of cysts. Recurrent cyst was not noted clinically or on postoperative MR images, despite the fact that the tibial and sural cysts were not decompressed in Cases 1 and 2 and the case represented in Fig. 16. In our experience mild postoperative changes are not uncommon and usually resolve over time because the joint connection has been obliterated. In contrast, if the joint connection has not been addressed at the operation, these fluid dynamic changes can lead to postoperative cyst reformation and further, even massive extension. It is conceivable that even a small intraneural cyst remnant could lead

to recurrence, perhaps even cross over and descend within previously unaffected terminal branches. This highlights the need for careful, long-term follow-up and suggests a benefit to eliminating any cyst remnant. In our experience, given that we have always disconnected and/or ligated the joint–nerve connection, we have not observed intraneural cyst recurrence or progression.

Could There be Another Explanation?

This unified theory is predicated on a joint–cyst connection originating either from a capsular rent, as seen with arthrography,³⁰ or from a synovial herniation. To us, the finding of an intraneural cyst not connected to a joint would be inconsistent with direct synovial herniation. We certainly also considered the possibility that such cases could represent exceptions to the unified theory. De novo multifocal cyst formation occurring from a degenerative process affecting three neighboring nerves does not seem likely, especially at locations away from a joint. Furthermore, it does not seem logical for two distinct pathological processes to be involved, that is, formation of one cyst from the joint (articular theory) and two separate cysts on the basis of some other process. As proponents of a unified articular theory³³ and Occam's razor, we believe that the finding of joint pathological conditions and cyst–articular connections is not coincidental but causal.

Conclusions

The pathogenesis of the intraneural ganglion cyst has been an issue of controversy for longer than a century. Despite many reports of such ganglia arising de novo without joint connections (degenerative theory), we believe that we have recently demonstrated the true nature of these cysts based on a unifying articular or “synovial” theory.³³ In fact, peroneal and tibial intraneural cysts share certain characteristic clinical, imaging, operative, and histological features that make their anatomical appearances predictable, stereotypical, and understandable.

A careful scrutiny of our atypical cases and of the literature has expanded our appreciation of the spectrum of presentations and imaging appearances assumed by intraneural cysts. It has certainly deepened our understanding of the mechanism(s) underlying their formation. These clinical observations have validated the articular theory. In summary, we have presented a dynamic explanation of intraneural cyst pathogenesis based on imaging, operative, and experimental evidence. The common principles for peroneal and tibial intraneural ganglia include the following: an articular branch connection from a degenerative joint; cyst extension along the path of least resistance;³³ and, ultimately, cyst dimensions and distributions determined largely by pressure fluxes, which in some cases can lead to the formation of multiple intraneural ganglia.

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