Adherence of intraneural ganglia of the upper extremity to the principles of the unifying articular (synovial) theory

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Object. Intraneural ganglia are nonneoplastic mucinous cysts contained within the epineurium of peripheral nerves. Their pathogenesis has been controversial. Historically, the majority of authors have favored de novo formation (degenerative theory). Because of their rarity, intraneural ganglia affecting the upper limb have been misunderstood. This study was designed to critically analyze the literature and to test the hypothesis that intraneural ganglia of the upper limb act analogously to those in the lower limb, being derived from an articular source (synovial theory).

Methods. Two patients with digital intraneural cysts were included in the study. An extensive literature review of intraneural ganglia of the upper limb was undertaken to provide the historical basis for the study.

Results. In both cases, the digital intraneural ganglia were demonstrated to have joint connections; one patient in whom an articular branch was initially not appreciated had evidence on postoperative MR images of persistence of intraneural cyst after simple decompression was performed. Eighty-six cases of intraneural lesions were identified in varied locations of the upper limb: the most common sites were the ulnar nerve at the elbow and wrist, occurring 38 and 22 times, respectively. Joint connections were present in only 20% of the cases published by other groups.

Conclusions. The authors believe that the fundamental principles of the unifying articular (synovial) theory (that is, articular branch connections, cyst fluid following a path of least resistance, and the role of pressure fluxes) previously described to explain intraneural ganglia in the lower limb apply to those cases in the upper limb. In their opinion, the joint connection is often not identified because of the cysts’ rarity, radiologists’ and surgeons’ inexperience, and the difficulty visualizing and demonstrating it because of the small size of the cysts. Furthermore, they believe that recurrence (subclinical or clinical) is not only underreported but also predictable after simple decompression that fails to address the articular branch. In contrast, intraneural recurrence can be eliminated with disconnection of the articular branch. (DOI: 10.3171/FOC.2009.26.2.E10)

Key Words • articular (synovial) theory • intraneural cyst • intraneural ganglion

Intraneural ganglia are nonneoplastic mucinous cysts that are found within the epineurium of peripheral nerves. Of the approximately 350 cases in the literature, the vast majority affect the peroneal nerve. For centuries these cysts have been considered curiosities. Their pathogenesis has been controversial and obscure. Recent evidence involving the peroneal nerve at the fibular neck region has demonstrated the lesion’s consistent origin from the superior tibiofibular joint and stereotypical appearance. The peroneal intraneural ganglion has served as the prototype for a unifying articular (synovial) theory.⁸⁷

Intraneural cysts in the upper limb are rare, incompletely described, and poorly understood. Joint connections have only seldom been identified in these cases. These features differ markedly from those of extraneural cysts which are common in clinical practice and in the literature and are well-known and understood by surgeons to be derived from synovial surfaces. Critical analysis and reinterpretation of the available literature on intraneural cysts in this rare location with a modern perspective has not been published previously. The purpose of this paper is to support the notion that joint connections are indeed present in all of these cases; to demonstrate that the principles of the unifying theory that have been previously identified for intraneural ganglia in the lower limb hold true in the upper limb; and to highlight the shared pathogenesis of intraneural and extraneural cysts.

Methods

This study was initiated by the senior author (R.J.S.) to test a hypothesis without any first-hand experience with this rare location of intraneural cyst. To illustrate the

Abbreviations used in this paper: FSE = fast spin echo; IP = interphalangeal.
entity, we included 2 cases of intraneural ganglia occurring in a rare site in the upper limb. We then undertook a thorough review of the world literature on intraneural ganglia and intraneural cysts as a whole to identify intraneural ganglion cysts reported in the nerves of the upper extremity. Standard Internet databases (MEDLINE, searched via PubMed, and Scopus) and Web search engines (Google and Yahoo) were used. All references of retrieved papers were cross-checked. Magnetic resonance images, when available, were analyzed by a musculoskeletal radiologist with experience with intraneural ganglia.

Illustrative Cases

Case 1

This 31-year-old woman, who had minor trauma to the volar side of her right dominant hand from weightlifting, immediately developed pain and tenderness along the index finger. Within a few days the pain resolved and numbness developed in the radial aspect of the index finger and a string-like mass was noted longitudinally along the course of its radial digital nerve. Three months after the onset of symptoms, the digital nerve was palpable where it crossed over the metacarpal head. A Tinel sign was elicited along the radial digital nerve starting from the midpalm. Two-point discrimination in the radial digital nerve distribution of the index finger was > 10 mm. An MR imaging study revealed an elongated cystic tubular abnormality in the volar radial aspect of the hand extending from the distal portion of the carpal tunnel to the level of the second metacarpal head. It measured 5–8 mm in diameter and 5 cm in length. No joint connection was identified prospectively. The MR images were not available for our review.

Five months after symptom onset the patient was evaluated at our institution. The mass had decreased in size. The radial digital nerve of the index finger was still palpable at the metacarpophalangeal joint level. There was a vague but deep soft tissue mass deep to the thenar muscle and tender to palpation. A Tinel sign was evident at the site of the mass and distally along the radial digital nerve. Two-point discrimination in the distribution of the nerve was 3 mm.

Over the next 3 months, the mass enlarged again and paresthesias developed in the dorsoradial aspect of the index finger. Surgical exploration was performed at the time of this visit. An intraneural ganglion cyst was seen coursing within the radial proper digital nerve to the index finger. Proximally the intraneural cyst was noted within the median nerve just at the take-off of the proper digital nerve. The mass also appeared to involve the take-off of the sensory nerves to the thumb, just tenting these structures (Fig. 1). Excision of the ganglion cyst with preservation of the nerve and identification and excision of the stalk to the second carpometacarpal joint were carried out.

Postoperatively, the patient experienced some neurogenic pain, which gradually resolved. There was still some hypersensitivity at the radial side of the index finger at 2 months postoperatively, and she regained good use of the hand.

Case 2

This 51-year-old woman noted the spontaneous onset of numbness and a mass on the dorsoulnar aspect of the right thumb for 3 months. The mass increased and decreased in size, just proximal to the metacarpophalangeal joint of the thumb. The mass transilluminated and was felt to be an extraneural ganglion cyst beneath the dorsal ulnar sensory nerve to the thumb. At operation, a ganglion cyst was noted within the dorsal digital nerve (Fig. 2). It was approximately 5 cm in length and was larger proximally. It extended distally beyond the level of the IP joint. The cyst was decompressed. No specific joint connection was noted. Postoperatively the numbness improved. While there was no clinical recurrence of swelling within the nerve, a sizable mucous cyst developed from the IP joint of the thumb and subsequently largely disappeared. A postoperative MR imaging study performed 4 months later demonstrated persistence of a small remnant of intraneural cyst and the development of the extraneural cyst, both connected to the IP joint (Fig. 3).
The patient also had a history of a recurrent extraneural ganglion on the volar ulnar aspect of the left wrist that arose from the distal radioulnar joint. Four years ago, the mass was resected again and the joint opening was oversewn with good results.

**Results**

We identified a total of 86 cases (involving 87 nerves) of intraneural ganglia affecting nerves of the upper limb described in 65 reports. One case that was published in 2 articles was recorded one time.63,94 For the purposes of this study, we considered the Zum Busch article100 as the earliest case in the upper limb as this is widely cited as such. (Note that earlier cases can be substantiated;88 see Discussion.) These cases were reported in the following languages: English (26), Japanese (25), German (8), Italian (3), French (2), and Korean (1). Of these cases only 56 (35 reports) were listed in PubMed. We excluded published cases in the following 3 categories: 1) cases affecting the axial cervical spine, including one case of a hypoglossal cyst presumably derived from the atlantooccipital joint.6,82 2) cases reported in the 19th and early 20th century and described as “blood cysts,” myxomas (fibromyxomas, myxofibromas), and cystic benign or malignant nerve sheath tumors (including “gliomas”); and 3) cases described in a manner that did not allow us to distinguish adequately between intraneural or extraneural ganglia or to substantiate the intraneural nature of the cyst.

Intraneural ganglia were identified in the following sites: suprascapular in the shoulder (6, 13, 16, 27, 58, 67, 69, 76), ulnar (3) at the elbow at the wrist, radial (1), and posterior interosseous at the elbow (1); 33 superficial radial (3);13,16,22 lateral antebrachial cutaneous (1);26 dorsal cutaneous branch of the ulnar (3);31,26,90 posterior antebra-
tions. Based on our interpretation of the cases included in this paper, we believe that the unifying articular (synovial) theory applies to these cases of intraneural ganglia in the upper limb and that the joint-related connection often goes unrecognized leading to the historical misconception of de novo formation (degenerative theory).

Unifying Theory

In 2003, we proposed a unifying (synovial) theory based on the peroneal nerve at the fibular neck and its connection to the anterior portion of the superior tibiofibular joint. We believe that capsular rents may lead to dissection of joint fluid into and along an articular branch leading to intraneural ganglia or into the neighboring tissues (apart from the articular branch) leading to extraneural ganglia. For intraneural ganglia at this site, we have demonstrated a stereotypical appearance that follows anatomical and hydrodynamic principles. Extraneural ganglia may arise from sources of synovium (joints, bursae, tendon sheaths, and so forth). Most commonly, these extraneural cysts present on the dorsal wrist and originate from the scapholunate joint through a nonneural “pedicle.” In our opinion, extraneural cysts do not invade epineurium and become intraneural in nature. Extraneural cysts can compress or adhere to nerve and be mistaken for intraneural cysts.

In the past few years, this theory has been tested and substantiated at other unusual sites in the lower limb by our group and others. Experience has allowed us to elaborate upon 3 fundamental principles for the formation and propagation of intraneural ganglia in the lower limb, which we believe are applicable to those cases in the upper limb.

Fundamental Principles

Joint Connections. Joint connections were identified by the original authors in only 22.1% of these cases (19 of 86)—20.2% (17 of 84) if we exclude the suprascapular nerve cases previously published by our group. (Note: illustrated cases were also not included.) In this review, all of these cases of upper limb intraneural ganglia were paraarticular and were derived from appendicular joints in the region. (Note: Information was typically insufficient to determine the specific wrist joint connection.) We have previously shown that even the sporadic intraneural ganglia described as remote from a joint, still have an unrecognized joint origin. Joint connections may be small, easily missed, and not imaged or explored, and cysts may still enlarge far from joints; these connections have not been identified routinely because of the cyst’s rarity and radiologists’ and surgeons’ unfamiliarity and inexperience with them. In many early cases there were no high-resolution MR imaging scans, such as can be performed with current imaging equipment, techniques, and parameters. All of these nerves affected with ganglia have de-
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scribed articular branches\textsuperscript{71} to the joints. Interestingly, in all examples of upper limb intraneural ganglia there was at least 1 case of a joint connection identified at each of the most commonly affected nerves/sites.

Our belief is bolstered by considering certain additional information. We have demonstrated this consistent finding with imaging and with operation in the lower limb.\textsuperscript{79–81,85–87} We have also shown this in 4 cases of intraneural ganglia at 2 rare sites in the upper limb. In 3 cases the joint connections were not identified initially; the cases presented to us sequentially were shown at reinterpretation or at follow-up examination to have joint connections (in Case 1 in this paper and in 2 cases of suprascapular intraneural ganglia that we reported in a previous article\textsuperscript{76}). We were able to identify previously unrecognized joint connections in 2 cases (ulnar\textsuperscript{10} and posterior intersosseus\textsuperscript{33} intraneural ganglia) in which appropriate images were published that could allow us to reinterpret films and identify a joint connection. Two historic cases reported before prior knowledge or imaging of theories on joint connections represent robust evidence to support a joint connection: 1) the earliest known case of an intraneural cyst (1810) located within the ulnar nerve, originally thought to be a serous cyst, has recently been reinterpreted as an elbow joint-related ganglion;\textsuperscript{12,88} and 2) a cadaveric specimen listed in a catalog (1929)\textsuperscript{4} of a cyst within the deep branch of the ulnar nerve connected to one of the carpal joints. One other case is particularly revealing: ironically, Jenkins\textsuperscript{41} who, like Cutler and Gross,\textsuperscript{18} believed that intraneural ganglia were derived from degeneration of cystic nerve sheath tumors, described one case in which it was necessary to “excise the pisiform to obtain access to the deepest part (of the cyst)”; to us, he is describing an articular connection to the wrist.

Certain data are especially informative regarding the underlying mechanism of the pathogenesis of these cysts. The strong association of degenerative joint disease and intraarticular pathology seen in the lower limb cases is also reflected in these upper limb cases. Trauma was identified in 19 (25\%) of 76 cases in which enough clinical information was reported. Nineteen (50\%) of 38 ulnar nerve cases at the elbow had dysplastic or degenerative findings. Labral tears were demonstrated in 2 cases of suprascapular nerve ganglia. Arthrography performed in 2 cases demonstrated communications of the joint with the cyst through a capsular tear.\textsuperscript{14,76} Still, we recognize that even with arthrography, delayed arthrography or exercise might be necessary to reveal the joint communication with the cyst (as is the case with extraneural cases).\textsuperscript{51,77} Furthermore two of the cases confirmed neural tissue histologically within the “pedicle/stalk” of the articular branch.\textsuperscript{34,60}

Occam’s razor would favor a shared pathogenesis of the unifying articular (synovial) theory—not only of intraneural ganglia in the upper limb following a mechanism similar to that of those in the lower limb, but also of intraneural ganglia following a mechanism similar to that of extraneural ganglia. This theory seems far more logical than other theories on the subject, especially the degenerative one.\textsuperscript{87}

Path of Least Resistance. Intraneural propagation within the epineurium occurs following the path of least

\begin{figure}
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\caption{Previously published case of an ulnar intraneural ganglion cyst with unrecognized joint connection. A: Axial T2-weighted image at the level of the distal humerus demonstrates the intraneural cyst within the ulnar nerve within the cubital tunnel (asterisk). Note displacement of the nerve fascicles around the cyst, the “signet ring” sign. The connection of the cyst (plus sign) to the elbow joint is seen on this image (arrow). ME = medial epicondyle; LE = lateral epicondyle; O = olecranon. B: Sagittal T2-weighted FSE image showing the longitudinal extent of the cyst (asterisk) and the connection of the cyst (plus sign) to the posterior elbow joint (arrow). Modified from Boursinos et al.: \textit{Hand} 2:12–15, 2007.}
\end{figure}
resistance. Just as in the lower extremity where extensive longitudinal dissection of cyst may occur (for example, buttoc level extension of a peroneal nerve) we identified a similar situation where an ulnar nerve cyst propagated from the cubital tunnel to the infracavicular brachial plexus. A suprascapular intraneural ganlula arising from the glenohumeral joint extended to the neck. We have also shown that when intraneural cyst extends to a major branch, be it the sciatic nerve for peroneal or tibial nerves in the lower limb, or the upper trunk for suprascapular nerve, it can cross over. For example, cyst within a primary neural pathway (such as the peroneal nerve) can fill the tibial nerve (a secondary pathway) after expanding within the sciatic nerve. These patterns of primary and secondary proximal ascent and distal descent are clearly dependent on pressure fluxes.

In the lower limb, we have shown that the preferential pathway often is in a proximal direction with more limited distal descent. The intraneural cyst typically has characteristic clinical and imaging features: a relatively narrowed neck ("tail" sign); a tubular appearance because of its confines within the nerve; a balloon-like expansion ("balloon" sign) wherein fascicles are displaced by cyst ("signet ring" sign); and further evidence of an ascending streak. These features suggest the common effects of intraarticular pressures along a path of least resistance.

The nature of this retrospective review of literature spanning 2 centuries has inherent limitations. Still, it seems clear to us that the initial phase of cyst propagation is "primary ascent" from a synovial joint along the articular branch. Directionality of further cyst propagation could not be assessed accurately due to the number of cases, paucity of high resolution MR images obtained, and limited operative descriptions. With some documented exceptions, predominant proximal ascent seems to occur but further study is required to confirm this pattern of extension in these rare lesions in the upper extremities. In addition, it is likely that pressures and pressure fluxes give rise to complex patterns of ascent, descent, and cross-over. For cases of ulnar intraneural ganglia at the elbow, different patterns have been described (with joint connections): many within the cubital tunnel; some with proximal extension; others with distal extension; and others perhaps with combinations of proximal and distal extension. Possible explanations for the apparent exaggerated distal descent (that is, other patterns) include: 1) increased pressures (for example, from scar tissue) causing the path of least resistance to be distal; 2) inaccurate representation (misunderstanding or misrepresentation) of pathology; and 3) misdiagnosis of an extraneural rather than intraneural cyst (these may appear similar). We suspect that scarring from previous surgery can lead to exacerbation of other pathways and distal descent. We demonstrated this in a sural intraneural case. Initially predominant ascent occurred. At operation the articular trunk was ligated but not at the level of the subtal joint of origin. Surgical ligation of a nerve led to increased resistance. Follow-up MR imaging revealed prominent descent down a remaining neural pathway. Furthermore, the extrinsic pressures of locations such as the carpal tunnel and cubital tunnel are likely to play a role in determining cyst size, shape, and dimensions that is not fully appreciated; patterns underlying these pressures need to be defined.

In addition, depending on the site of the capsular rent, the path of least resistance can occur within nerve and/or outside of nerve leading to intraneural and/or extraneural cyst. This combination of different types of cysts has been seen in the lower limb as well as in Case 2 in the present paper. Intraneural and extraneural cysts can coexist or occur sequentially. Other cases of less common, more complex (adventitial) ganglia also may present similarly. The one case in which 2 separate digital intraneural cysts were reported may well represent simultaneous intraneural cyst development along 2 different nerves from a single joint. Another possibility for 2 different intraneural nerves would be the cross-over phenomenon.

Finally, 2 cases interpreted as intraneural ganglia were excluded from our data analysis based on their MR images. Limited MR images available for review suggested that the lesions were extraneural ganglia without close proximity to a nerve with their joint connections to the shoulder joint probably unrecognized at the time of initial imaging and subsequent surgery.

**Pressure and Pressure Fluxes.** Pressure fluxes, presumably related to increased intraarticular pressures (such as in strenuous activity), have been described in lower limb intraneural cysts as responsible for intermittent symptoms and fluctuating findings on examination and imaging. Similarly, several cases of fluctuating symptoms and cyst size occur in the upper limb for example, in our 2 illustrative cases). The abrupt nature of the decrement in the cyst size suggested that cyst rupture (along with resorption) can result in pressure fluxes in certain cases. The intermittent, episodic nature of the symptoms and fluctuating cyst size is well known to hand surgeons from their experience with the common simple extraneural ganglia. Pressure and pressure fluxes without doubt lead to more extensive extension of cysts along the path of least resistance as described above.

**Implications of This Study**

Potentially, any articular branch to a synovial joint can be affected by an intraneural ganglion. We believe that the number of cases is underestimated; many isolated cases are unreported; and at least some of the early cases of intraneural cysts with limited descriptions and different pathologic diagnoses likely represent intraneural ganglia. We also suspect that other cases of intraneural ganglia may go unrecognized and be causes of pain syndromes, such as those involving the posterior interosseous nerve at the wrist.

The purpose of this study is not to establish treatment guidelines or to be definitive about the elimination of recurrences. Based on our experience with these ganglia, we believe that cyst decompression should be performed along with disconnection of the articular branch. Intraneural recurrence can be eliminated when the articular branch is disconnected at or near the joint of origin.
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believe that resection of the entire cyst and its wall is unnecessary; this only results in unnecessary intraneural dissection and risk of neural injury. The joint seems to be the root of the pathology and wherever possible the reversal of intraarticular pathology would seem to be the most direct means of correcting the problem. Although we have recommended resection of the superior tibiofibular joint (synovium) in cases of peroneal or tibial intraneural ganglia arising from this joint, resection of other joints should not be performed. We anticipate that arthroscopic methods to treat these connections can be designed in the future. We anticipate that a joint-derived procedure could potentially address all of the pathology.

While recurrences for lower limb intraneural ganglia have been reported to be as high as 30% when simple decompression was done without disconnection of the articular branch, they were not described in any of these cases. In many cases follow-up information was unavailable, and postoperative MR imaging studies were rarely performed. We are aware of one case that became apparent after publication. In certain instances we predicted intraneural persistences/recurrences and then demonstrated examples (in illustrated Case 2 of the digital nerve in this paper and the suprascapular nerve case previously reported). We believe that this incidence of symptomatic or subclinical recurrences is underestimated and that long-term follow-up and postoperative MR imaging is necessary for accurate surveillance. In our opinion there is a logical explanation for the apparent lower recurrence rate noted in this review. In many of these cases in the upper limb, especially where mobilization of proximal and distal “normal” nerve is obtained (for example, when the ulnar nerve is transposed at the elbow), the articular branch may be unknowingly disconnected. Extraneural recurrences which in our experience are often subclinical can still occur and are reflective of the pathologic degenerative joint.

Conclusions

Previous research on the prototype peroneal intraneural ganglia set the stage for the unifying articular (synovial) theory. This theory, which has been tested at other nerves and sites in the lower limb, can now be generalized to both common and rare sites of intraneural ganglia in the upper limb. With further experience with these cysts, predictable patterns of cyst propagation will be appreciated in these lesions, much as they have been in those in the lower limb. As with lower limb intraneural ganglia careful attention to image acquisition and interpretation of images and intraoperative pathology is required to prospectively identify joint connections and true extent of the intraneuralt cysts in the upper limb.

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Disclaimer

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

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