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CLINICAL ARTICLE

Extreme subparaneurial ganglion cysts. Part 1: Principles and implications

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OBJECTIVE The formation and propagation of intraneural ganglion cysts (INGCs) is being elucidated by the unified articular theory. Its principles include a connection for joint fluid to egress from a synovial joint via an articular branch to a parent nerve and cyst following the path of least resistance, dependent on pressures and pressure fluxes. The occurrence of so-called extreme peroneal or tibial INGCs in the popliteal fossa extending to the sciatic nerve has been reported. One rarely described variant with a circumferential cyst within the subparaneurial compartment outside the epineurium of nerve(s) has been previously illustrated, but its mechanism and morphology have not been clarified. In this study, the authors aimed to investigate this type of cyst to challenge the principles of the unified articular theory.

METHODS Four novel cases of patients with peroneal INGCs and "extreme subparaneurial cyst(s)" of the sciatic nerve and its distal branches were investigated: 3 arose from the superior tibiofibular joint (STFJ) and 1 from the knee joint. Three other cases of recognized extreme subparaneurial cyst (2 peroneal and 1 tibial from the STFJ) and 1 case of a peroneal subparaneurial cyst in the literature were reinterpreted. Data on clinical presentation, MR images, and surgical results were analyzed.

RESULTS In all 8 cases, subparaneurial extension was observed to different degrees along the sciatic, tibial, common peroneal, sural, and deep and superficial peroneal nerves, as was subparaneurial-to-subparaneurial communication at the sciatic nerve bifurcation (i.e., crossover). Sequential MRI performed in 7 patients showed variable dynamic changes, including extreme ascent and descent. Extraneural rupture of the subparaneurial cyst, with spread into the surrounding tissue, was present at the sciatic nerve bifurcation in 6 cases.

CONCLUSIONS The authors provide pathoanatomical and pathophysiological evidence supporting that extreme subparaneurial cysts follow the principles of the articular theory. They propose a distribution pattern that explains the occurrence and evolution of extreme subparaneurial cysts along the sciatic nerve and its distal branches in patients with peroneal or tibial INGCs and subepineurial cysts. Crossover in the subparaneurial compartment allows potentially extensive circumferential distribution within connected nerves. Also, dynamic factors can lead to dramatic changes in cyst size and appearance from reabsorption or extraneural rupture. In Part 2 of this study, the authors provide evidence showing that a fenestration in the epineurium allows cysts to pass from the subepineurial-to-subparaneurial, subparaneurial-to-subparaneurial, and subparaneurial-to-subepimyseal compartments.

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KEYWORDS peripheral nerve; MRI; intraneural; layer; ganglia; evolution; extension; propagation; distribution; compliance; pressure fluxes; rupture; tumor; neurosurgical education

Intraneural ganglion cysts (INGCs) are mucinous cysts that are usually located below the epineurium of peripheral nerves. The common peroneal (fibular) nerve (CPN) at the fibular neck is the most common site for INGCs to occur. The formation and propagation of INGCs is being elucidated. In 2003, the unified articular (synovial) theory[1] was introduced to explain the pathophysiological mechanism by which cyst formation and

ABBREVIATIONS CPN = common peroneal nerve; DPN = deep peroneal nerve; EHL = extensor hallucis longus; INGC = intraneural ganglion cyst; MRC = Medical Research Council; SPN = superficial peroneal nerve; STFJ = superior tibiofibular joint; TA = tibialis anterior; TE = toe extension; TN = tibial nerve.

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propagation occurs. Using the CPN as the prototype, cyst fluid exits from the anterior aspect of the superior tibiofibular joint (STFJ) along the articular branch into and along the CPN (i.e., the parent nerve). The fluid may become thickened (mucoid cyst) as it is no longer contained within the joint. Depending on intra-articular pressure and pressure fluxes and the path of least resistance, the cyst may have variable extents and attain considerable size or length. It ascends below the epineurium of the CPN (phase I, primary pathway), characteristically taking on a balloon-like appearance;[2,3] crosses over at the distal sciatic nerve bifurcation (phase II);[4] and descends within the CPN (phase IIIA) and tibial nerve (TN; secondary pathway) (phase IIIB).[5,6] Analogously, this theory may explain the propagation of tibial INGCs arising from the posterior aspect of the STFJ along a tibial articular branch extending to the sciatic nerve and crossing over to the CPN.[7] These principles have been demonstrated at many other synovial joints, including the knee, using articular anatomy supported by Hilton's law[8] and have been widely supported.[9]

The extension of INGCs arising from the STFJ or knee joint to the sciatic nerve in the thigh or lower buttock is rare,[10–17] and these cysts have been called "extreme."[18] Reports of such INGCs described prior to MRI concentrated on extent, but not on the morphology or pathophysiological mechanism.[19–22] One intriguing type of extreme INGC, which was first reported in 2007,[6] has a component of the cyst within the epineurium (subepineurial cyst) in addition to cyst outside the epineurium, under a separate layer called the paraneurium (or circumneurium[23]). This type of cyst was termed a subparaneurial ganglion cyst, a description that included both circumferential and partial circumferential cysts.[5] In this article, we look in more detail at cases of "extreme subparaneurial ganglion cysts." This extreme type of extreme cyst has been illustrated before but is not understood. We therefore investigated this type of extreme subparaneurial ganglion cyst to challenge the principles of the unified articular theory.

Methods

The clinical records and MR images of all novel cases of patients with extreme subparaneurial ganglion cysts evaluated at the Mayo Clinic and Haaglanden Medical Center between 2001 and 2023 were retrospectively reviewed. We also reviewed our prospectively maintained literature database of approximately 1000 cases of INGCs[24] to identify and reinterpret any identified case of a recognized or unrecognized MR image supporting a peroneal or tibial subparaneurial ganglion cyst from the STFJ or knee joint.

Strict inclusion criteria were used to define extreme subparaneurial ganglion cysts, including 1) the presence of a substantial (thick) circumferential cyst in the subparaneurial space around the epineurium of the affected parent nerve, which can be observed on axial images (Fig. 1A); 2) the extension of the circumferential cyst in the subparaneurial space over long distances, including the sciatic nerve for peroneal or tibial INGCs, which can be observed on sagittal and/or coronal images (Fig. 1B and C); and 3) the presence of a circumferential subparaneurial cyst in another affected nerve, such as a branch below the sciatic nerve bifurcation (e.g., sural communicating branch), or nerve(s) distal to the parent nerve or in the opposite (secondary [cruciate]) pathway (due to extreme extension into the sciatic nerve and crossover at the level of the sciatic nerve bifurcation, and descent into the CPN or TN). Cases with (thin) small amounts of circumferential cyst in the subparaneurial space (such as the wedding ring sign[6]) and cases with signs suggestive of cyst rupture within the subparaneurial space, but not fulfilling the abovementioned criteria, were excluded.

Clinical Assessment

Patient age and sex were noted, as well as duration of symptoms at presentation, distribution of pain symptoms, sensory deficit, and any motor weakness in TN and CPN innervated muscles. Surgical notes were reviewed. The outcome was reported for the recovery of symptoms, sensation, and motor weakness using modified Medical Research Council (MRC) grading.

MRI Analysis

All available MR images were reviewed to characterize the origin, extent, and morphology and propagation patterns of these INGCs. Interpretation was performed by fellowship-trained musculoskeletal radiologists (K.K.A. and B.M.H.) and neurosurgeons (G.C.W.D.R. and R.J.S.), all experienced with the diagnosis and treatment of INGCs. Several MRI examination sessions were performed focusing on different aspects, including joint connections, distribution of cyst at different levels and in different compartments of the sciatic nerve and its distal branches, and dynamic changes of cyst(s) over time.

MRI signs were assessed using T2-weighted images. Joint connections were determined by the presence of a tail sign.[25] The presence and size of a subepineurial cyst eccentrically within the parent nerve was evaluated for a signet ring sign[25] (for a cyst involving the CPN, this cyst would be localized to the deep peroneal nerve [DPN] fascicular bundle). Evidence of sciatic crossover was determined by the presence of a subparaneurial cyst along the sciatic nerve and all its distal nerve branches (TN, CPN, sural communicating branches, DPN, and superficial peroneal nerve [SPN]). Different degrees of subparaneurial extension were thereby distinguished, including thin, faint cyst(s) concentrically around the epineurium of nerve(s), creating a wedding ring sign or more prominent cyst(s) assuming an owl-eye appearance (owl-eye sign, previously called an extreme wedding ring sign[6]) on axial images (Fig. 1A). Evidence was also determined by a long segment of smooth, continuous cyst fluid with a parallel hyperintense signal in the outermost layer of the nerve creating a tram-track appearance[26] on coronal or sagittal images (Fig. 1B and C). Subparaneurial-to-subparaneurial communication was best seen on coronal images (Fig. 1B and C). Finally, the presence of a cyst within a cyst (i.e., subepineurial cyst within a nerve with a circumferential subparaneurial cyst) was noted on axial images (Fig. 1D).

Dynamic changes were analyzed by comparing MR

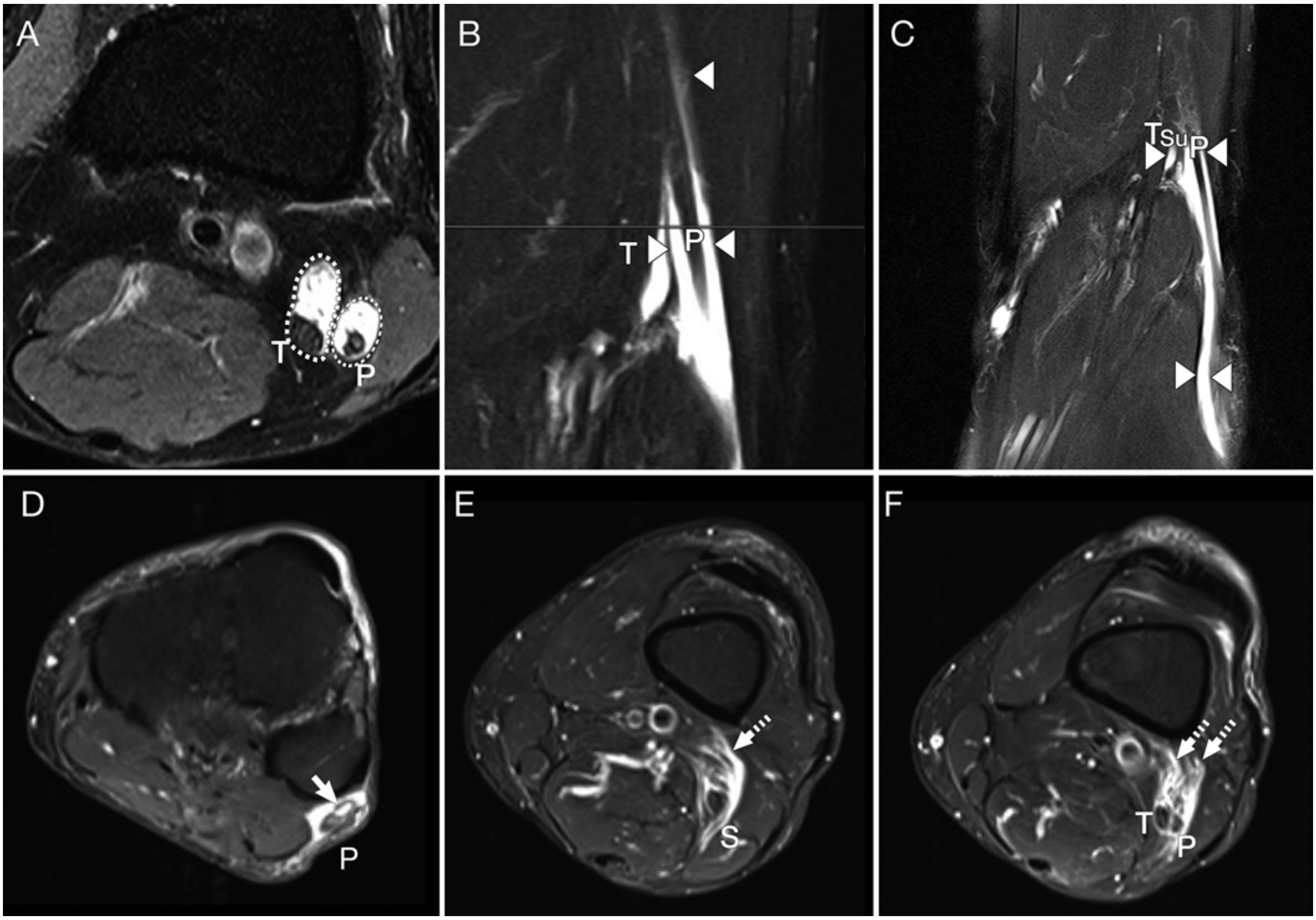

FIG. 1. Case 1. MR images showing the various signs. **A:** Axial T2-weighted MR image obtained just above the knee joint, showing the owl-eye sign, which is also caused by subparaneurial distribution of the cyst (*dashed circles*), here around the epineurium of the CPN (P) and TN (T) just below the sciatic nerve bifurcation. A slit-like subepineurial cyst is seen within the CPN. **B and C:** Sequential coronal T2-weighted MR images with fat suppression showing parallel tracks of hyperintense signal (tram-track sign) contained within the subparaneurial layer (*arrowheads*) around the CPN just distal and proximal (peroneal division) to the sciatic nerve bifurcation in the distal/midthigh. Tram tracks extend along the CPN, sural nerve (Su), and TN distal to (to the level of the fibular neck region), at, and above the sciatic nerve bifurcation. **D:** Axial T2-weighted image demonstrating the cyst-within-cyst appearance: subepineurial cyst (*arrow*) within a subparaneurial cyst within the CPN at the level of the fibular head. **E and F:** Axial T2-weighted images obtained 1 week after the ones in panels A–D, showing the rupture of the paraneurial layer with extraneural cyst rupture (*dashed arrows*) at the level of the sciatic nerve (S) bifurcation in the distal thigh (E) and around the CPN and TN (F).

images obtained at different times. For patients in whom sequential MR images had been performed preoperatively, the distribution of cyst(s) in these nerves at various levels was compared at the different time points, and we looked for signs of regression or expansion over time. MR images were analyzed for the presence of cysts, cyst grading (mild to severe), and location of acute/subacute changes of extraneural rupture of the cysts (i.e., the presence of extraneural free fluid between muscles, around neurovascular structures, or extending along fascial planes) (Fig. 1E and F).[27] Finally, postoperative MR images were evaluated for the persistence or recurrence of intra- or extraneural cysts.

Results

Four novel cases of patients with a peroneal subparaneurial cyst treated at Haaglanden Medical Center by the first author were identified. The peroneal INGCs originated from the anterior aspect of the STFJ (n = 3) and the posterolateral aspect of the knee (tibiofemoral) joint (n = 1).

Our literature review revealed 3 previously recognized cases of extreme subparaneurial cysts reported by the senior author (2 peroneal and 1 tibial from the STFJ).[5,18,28] Two other examples of subparaneurial cysts involving the CPN arising from the STFJ were identified, but their description or published MR images did not extend to the sciatic nerve and therefore did not meet our criteria for extreme subparaneurial cysts. One case was a recognized (sub-)paraneurial cyst involving the CPN arising from the STFJ, reported by Kim et al.;[29] the other[30] was noted by us on review of the published MR image to have a subparaneurial cyst involving the CPN as well as descent into the DPN and SPN, but this was not noted by the authors. We obtained the original films from the senior author of

TABLE 1. MRI findings for all novel cases of extreme subparaneurial ganglion cysts

Case No.	Age, yrs	Sex	Side	Primary Nerve Affected/Origin From Joint	Sequential MRI Time Points	Subparaneurial Findings							Extraneural Rupture		
						Axial						Coronal or Sagittal			
						Sc	TN	Su	CPN	DPN	SPN		Nerve	Location	Severity
1	78	M	Lt	Peroneal/anterior STFJ	3 wks preop	NI	O	O	O	O	O	TT			
					2 wks preop	O	O	O	O	NI	NI	TT	Sc	Thigh	Severe
2	59	M	Rt	Peroneal/anterior STFJ	12 wks preop	NI	NI	O	O	O	O	TT	CPN	Knee	Slight
					10 wks preop	W	W	NI	–	NI	NI	TT			
3	38	M	Rt	Peroneal/anterior STFJ	0*	NI	O	O	O	O	O	TT	No signs of rupture		
					24-wk interval*	–	–	–	W	–	–	–			
4	38	F	Rt	Tibial/posterolat knee	5 wks preop 1	O	W	W	O	W	W	TT			
					4 wks preop 1	W	W	W	W	W	W	–			
					16 wks preop 2	O	O	O	O	O	O	TT	Sc	Knee	Severe
					6 wks preop 2	O	O	O	W	W	W	TT			

NI = not imaged; O = owl-eye sign present; Sc = sciatic nerve; Su = sural nerve branches; TT = tram-track sign present; W = wedding ring sign present; – = absent.
* The patient in case 3 did not undergo surgery.

the first publication (B.C.S.)[29] to test our hypothesis that unrecognized crossover occurred. Reinterpretation confirmed an extreme subparaneurial cyst. These data were included in this study, but the second case, which was unable to be analyzed, was not included.

Patient characteristics and MRI features of these 8 patients are summarized in Tables 1 and 2. Illustrative findings from all novel cases and our reinterpretation of the case of Kim et al.[29] are presented in Figs. 1–5.

Clinical Data

Novel Cases

The three peroneal INGCs arising from the STFJ had tibialis anterior (TA) muscle weakness grades 3 (case 1), 0 (case 2), and 2 (case 3). The patient with the INGC arising from the knee joint (case 4) had a foot drop and DPN denervation on MRI before the first surgery, but at presentation to us had normal TA strength. All patients experienced excruciating pain in the distribution of the CPN. Cases 1–3 had a Tinel's sign at the fibular head. Two patients (cases 1 and 4) also experienced radiating pain from the calf to the plantar aspect of the foot.

Cases 1 and 2 were operated on using the same technique (cyst decompression by opening of the paraneurial layer and transection of the articular branch to the STFJ) through a small incision in the fibular neck region. Drainage of the subepineurial cyst was not performed. The patient in case 3 did not want to undergo surgery. The patient in case 4 had been previously operated on elsewhere; the same incision was used to expose the TN and CPN at the level of the popliteal fossa.

In all cases, pain quickly improved after the surgery. Motor deficit slowly recovered in time. In case 1, TA weakness and toe extension (TE) had improved 3 months after the surgery from MRC grade 4 to grade 5−. Strength in the extensor hallucis longus (EHL) was still decreased (MRC grade 4). After a half year, strength recovered completely. In case 2, the complete loss of dorsiflexion and eversion function improved to MRC grade 5 TA and eversion 5–8 months after the surgery. Sensory deficit completely recovered in both cases. Case 3 was not followed.

TABLE 2. MRI findings for previously reported extreme subparaneurial ganglion cysts

Authors & Year	Case No.	Age, yrs	Sex	Side	Primary Nerve Affected/ Origin From Joint	Sequential MRI Time Points	Subparaneurial Findings							Extraneural Rupture		
							Axial						Coronal or Sagittal			
							Sc	TN	Su	CPN	DPN	SPN		Nerve	Location	Severity
Spinner et al., 2007[34]	5	41	M	Lt	Peroneal/anterior STFJ	6 wks preop	O	O	O	O	O	O	TT			
						3 wks preop	O	O	–	O	–	–	NI	Sc	Thigh	Severe
Colombo et al., 2014[28]	6	34	M	Rt	Peroneal/anterior STFJ	14 wks preop	W	W	O	O	O	O	TT			
						2 wks preop	–	–	–	–	O	O	TT	CPN	Thigh	Slight
Spinner et al., 2007[7]	7	46	M	Lt	Tibial/posterior STFJ	10 wks preop	–	–	–	–	–	–	–	TN	Knee	Severe
						9 wks preop	O	O	O	NI	NI	O	TT			
						1 wk preop	W	O	–	–	–	–	–			
Kim et al., 2018[29]	8	30	M	Lt	Peroneal/anterior STFJ	0.5 wk preop	NI	W	O	O	O	O	TT	No signs of rupture		

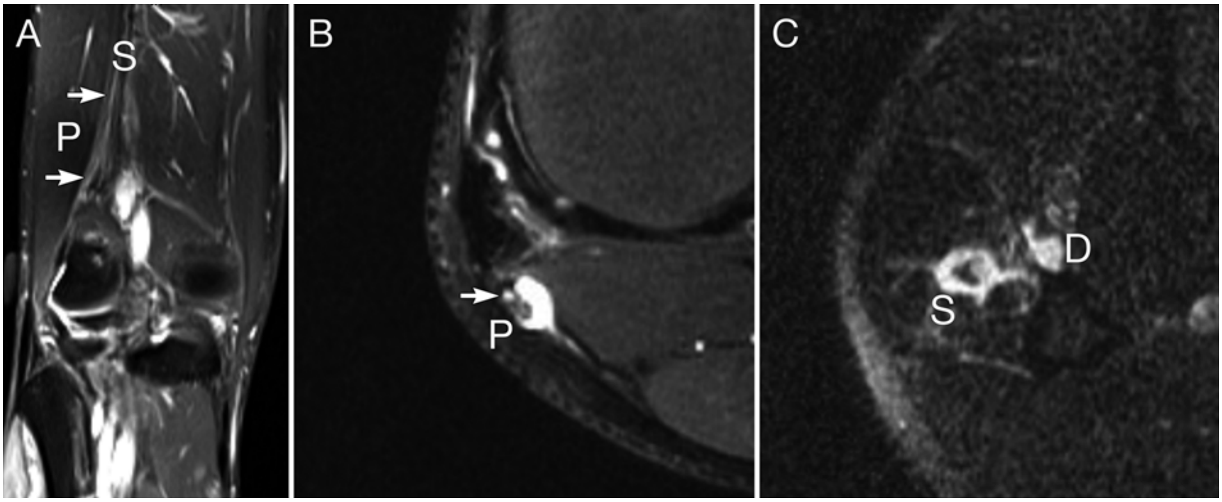

FIG. 2. Case 2. T2-weighted MR images with fat suppression showing a peroneal INGC with extreme subparaneurial descent. **A:** Coronal image showing faint tram tracking (*arrows*) in the CPN (P) extending proximally to the sciatic nerve (S) bifurcation. **B:** Axial image above the level of the fibular head of the CPN, displaying both a near-complete owl-eye sign and a signet ring sign (*arrow*) comprising a ring within a ring. **C:** Axial image below the level of the fibular neck in the proximal leg, demonstrating two separate subparaneurial cysts around the SPN (S) and DPN (D) branches of the CPN.

Case 4 improved in symptoms but already had maximum strength prior to the second surgery.

Cases Previously Reported in the Literature

Three cases (cases 5–7) of extreme subparaneurial cysts (2 peroneal INGCs and 1 tibial INGC arising from the STFJ) were previously published by the senior author.[6,18,28] In these patients, the articular branch was disconnected, the subparaneurial cyst was decompressed, and the STFJ was also resected. In case 5, strength slowly recovered in time for TA (grade 2 at 4 months, grade 5− at 18 months and 2.5 years), TE (grade 1+ at 4 months, grade 5− at 18 months and 2.5 years), and EHL (grade 0 at 4 months, grade 3+ at 19 months, and grade 4+ at 2.5 years). Mild paresthesias persisted in the first web space 2 years postoperatively. In case 6, at 3 months the patient regained grade 5− TA, TE, and EHL and eversion grade 5. At the 1-year follow-up, he regained full motor function, and by 2 years, normal sensation. The patient with the tibial INGC (case 7) presented with 4 months of anterolateral shin pain and tibial regional pain. He had weakness of the gastrocnemius, toe flexors, and posterior tibialis muscle force (MRC grade 3); dorsiflexion and eversion were normal. Postoperatively, symptoms significantly improved: the patient had

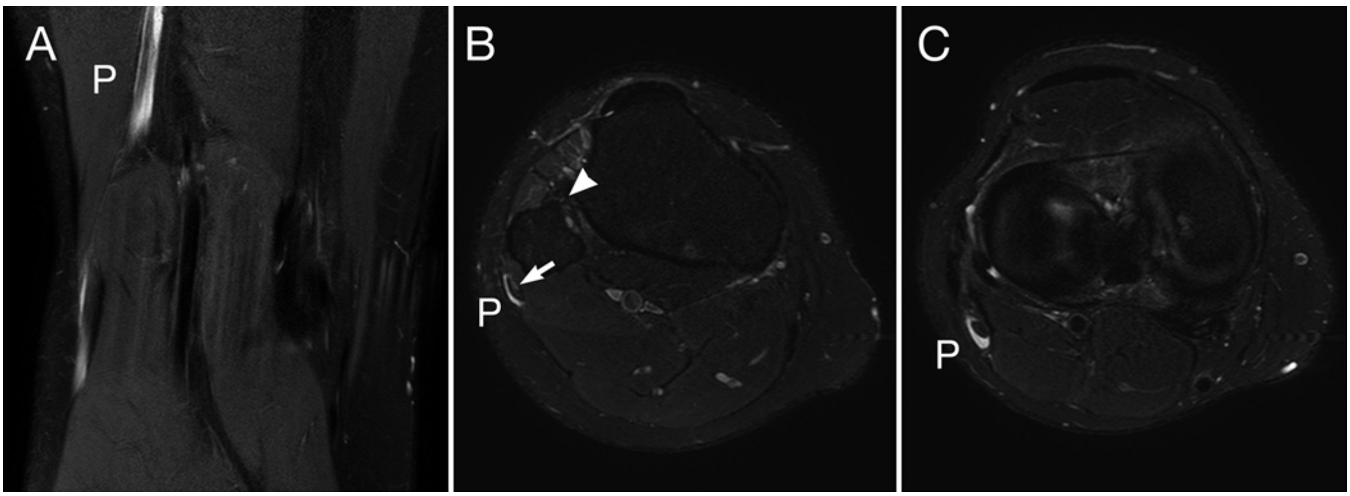

FIG. 3. Case 3. T2-weighted MR images with fat suppression showing the spectrum of subparaneurial cysts. **A:** Coronal image showing the tram tracks of a subparaneural cyst in the CPN (P) extending from the fibular head region to the distal thigh (maximal proximal extent on this sequence). **B:** Axial image showing the partial subparaneurial cyst in the CPN at the level of the fibular head along with the intraepineurial cyst (*arrow*). The connection to the STFJ (*arrowhead*) is also seen. **C:** Axial image showing a circumferential subparaneurial cyst (owl-eye sign) in the CPN at the level of the knee.

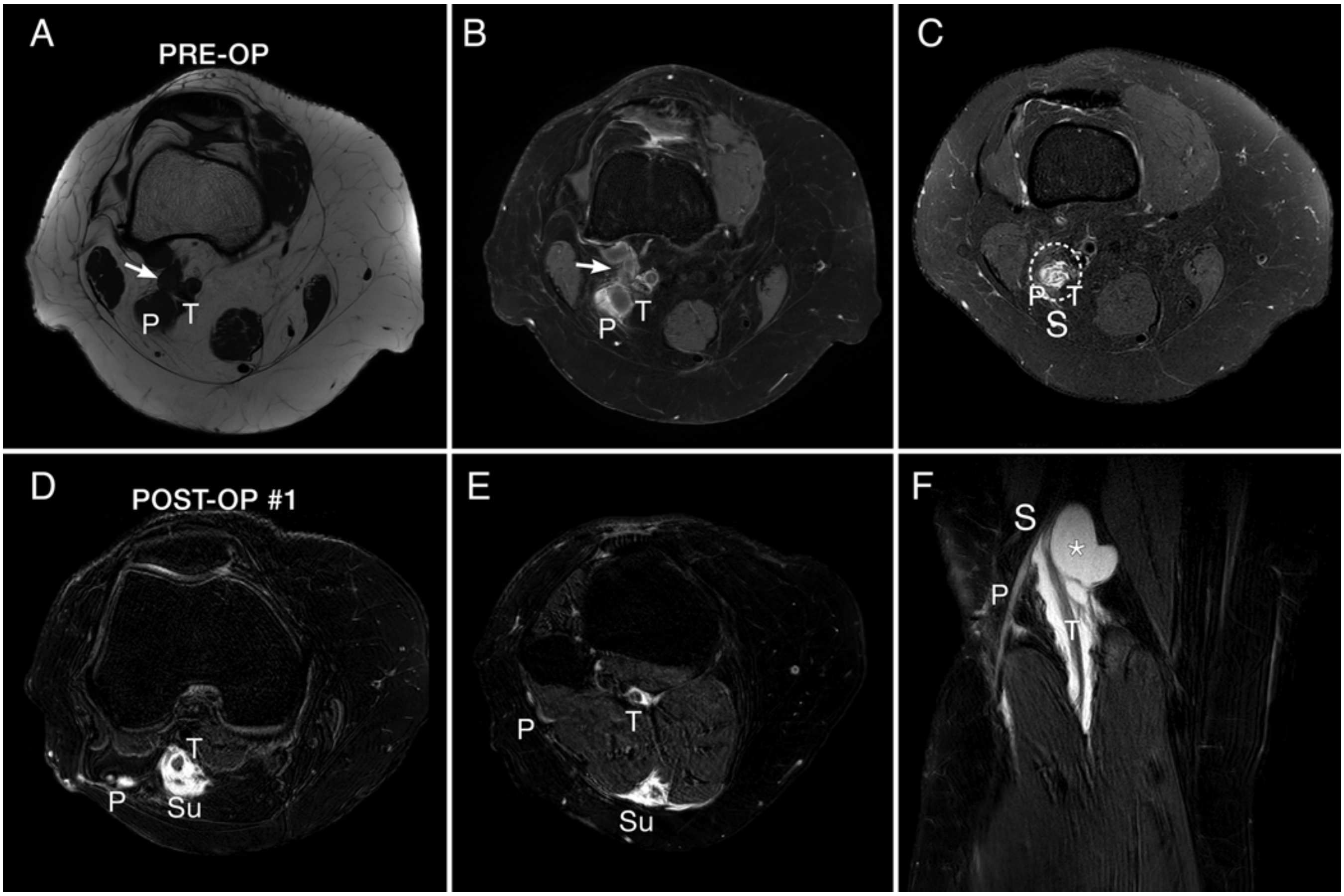

FIG. 4. Case 4. MR images showing the development of subparaneurial cysts postoperatively. **A:** Axial T1-weighted MR image at the level of the distal femoral metadiaphysis, showing an intraneural cyst within the CPN (P) just distal to the sciatic nerve bifurcation. The *arrow* indicates the connection to the posterolateral knee joint at the most superior aspect of the joint capsule. T = tibial nerve. **B:** Axial T1-weighted MR image with fat suppression after the administration of intravenous gadolinium contrast at the same level, showing the nonenhancing intraneural cyst and the joint connection (*arrow*). **C:** Axial T2-weighted MR image with fat suppression proximal to panels A and B at the level of the sciatic nerve (S) bifurcation, showing crossover with a small amount of cyst present surrounding the distal sciatic nerve (*dashed circle*). **D:** Postoperative axial T2-weighted MR image with fat suppression at the level of the knee obtained 6 months after surgery, showing the development of owl-eye signs with cyst surrounding the TN and sural nerve (Su) within the subparaneurial space. The CPN is enlarged and hyperintense without discrete cyst. **E:** Axial T2-weighted MR image with fat suppression distal to panel D (at the level of the fibular head), showing circumferential cyst in the subparaneurial space surrounding the tibial and sural nerves. The CPN has subtle changes on this image. **F:** Coronal T2-weighted MR image with fat suppression demonstrating the sciatic nerve bifurcation with a tram-track sign involving the TN. The *asterisk* indicates the level of sciatic nerve bifurcation. The CPN shows mild T2 hyperintensity but is otherwise normal with no cyst.

no pain after 2 months. Weakness had partially recovered (gastrocnemius: MRC grade 4+, posterior tibialis: MRC grade 3+, toe flexors: MRC grade 5−). At the 1-year follow-up, his strength returned to 85% of normal. The previously reported case with a peroneal subparaneurial ganglion cyst (case 8)[29] presented with symptoms for 2 months of progressive weakness and pain in the anterolateral shin. He had MRC grade 1+ TA and TE. The subparaneurial cyst was decompressed and the articular branch was divided. Strength completely recovered after 2 months, and there were no recurrent symptoms at 12 months.

MRI Analysis

Signs for All Cases

Results from the MRI studies are shown in Table 1, including the distribution and extent of INGCs. In all cases, there was MRI evidence of a joint connection to the STFJ (tail signs). All cases, including the case by Kim et al.,[29] had evidence of a subepineurial cyst in the parent nerve (Fig. 5C and D). All cases had subparaneurial cysts (wedding ring and/or owl-eye and tram-track signs and a combination of subparaneurial and subepineurial cyst [ring-within-ring sign]) in the parent nerve (Figs. 1D and 2A). All cases, including the case by Kim et al.[29] (Fig. 5E and F), exhibited radiological features consistent with crossover with subparaneurial-to-subparaneurial communication at the sciatic nerve bifurcation.

Seven patients had sequential MRI studies. The dynamic nature of these cysts was quite apparent as the degree of extension or regression showed variable changes over time: from considerable cyst expansion (with extreme sub-

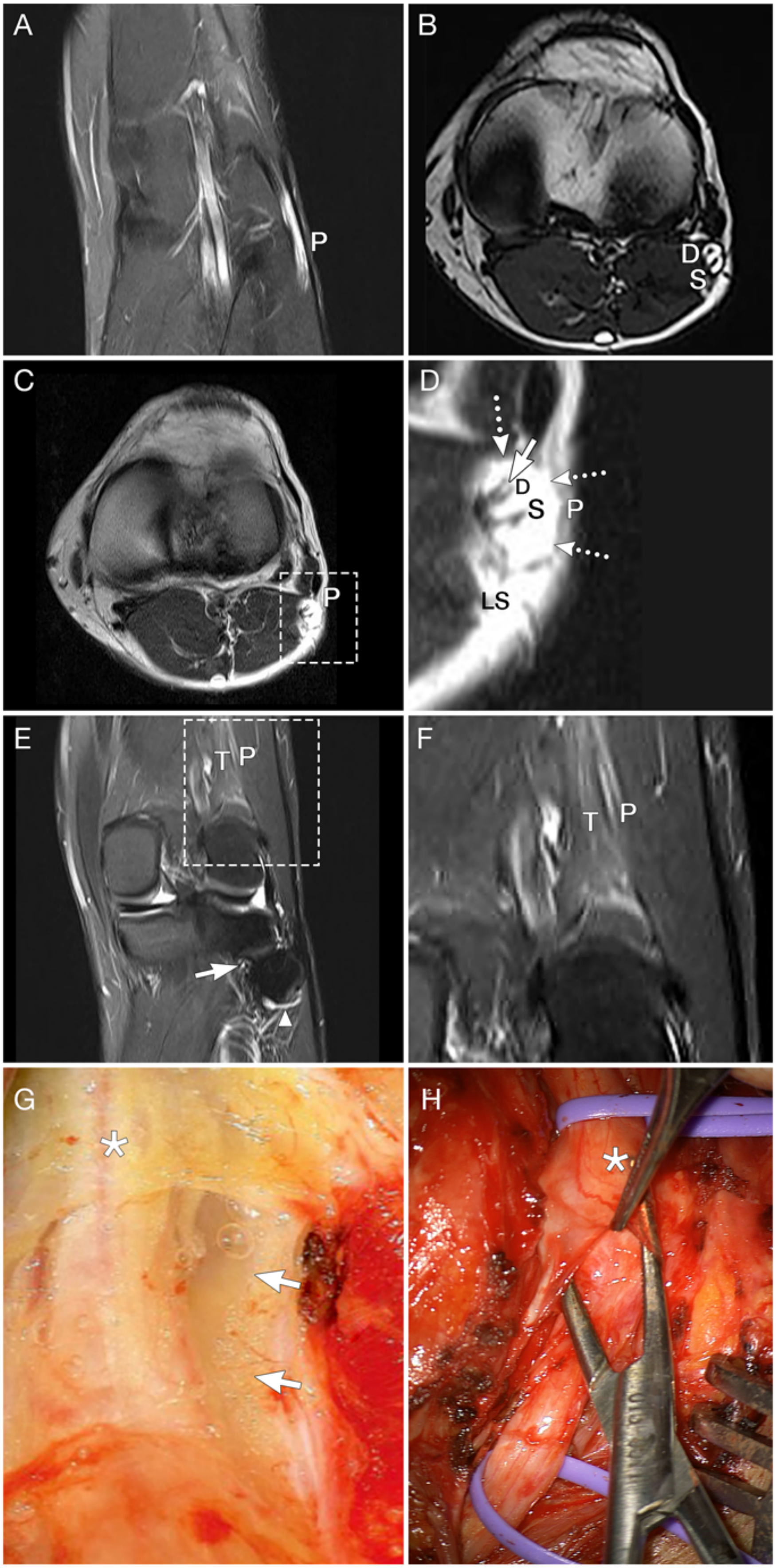

FIG. 5. Case 8. Reinterpretation of the previously reported peroneal intraneural ganglion with extreme subparaneurial cyst illustrating an unrecognized subepineurial cyst and sciatic crossover.[29] **A:** Coronal T2-weighted MR image with fat suppression showing a subparaneurial cyst in the CPN (P) at the level of the fibular head and knee joint. **B:** Axial T2-weighted MR image without fat suppression at the level of the knee joint, showing cyst around the DPN (D) and SPN (S) bundles of the CPN. **C:** Axial T2-weighted MR image without fat suppression showing the subparaneurial cyst within the CPN. **D:** Photographic enlargement of *outlined area* in panel C, showing the subepineurial cyst in the DPN fascicular bundle (*solid arrow*) within the CPN subparaneurial cyst (*dashed arrows*). A subparaneurial cyst in also seen involving the lateral sural (LS) communicating branch. **E:** Coronal T2-weighted MR image with fat suppression showing the peroneal intraneural cyst arising from the STFJ (*arrow*; tail sign). A cyst within the articular trunk (*arrowhead*) of the CPN is seen along the fibular neck. A subtle tram-track sign can be seen around the TN (T) and CPN just distal to the sciatic nerve bifurcation in the distal thigh. This is consistent with crossover in the sciatic nerve and descent down the CPN and TN in the subparaneurial layer. **F:** Photographic enlargement of *outlined area* in panel E. **G:** Intraoperatively, there was a clear transparent subparaneurial layer with cyst fluid (*arrows*) clearly visible through this layer around the CPN (*asterisk*). **H:** The hemostat is within the subparaneurial compartment (the *asterisk* indicates the subparaneurial layer) around the CPN (in vasoloops proximally and distally).

paraneurial cyst ascent and descent) to dramatic cyst redistribution or regression (e.g., cases 5[34] and 7[7]). Extraneural rupture of the subparaneurial cyst into surrounding tissues was noted in 6 cases (5 at the level of the sciatic nerve bifurcation) (Fig. 1E and F). There was no obvious correlation between size of the cyst and neurological symptoms.

MRI confirmed no residual or recurrent INGC in 5 cases and 1 residual cyst stump (in the transected articular branch to the knee) in 1 case (case 4): case 1 at 6 months, case 2 at 3 months, case 4 at 3 and 12 months, case 5 at 2 and 12 months, case 6 at 3 and 11 months, and case 7 at 3 months. Case 3 did not undergo operation. No postoperative imaging was performed in the case of Kim et al. (case 8).[29]

Novel Cases

In all cases, there was evidence of extreme subparaneurial cyst(s) at different levels of nerves in the primary and secondary pathways. In 3 peroneal cases, there was MRI evidence of an STFJ connection to the anterior portion of the STFJ. A subparaneurial cyst in the distal sciatic nerve was present in all our peroneal INGCs; in case 1, there was an owl-eye sign at all levels (sciatic, peroneal/tibial, DPN, and SPN) on MR images obtained at one time point (Fig. 1). In case 2, faint sciatic crossover was present with more easily visible extreme subparaneurial descent extending down the CPN, DPN, and SPN (Fig. 2). In case 3, a subparaneurial cyst was present within the CPN to the level of the sciatic nerve (Fig. 3) without distal descent into the DPN or SPN; 5 months later, MRI showed a subparaneurial cyst extending from the STFJ to the fibular head with descent into the DPN, SPN, and intramuscular cyst in the TA muscle. In the peroneal INGC arising from the knee joint (case 4, Fig. 4), owl-eye signs could be seen at all levels when combining serial imaging studies. Extraneural rupture was present in 3 cases (Fig. 1E and F).

Literature Cases

In the senior author's previously reported cases, 1 case had an owl-eye sign at all levels (sciatic, peroneal/tibial, DPN, and SPN) on MR images obtained at one time point (case 5). In case 6, a thin wedding ring sign was present in the distal sciatic and proximal tibial nerves, and an owl-eye sign was present around the CPN, DPN, and SPN. In the tibial INGC (case 7), on the first set of MR images, the cyst extended to the level of the knee with subparaneurial cyst in the CPN, DPN, and SPN. The distal thigh was not well visualized. Two months later, MRI showed an extensive subparaneurial cyst (with owl eyes) in the sciatic nerve to the proximal thigh. There was evidence of extraneural rupture in the thigh. The knee and STFJ were not well visualized. In the case by Kim et al.,[29] while axial MRI studies did not extend to the level of the sciatic nerve bifurcation, coronal imaging did show cyst with a tram-track sign in the proximal TN (Fig. 5E and F). No signs for rupture were found, and sequential imaging was not performed.

Discussion

Principles

We present evidence to show that extreme subparaneurial ganglion cysts can be explained by the three underlying principles put forth by the unified articular theory for INGCs.[17,18] In this study, we focused on the most frequent INGCs of the CPN arising from the STFJ, which has been used as the prototype for the articular theory. We then generalized our findings to a less frequently affected nerve (TN) at the same joint of origin (STFJ) and another joint of origin (the knee), and we further challenged our findings by retrieving and examining the only known similar case, previously reported by Kim et al.[29] Their case was reported as a subparaneurial variant with a circumferential subparaneurial cyst around the CPN without evidence of a subepineurial cyst or sciatic nerve crossover; reanalysis showed subtle evidence of both radiological features (Fig. 5). These findings strengthen the proposed mechanisms. While the spectrum of INGCs ranges from the nearly invisible[31] to the extreme,[7] we believe the same principles apply. These extreme subparaneurial cysts develop from the typical and extreme INGCs. For extreme subparaneurial cysts, the increased dimensions, extents, and configurations of the cysts are related to underlying pathoanatomical (e.g., anatomical layers) and pathophysiological (e.g., pressure and rupture) considerations that have yet to be elucidated (Fig. 6).

Joint Connections

Joint connections are the basis for the articular theory. These examples of extreme subparaneurial cysts arose from the most common joint origin for cyst formation of INGCs, the STFJ, as well as a rare site, the knee joint. The fact that reinterpretation of published cases by others has revealed previously unrecognized joint connections and crossover strengthens the principles of the articular theory in these extreme cases.[7,18,32–34]

Path of Least Resistance

All these cases of extreme subparaneurial cysts had communication of subparaneurial-to-subparaneurial compartments at the sciatic nerve bifurcation. We believe that in these cases, cyst ascends within the epineurium of the parent nerve to the sciatic nerve bifurcation, where an actual defect (e.g., a fenestration) allows cyst fluid to transfer from the subepineurial space into the subparaneurial space, and subsequently fills this space completely, surrounding the epineurium of the nerve. In a previous article, several potential pathophysiological mechanisms for subepineurial communication with the subparaneurial space were postulated (including other branching sites), but the exact pathophysiological mechanism for this distribution was not provided.[5] In case 4, scarring in the CPN at the sciatic nerve bifurcation from previous surgery altered the fluid mechanics, favoring subparaneurial extension within the TN (Fig. 4).

Pressures and Pressure Fluxes

Phase III subsequently is more complicated. The spectrum is broad because a cyst below the paraneurium can go up and down every nerve it communicates with. This propagation seems to occur relatively easily; after crossover, extreme subparaneurial distribution can occur over a considerable distance longitudinally, up (extreme subpara-

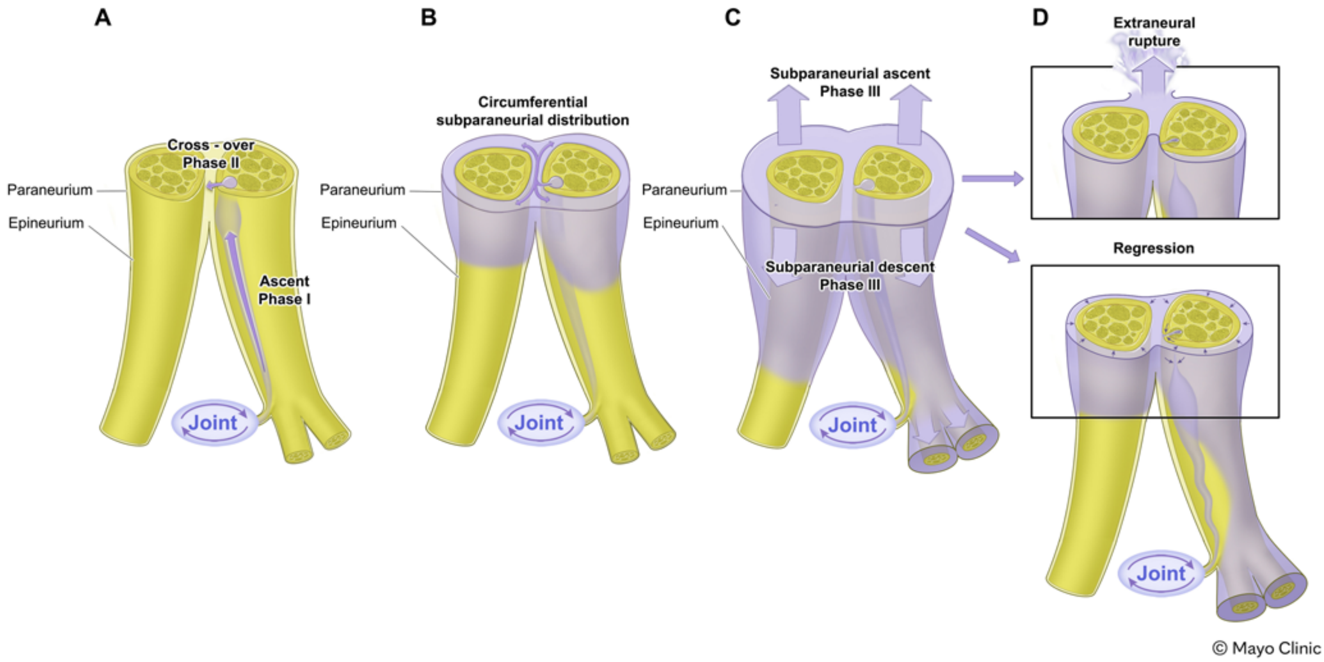

FIG. 6. Illustrations demonstrating the mechanism underlying the formation and propagation of extreme subparaneurial ganglion cysts. **A:** Cyst fluid coming from the STFJ passes along the articular branch into the CPN, below the epineurium. With an increased intra-articular pressure, the cyst may ascend in the CPN (phase I). Once the cyst has reached the level of the sciatic nerve bifurcation, the fluid can pass through an opening in the epineurial layer, entering the subparaneurial space, which leads to crossover (phase II). **B:** The combination of high pressure inside the nerve and low compliance of the shared paraneurial layer leads to a rapid distribution of cyst around the tibial and peroneal nerves at the level of the sciatic nerve bifurcation. **C:** The rapid filling below the paraneurial layer may lead to extreme subparaneurial ascent outside the epineurium of the sciatic nerve and descent (phase III) around the CPN, the sural branches (not illustrated in this image), and the SPN and DPN branches over long distances. **D:** The buildup of pressure or pressure fluxes may lead to extraneural cyst rupture (*upper*). Spontaneous regression/resorption (*lower*) may also occur by an ill-defined mechanism. In Part 2, we show that this sequence of events resembles the eruption of a geyser. Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.

neurial ascent) the sciatic nerve and down (extreme subparaneurial descent) all the distal branches of the sciatic nerve, giving the appearance of tram-track signs. In addition, a cyst in the subparaneurial space can also expand dramatically, leading to the owl-eye appearance. Both the extreme extension and expansion can be explained by a higher compliance of paraneurium compared with the epineurium. At the same time, this extreme filling of the subparaneurial compartment (the path of least resistance) seems to lead to deflation of the cyst in the subepineurial compartment; in all extreme subparaneurial cases, the size of the subepineurial cyst (Fig. 1D) was often relatively small in comparison with the size of the subparaneurial distribution (Fig. 1A).

The extreme subparaneurial distribution patterns can explain the occurrence of extreme cases described in the literature prior to MRI.[4,7,9,26] Within this subparaneurial layer, descent may follow the branching point, giving rise to multiple interconnected subparaneurial cysts. Owl-eye signs can be identified spanning from the sciatic nerve, the CPN or TN, the sural nerve, or further distally around the DPN and SPN or potentially the TN muscular branches. The occurrence of multiple INGCs seemingly remote from a joint was once used to support the degenerative theory rather than the synovial theory.[35] In 6 patients (cases 1, 3, 4, 5, 6, and 7), we observed extreme ascent and descent resulting in dramatic shifts of cyst sizes and compartmental configuration, even within days.[17] In case 4, extreme subparaneurial cysts in the tibial and sural nerves only became apparent after cyst decompression of a peroneal INGC arising from the knee joint (done elsewhere); this surgery resulted in scarring in the popliteal fossa and distal thigh, which altered the flow dynamics of the cyst propagation (Fig. 4). We noted extraneural rupture near the sciatic nerve bifurcation in 6 cases, which could be caused by the vulnerability of this layer and/or another potential fenestration.

Implications

Understanding the mechanisms is important in the evaluation and treatment of patients with extreme subparaneurial ganglion cysts.

Clinical

Patients with extreme subparaneurial cysts may have symptoms and signs beyond the distribution of the INGC of the parent nerve, potentially involving the nerve/division of the secondary pathway from either ascent within the sciatic nerve or descent in the opposite terminal branch of the sciatic nerve (cases 1 and 4). This was noted in 2 of our previously published extreme subparaneurial cases (cases 5 and 7) and several cases in the literature.[10,15,36]

Radiological

Imaging in these cases should include high-resolution fluid-sensitive sequences with robust fat suppression (which was not available in all cases). Still, the MRI signs for INGCs (such as those for joint connections) have consistently been present. Small joint connections often go unrecognized as attention may be directed to the larger, more complex cyst. We have previously identified unrecognized joint connections in examples of extreme cases.[4,7,9,13,26,32] Dynamic changes may result in cyst regression/redistribution, which may make radiological signs completely or partially disappear[17] and easy to miss or misinterpret: signs may be ghostlike, appear like faint silhouettes, or be partial. Radiological evidence for crossover may be subtle or be underrecognized, as in the case of Kim et al.[29] (which had a substantial subparaneurial cyst). The finding of a subparaneurial cyst distal to the sciatic nerve bifurcation in the CPN is an indication that crossover has occurred (extreme subparaneurial descent in the secondary pathway) and, as our cases show, is often accompanied by a subparaneurial cyst higher up in the sciatic nerve and down into the TN (although the amount of subparaneurial cyst may be less, with only a slight hyperintense ring [wedding ring sign]). Subparaneurial cysts may not be recognized on imaging review (as in the case of Stamiris et al.[30]) or captured due to limitations of standard imaging done at a few time points. A single MRI study provides only a single snapshot in time and does not reflect the full radiological spectrum of the extreme pathoanatomy that may potentially appear markedly different depending on the timing of the imaging: ranging from an owl eye to a complete or partial wedding ring to a faint rind (or silhouette) to the complete absence of cyst. For extreme INGCs (including subparaneurial forms), while MRI at all levels would be helpful to understand better the pathoanatomy and serial studies would allow further insight into the dynamic changes, they would not likely change the surgical treatment.

Surgical

The surgical treatment for extreme cysts is based on the same principles outlined previously by the unifying articular theory[1,16,23] for smaller and less complex INGCs.[17,21,22,29] After transection of the articular branch, cyst inside the subparaneurial and subepineurial space will be resorbed over time. Prominent accessible subparaneurial or subepineurial cyst can be decompressed in a limited fashion. When encountering a subparaneurial cyst intraoperatively (that was not detected or appreciated on preoperative imaging), it is thus not necessary to open this layer over its entire length or dissect the sciatic nerve.[12] We do not advise extensively draining the subepineurial cyst, because this would require interfascicular dissection, which might lead to nerve injury. Case 4 (which was first operated on elsewhere) shows that decompression (without transection of the articular branch) often leads to recurrence of symptoms and cyst (with changes in the pattern of the cyst propagation). We favor resection of the synovial surface when treating INGCs arising from the STFJ. This cannot be done for cysts arising from the knee. Ligation of the articular branch can result in a stump of cyst (case 4). Our surgical series shows that excellent clinicoradiological results can be achieved for these extreme subparaneurial ganglion cysts by addressing their articular pathology and origin.

Limitations

In many cases, full assessment of the nerves, especially at the sciatic nerve bifurcation and the cysts, was compromised by limitations on in-plane resolution, field of view, bilateral studies, no intravenous contrast, motion artifact, and protocols performed for routine joint imaging that did not fully interrogate the nerve pathology. Given the dynamic nature of these cysts, it is difficult to know the full extent of many INGCs. Considering the lack of imaging sequentially over time and the relatively few cases of extreme subparaneurial cysts (with full imaging available), we do not know their prevalence, if there is always evidence of subepineurial cyst, if proximal or distal extension in the subparaneurial space is preferential, or if there is an effect of gravity.

Conclusions

The occurrence and propagation patterns of extreme subparaneurial cysts can be explained by the unified articular synovial theory. We believe that extreme subparaneurial cysts are not as rare as is currently thought and represent an important phase of the dynamic life cycle of INGCs. In Part 2,[37] we discuss the pathoanatomical and pathophysiological mechanisms for the development of extreme subparaneurial cysts.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Spinner, de Ruiter, Howe, Amrami, Reina. Acquisition of data: Spinner, de Ruiter, Son, Hayford, Amrami. Analysis and interpretation of data: Spinner, de Ruiter, Howe, Amrami, Reina. Drafting the article: Spinner, de Ruiter, Howe, Amrami, Reina. Critically revising the article: Spinner, de Ruiter, Son, Howe, Amrami, Reina. Reviewed submitted version of manuscript: Spinner, de Ruiter, Son, Reina. Approved the final version of the manuscript on behalf of all authors: Spinner. Administrative/technical/material support: Spinner, Hayford. Study supervision: Spinner.

Supplemental Information

Companion Papers

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