The almost-invisible perineurioma

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Intraneural perineurioma is a rare, benign slow-growing lesion arising from the perineurial cells that surrounds the peripheral nerve fibers. Typically it presents during childhood and young adulthood as a motor mononeuropathy. MRI plays an essential role in the diagnosis and localization of the lesion, which appears as a fusiform enlargement of the nerve fascicles that enhances intensely with gadolinium. Despite the typical clinical and radiological features, intraneural perineurioma remains largely underdiagnosed because of the lack of familiarity with this entity, but also as a result of technical limitations with conventional MRI that is typically performed as a screening test over a large field of view and without contrast sequences. The purpose of this article is to present the pitfalls and pearls learned from years of experience in the diagnosis and management of this relatively rare condition.

Clinical suspicion and detailed neurological examination followed by high-quality electrophysiological studies (EPS) must lead to an adequate preimaging localization of the lesion and narrowing of the imaging area. The use of high-resolution (3-T) MRI combined with gadolinium administration will allow adequate visualization of the internal anatomy of the nerve and help in differentiating other causes of neuropathy. In cases where the lesion is not recognized but clinical suspicion is high, possible errors must be assessed, including the EPS localization, area of imaging, MRI resolution, and slice thickness.

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INTRANEURAL perineurioma is a rare, benign slow-growing lesion arising from the perineurial cells that surrounds the peripheral nerve fibers.⁶ Based on our experience and recent published information related to this lesion, it has a characteristic presentation and features that allow early diagnosis and help to distinguish it from other pathological entities clinically, radiologically, and histologically. Typically it presents in young patients as a motor mononeuropathy mainly affecting major nerves such as the sciatic nerve or one of its branches. MRI plays an essential role in the diagnosis and differentiation from other conditions such as hereditary neuropathies, demyelinating conditions, peripheral nerve sheath tumors (PNSTs), and infiltrative nerve diseases. On MRI intraneural perineurioma typically appears as a fusiform enlargement of the nerve fascicles with avid enhancement after intravenous gadolinium.⁸ Histologically, intraneural perineurioma typically forms concentric whorls of perineurial cells around the nerve fibers (known as pseudo-onion bulbs) that are

often confused with the true onion bulb lesions seen in inherited and demyelinating neuropathies. Only with the introduction of the perineurial cell marker endothelial membrane antigen (EMA) and the Schwann cell marker S-100 has it been possible to make a clear differentiation between them⁶ histologically.

Intraneural perineurioma is often not diagnosed or is misdiagnosed. The main reason for this underrecognition is the lack of familiarity with the disease along with technical limitations with imaging that can render the lesion “invisible” to the untrained eyes. The purpose of this article is to present the pitfalls and pearls we have learned from years of experience in the diagnosis and management of the disease; the Mayo Clinic series now includes more than 50 patients, and every year approximately 5 new patients are being evaluated in the institution. We believe this lesion is more common than currently appreciated and should be considered as a potential diagnosis in children with progressive neuropathy.

ABBREVIATIONS CIDP = chronic inflammatory demyelinating polyneuropathy; CMT = Charcot-Marie-Tooth disease; EMA = endothelial membrane antigen; EPS = electrophysiological studies; GBS = Guillain-Barré syndrome; PNST = peripheral nerve sheath tumor; SPGR = spoiled gradient.

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Pitfall 1: Unknown Entity and Unknown Clinical, Electrophysiological, and Radiological Features

Clinical

Perineuriomas have historically been confused with other conditions that have similar clinical, radiological, and histological presentations. In initial reports, most authors described the lesion as a reactive or inflammatory process probably related to trauma, hence the misleading historical names of this entity, including interstitial hypertrophic neuritis, localized hypertrophic neuropathy, and hypertrophic neurofibrosis.

Until recently, little was known about the characteristics and natural history of the disease based on published case reports and small series. In 2007, Boyanton et al. published the first extensive review of the literature, which included 53 patients;² in 2009, Mauermann et al. published the largest cohort (32 patients) with a detailed description of their clinical, electrophysiological, radiological, and pathological features and long term follow-up.⁸ Based on these publications it is now known that intraneural perineurioma mainly manifests during childhood and young adulthood, with a median age for symptoms to appear between 14 and 23 years (no sex prevalence). Patients normally present with symptoms and signs of weakness/atrophy in 90% of cases. In 10% of patients, the initial presentation can be numbness or pain; over time, however, all patients with intraneural perineurioma will develop progressive weakness. Typically, the onset of the symptoms is slow and gradual; at the beginning, the patients or their relatives commonly notice a subtle change in a normal motor pattern (e.g., gait abnormalities) that becomes more evident during activity (playing, running, jumping). Frequently, however, the changes and disability are underestimated and/or even considered within the realm of normal variation, even when assessed by the primary care physician. Over time, the neurological impairment progresses (e.g., foot drop) and visible deformities appear in the affected extremity as a result of muscle atrophy. When the initial presentation is in early childhood, the findings can mimic and be confused with other congenital disorders, such as clubfoot, or misinterpreted as a hereditary neuropathy. The motor involvement is typically focal and limited to the affected nerve; nevertheless, occasionally the plexus or multiple nerves can be affected. In both of these studies the most common localization was the sciatic nerve or its branches (21%–47%), followed by the ulnar, radial (12%–17%), and median nerves (6%–11%). Interestingly the median time from symptom onset to diagnosis has been 3 years with a range between 6 months and 30 years; this prolonged time clearly reflects the difficulties in accurate diagnosis and early recognition.

Electrophysiological

The most common pattern found in intraneural perineurioma is a focal neuropathy associated with axonal degeneration. It has a motor predominance, however, sensory involvement is also frequently present.⁸ A combination of a detailed neurological examination with high quality electrophysiological studies (EPS) can help to narrow the

anatomical site to optimize imaging studies. Careful attention must be taken for those lesions that are proximal and inaccessible to EPS, as well as those cases in which there is an incomplete involvement of the nerve; in addition, the presence of multifocal disease can be an additional confounding factor in localization. EPS are highly operator dependent with significant variability in skills, anatomical knowledge, technical expertise, and experience. Because of this it is possible to incorrectly or inadequately localize lesions prior to imaging. A thoughtful approach considering all available information is important to optimize imaging of the correct area of interest (Fig. 1).

Radiological Characteristics

Currently peripheral nerve MRI is being routinely used as part of the diagnostic work-up for most neuropathies; however, few radiologists are trained in this field and the images can be frequently misinterpreted due to the variety of mass-like lesions associated with nerves that can be encountered. On MRI intraneural perineurioma has a stereotypical appearance when optimally imaged. The affected nerve overall shows fusiform enlargement, but close inspection on high resolution imaging will demonstrate that individual nerve fascicles are enlarged while nerve “architecture” is maintained. Histologically the enlarged individual fascicles (surrounded by the neoplastic perineural cells) correlate in the MR with the nerve fascicles appearing isointense on T1-weighted (Fig. 2A) and hyperintense on T2-weighted (Fig. 2B) images. Intraneural perineuriomas characteristically show avid enhancement after contrast administration (Fig. 2C), differentiating this entity from hereditary and inflammatory neuropathies which also show fascicular enlargement but no or very minimal enhancement. Another common finding on MRI is the fatty atrophy of muscles in the affected nerve territory. While this is nonspecific it is much less common in other types of hypertrophic neuropathies. We believe that contrast enhancement is an important part of MR imaging of most cases of peripheral neuropathy, but it is absolutely required when intraneural perineurioma is suspected by history.

Lesions With Similar Imaging Features

There are numerous conditions that can present clinically as a mononeuropathy. Among the broad range of differential diagnoses are the hereditary, inflammatory, and autoimmune neuropathies; toxic and metabolic diseases including diabetes; PNSTs, as well as hematological disorders such as leukemia and lymphoma, sarcoidosis, and amyloidosis; and trauma. Each pathology will have its own clinical characteristics and complementary work-up; however more advanced tools such as imaging and sometimes biopsy are often needed for a definitive diagnosis.^{3,7} We have summarized the most common cases of tumor-like lesions seen in the MRI that can be mistaken for the intraneural perineurioma, emphasizing their clinical characteristics and imaging appearances.

Hereditary Neuropathy. The most common type is the sensorimotor neuropathy also known as Charcot-Marie-Tooth disease (CMT). Symptoms and presentation may

FIG. 1. Case 1. Axial T1-weighted (A), T2-weighted (B), and T1-weighted contrast-enhanced (C) MR images and photograph (D) obtained at evaluation of a 7-year-old boy with a classical presentation of intraneural perineurioma along with an intraoperative photograph obtained during the biopsy surgery (E) and photomicrographs showing results of histological analysis of the biopsy specimen (F). When the patient was 3 years old, his mother started noticing his left foot turning in. When he was between 5 and 6 years of age, it became apparent that his foot and leg were internally rotated, the muscles were wasting, and that he had a foot drop (D). His running became awkward, although he was still able to play sports. The foot drop progressed, and he underwent tendon transfer surgery at the age of 7. An electrophysiological study was finally done, and it showed a left chronic sciatic neuropathy with ongoing denervation affecting the peroneal division more than the tibial. MRI revealed a fusiform enlargement of the sciatic nerve from the sciatic notch to the distal thigh affecting primarily the peroneal division (A), which appears bright on the T2-weighted (B) and T1-weighted contrast-enhanced images (C). Consequently, a targeted fascicular biopsy was performed in the thigh, confirming the enlargement of the peroneal division of the nerve (E). Histological analysis (F) showed the whorled onion bulb-like formations (in H & E-stained section, *left*) reacting to EMA (*middle*) but not to S-100 (*right*) immunostaining, characteristic of intraneural perineurioma. Original magnification $\times 640$.

vary depending on the type of CMT, but usually the condition manifests during the first 2 decades of life as a gradual and progressive neurological impairment affecting predominantly the lower extremities and causing weakness, decreased tendon reflexes, atrophy, and skeletal deformities of the feet; usually multiples nerves are involved.⁹ On MRI, bilateral nerves and the lumbosacral plexus appear enlarged and may have a fusiform mass-like appearance that is isointense on T1-weighted images and hyperintense on T2-weighted images; abnormal enhancement with gadolinium can be seen; however, it is usually minimal.¹ The presence of a family history and genetic abnormalities are key points for the diagnosis. The diffuse nature of the clinical and imaging findings are distinctive and should help to distinguish CMT from intraneural perineurioma, which is always more focal.

Acquired Immune-Mediated Neuropathies. These can be divided into acute/subacute entities such as Guillain-Barré syndrome (GBS) and more chronic conditions such as chronic inflammatory demyelinating polyneuropathy/mononeuropathy (CIDP/CIDM). These disorders are characterized by an immune response that causes inflammation and destruction of the nerves. These entities can

cause both motor and sensory disturbances typically affecting multiple nerves. They are most commonly seen in adults, and the clinical course is gradual and progressive in CIDP as opposed to the acute onset of GBS. CIDP more frequently affects the lower extremities.⁵ On MRI, CIDP appears as a focal or diffuse element on the nerve fascicles that is isointense on T1-weighted images (Fig. 2D) and hyperintense on T2-weighted images (Fig. 2E) and can have a mild contrast enhancement¹ (Fig. 2F). Lumbar puncture typically demonstrates albuminocytological dissociation in GBS and CIDP. GBS may be associated with antecedent viral or other illness, but this correlation may not be obvious.

Peripheral Nerve Sheath Tumors. As an isolated lesion not related with any of the neurofibromatosis syndromes, peripheral nerve sheath tumors (PNSTs)—schwannomas and neurofibromas—are commonly found in young to middle-aged patients. Classically, the patient presents with a painless or a mildly painful slow-growing mass; mechanical pressure over the mass often causes sensory disturbance, but findings on neurological examination tend to be normal. On MRI, a benign PNST typically appears as a well-circumscribed oval or circular mass that

FIG. 2. Axial MR images obtained in 6 different cases demonstrating the differential diagnosis. The MR images in the left column are all T1-weighted, those in the middle column T2-weighted, and those in the right column Gd-enhanced T1-weighted. **A–C:** Intraneural perineurioma affecting both divisions of the sciatic nerve at the level of the upper thigh. **D–F:** Chronic inflammatory demyelinating polyneuropathy affecting the lumbosacral plexus and sciatic nerve at its origin. **G–I:** Schwannoma affecting the tibial nerve at the level of the knee. **J–L:** Intraneural ganglion cyst affecting the tibial nerve at the level of the knee. **M–O:** Amyloidosis affecting the sciatic nerve in the distal thigh. **P–R:** Traumatic neuroma of the ulnar nerve at the level of the elbow.

arises from a nerve fascicle; the nerve can be seen entering and exiting the lesion (“tail” sign). In the case of a schwannoma, the lesion may be eccentrically located relative to the nerve and may displace nerve fascicles, whereas a neurofibroma may be more centrally located. Both neurofibromas and schwannomas may have more conventional, mass-like appearances or may be wholly or

partially plexiform. The lesions normally appear isointense (relative to muscle) on T1-weighted images (Fig. 2G) and hyperintense on T2-weighted images (Fig. 2H) and show characteristic homogeneous enhancement after gadolinium administration^{1,12} (Fig. 2I). A “target” sign may sometimes be seen related to collagen deposition in the center of the lesion. Plexiform neurofibromas or schwannomas may not enhance but are usually easily identified by their appearance along a nerve.

Intraneural Ganglion Cyst. Nonneoplastic cystic lesions arise from joints and propagate along the nerves that innervate joints (articular branches). This is thought to be related to degenerative or posttraumatic changes in the joint capsule that allows extension of mucinous material from the joint along the nerve where it perforates the joint capsule. The cyst material extends through the epineurium causing displacement of the fascicles and functional impairment. The most common nerve affected is the common peroneal nerve, although involvement of other nerves has also been reported.¹⁰ On MRI, the normal morphology of the nerve is replaced by a unilocular or multilocular cystic lesion that follows the path from the joint along the parent nerve. Cysts appear hypointense on T1-weighted images (Fig. 2J), hyperintense on T2-weighted images (Fig. 2K), and show peripheral enhancement of the cyst wall on contrast images¹ (Fig. 2L).

Infiltrative Nerve Diseases. Some hematological malignancies, such as leukemia and lymphoma, and systemic diseases such as sarcoidosis and amyloidosis (Fig. 2M–O) may infiltrate nerves, causing different degrees of neurological deficit. The clinical presentation of these cases may be confusing, as several organ systems may be affected, and the subtle neurological deficits may be overlooked. MRI commonly demonstrates diffuse multifocal nerve enlargement with variable degrees of enhancement; lymphoma is relatively more commonly seen and is characterized by more intense enhancement.^{1,12}

Traumatic Neuroma. Traumatic neuromas are caused by a disorganized regrowth of axonal fibers in response to a direct injury of an individual nerve. Symptoms and signs will vary depending on the affected nerve and the degree of damage; nonetheless, there is always a history of trauma. On MRI, the neuroma appears as a bulbous mass over the injured area that may or may not be in continuity with the nerve, depending on whether the lesion is partial or complete. When nerves are completely transected, the proximal portion of the nerve may be retracted and enlarged. An important imaging feature of neuromas is the loss of normal fascicular architecture. Signal intensity may be intermediate on both T1-weighted (Fig. 2P) and T2-weighted (Fig. 2Q) imaging, and the contrast enhancement tends to be variable^{1,12} (Fig. 2R).

Pearl

The most important factor in correctly diagnosing intraneural perineurioma is clinical suspicion.

Pitfall 2: Magnetic Resonance Imaging

One of the main reasons for the growing use of MRI in peripheral nerve pathologies is improved ability to direct-

ly image nerves due to advances in tools such as dedicated receiver coils and the wide availability of high-field (3-T) magnets. The increasing availability of high-field MRI and emerging imaging techniques such as “MR neurography” have been essential for direct visualization of nerves, including their internal anatomy and tissue characteristics. A 3-T MRI scanner gives a greater signal-to-noise ratio than a 1.5-T scanner and can be translated to higher plane resolution, thinner slices, and faster imaging.¹¹ Careful attention to technique when performing nerve imaging is essential. Unfortunately many institutions around the world rely on less than optimal techniques for imaging peripheral nerves, and people fail to administer contrast medium or adequately localize studies for optimal resolution and image quality. These lapses can contribute to the difficulty of identifying and characterizing small or otherwise subtle lesions in the nerves such as intraneural perineurioma (Fig. 3).

Pearl

We highly recommend using 3-T MRI with dedicated receiver coils, which allow the best opportunity to localize lesions and visualize their imaging characteristics. The use of a contrast agent is critical when perineurioma is even a remote clinical consideration.

Pitfall 3: The “Invisible” Perineurioma—Small and Hard to Localize

As the neoplastic perineurial cells that surround the nerve fibers proliferate, the fusiform enlargement becomes progressively more detectable with MRI. The size of the lesion at the time of diagnosis can be variable and does not necessarily correlate with the severity of symptoms, meaning that small lesions can cause serious neurological impairment. Boyanton et al. found that the average maximum size was 5.4 cm with a median of 4 cm and a range

FIG. 3. Case 2. Axial spoiled gradient (SPGR) post-contrast 1.5-T (left) and 3-T (right) MR images obtained in a patient with intraneural perineurioma illustrating the importance of high-resolution MRI. A 54-year-old man was referred for further management of a sciatic PNST found as part of an imaging study for tibial mononeuropathy. When the patient was interviewed, he recalled first noticing some degree of limitation and weakness in his left foot about 20 years previously and that it had worsened slowly with time. The initial MR image (left) showed a rounded enhancing mass lesion localized in the sciatic nerve at the level of the thigh. When the imaging study was repeated using a 3-T magnet, the intraneural anatomy was clearly visualized and showed an enlargement of the nerve fascicles that enhanced with contrast administration in the tibial component of the sciatic nerve (right). A targeted fascicular biopsy was done, and the pathology was conclusive for intraneural perineurioma.

of 0.5 to 18 cm; although they did not discriminate between the different axes,² the largest dimension usually refers to length. Mauermann et al. reported that the median values for lesion diameter and length were 1.2 cm (range 0.4–2.3 cm) and 8.0 cm (range 2.5–32 cm) respectively, reflecting the fusiform arrangement of the lesion and the degree of variability along the longitudinal axis. In the same study, 11 patients had follow-up imaging (mean time of 38 months) that showed no significant change in the lesion size despite mild progression of the neurological deficit.⁸

Size (and therefore conspicuity) can be a determinant for the accurate identification of any lesion. The slice

FIG. 4. Case 3. Coronal T1-weighted contrast-enhanced (A), sagittal SPGR post-contrast (B), axial T2-weighted (C), and axial SPGR post-contrast (D) MR images obtained in an 8-year-old girl illustrating why this lesion was considered almost invisible. The patient had a long-standing and slowly progressive history of left-sided foot drop. Symptoms were first noted at age 4. EPS showed a chronic peroneal neuropathy and localized the lesion distal to the branch of the short head of the biceps femoris. An MRI study of the knee was done, showing an atrophy of the anterior compartment of the leg but no structural lesion. A second MRI study was performed, this time a high-resolution study that included the pelvis and thighs (A), again without any abnormal finding besides the atrophy. As the clinical presentation was highly suspicious, the high-resolution MRI study was reviewed by a radiologist with expertise in nerve imaging who noticed a very subtle focal lesion in the peroneal division of the sciatic nerve in the mid-thigh. This was only visible on one of the slices and was identified in the sagittal sequence where the length of the tumor was the largest (B). Imaging was repeated using a 3-T magnet with dedicated imaging (2-mm slices) over the focal area seen on the larger-field-of-view images, and this study showed with greater detail a short segment area of fusiform enlargement with loss of architecture in the peroneal division of the sciatic nerve that was mildly hyperintense on T2-weighted images (C) and avidly enhanced after contrast administration (D).

thickness of conventional MRI varies widely depending on the area under interrogation. Fields of view also vary widely, ranging from 4–6 cm for a finger to up to 45 cm when imaging the abdomen or pelvis. As field of view increases in size, resolution decreases unless the examination time is prolonged. Thicker slices may be needed to cover large areas (for example, when imaging along the entire course of the sciatic nerve), and there may be a gap between images. Partial volume effects for tiny lesions not contained within an individual slice can further compound the difficulty in seeing very small lesions. Nerves may have incomplete involvement—sometimes only a single nerve fascicle in a large nerve is affected, which can lead to a confusing picture in downstream denervation effects. Subtle fusiform enlargement in a large nerve may be very difficult to recognize, especially when side-to-side comparisons are not available (Fig. 4).

Pearl

In cases in which there is a high clinical suspicion and clear geographic localization but initial imaging results are “negative,” dedicated imaging using the highest possible resolution, beginning proximal to the affected nerve territory, can be performed to help visualize small lesions missed in the initial scan. Coronal and sagittal series may be especially helpful for seeing lesions over their length that may be harder to see in the axial plane. The use of all 3 planes can be helpful to distinguish the affected segment from normal nerve.

Pitfall 4: Management

In view of the enlarging experience with intraneural perineuriomas, we are not routinely performing biopsies in patients with typical features (clinical, EPS, and imaging) at present. When the diagnosis is unclear despite optimized imaging or histological confirmation is desired, we have favored the use of targeted fascicular biopsy.

Management of intraneural perineurioma varies. Boy-

anton et al. reported that the most common practice was resection with or without nerve grafting, with the next most common treatment options being excisional biopsy and neurolysis.² Some authors support resection of the lesion to avoid further progression;⁴ however, Mauermann et al. demonstrated that there was no significant change in lesion size at long-term follow-up. Some authors have argued that surgery should be done to preserve remaining function, including the use of distal nerve transfers. Unfortunately, most patients present with severe and irreversible muscle atrophy, making functional recovery unlikely if only the nerve is addressed surgically; in such cases, there is always the possibility of worsening disability or pain after surgical treatment of the nerve. Other secondary reconstructive procedures, including tendon transfers, can be considered to restore function. Follow-up MRI is typically recommended when confirmatory histology is not available to be sure that the lesion does not change in size.

Pearl

Based on the follow-up of our patients we now believe that targeted fascicular biopsy is not necessary if the clinical presentation and the MR images are typical of an intraneural perineurioma. The most important imaging characteristics are avid enhancement of fusiform lesions of nerve with downstream atrophy in the affected nerve territory. Further neurological decline can be expected in such cases, and the patient must be reassured and counseled about possible secondary procedures to restore function.

Conclusions

Recognition of intraneural perineurioma as a cause of progressive neuropathy in children and young adults is slowly increasing as the clinical and imaging features become more familiar to practitioners (Table 1). Until recently little was known about its clinical presentation, radiological features, and long-term outcome. Because it is uncommon, general knowledge among physicians is lack-

TABLE 1. Features of intraneural perineurioma

Clinical characteristics
Disease of childhood and young adulthood.
No sex predilection.
Affects equally upper and lower extremities, but is most commonly located in sciatic nerve or its branches.
Typically limited to 1 nerve (focal); however plexus or multiple nerve involvement can also occur.
Electrophysiological studies commonly show a focal motor neuropathy with axonal degeneration. Sensory function is also frequently affected.
No family history, no syndrome stigmata.
Imaging studies (MRI)
High-resolution MRI (3 T) shows a fusiform enlargement of the nerve, with conserved architecture but enlarged fascicles. Isointense on T1-weighted and hyperintense on T2-weighted images.
Avid enhancement with contrast administration.
Muscle atrophy localized in the muscles innervated by the affected nerve.
Histopathological characteristics
Concentric whorls of perineurial cells around the nerve fibers.
Strong immunoreaction to the perineurial cell marker EMA, and negative for the Schwann cells marker S-100.
Management and prognosis
Targeted biopsy can be done for diagnosis confirmation but is not necessary if the clinical history and imaging are characteristic.
Reassure the patient and if applicable offer secondary surgical options for functional restoration.
Follow-up MRI is typically obtained if tissue diagnosis is not established and for routine surveillance to establish the natural history.

ing which may have historically led to mistakes or delay in the diagnosis. Even when intraneural perineurioma is a clinical consideration, localization with clinical examination and EPS can be challenging which then leads to difficulties in optimizing imaging over a large area of interrogation. Persistence and patience is required to find and characterize what are often small and subtle lesions. Based on our growing experience, we now consider that targeted biopsy is not necessary when characteristic clinical and imaging findings are present, meaning that there must be a clear clinical history of slowly progressive painless neuropathy and weakness in a child or young adult, supportive EPS, and classical imaging MRI findings, including identifying a fusiform lesion arising from a nerve with avid enhancement. In cases where lesions are not recognized but clinical suspicion is high we recommend reviewing step by step the work-up sequences, making sure that an adequate preimaging localization based on physical examination and EPS was performed and that high resolution, targeted imaging was done in the appropriate nerve territory. Dogged pursuit of a structural lesion using optimized assessment, including a thorough clinical history, a physical examination, EPS, and imaging will have its reward in the accurate diagnosis of this important but underappreciated cause of neuropathy.

References

1. Ahlawat S, Chhabra A, Blakely J: Magnetic resonance neurography of peripheral nerve tumors and tumorlike conditions. **Neuroimaging Clin N Am** **24**:171–192, 2014
2. Boyanton BL Jr, Jones JK, Shenaq SM, Hicks MJ, Bhattacharjee MB: Intraneural perineurioma: a systematic review with illustrative cases. **Arch Pathol Lab Med** **131**:1382–1392, 2007
3. England JD, Asbury AK: Peripheral neuropathy. **Lancet** **363**:2151–2161, 2004
4. Gruen JP, Mitchell W, Kline DG: Resection and graft repair for localized hypertrophic neuropathy. **Neurosurgery** **43**:78–83, 1998
5. Lehmann HC, Meyer Zu Horste G, Kieseier BC, Hartung HP: Pathogenesis and treatment of immune-mediated neuropathies. **Ther Adv Neurol Disorder** **2**:261–281, 2009
6. Macarenco RS, Ellinger F, Oliveira AM: Perineurioma: a distinctive and underrecognized peripheral nerve sheath neoplasm. **Arch Pathol Lab Med** **131**:625–636, 2007
7. Maravilla KR, Bowen BC: Imaging of the peripheral nervous system: evaluation of peripheral neuropathy and plexopathy. **AJNR Am J Neuroradiol** **19**:1011–1023, 1998
8. Mauermann ML, Amrami KK, Kuntz NL, Spinner RJ, Dyck PJ, Bosch EP, et al: Longitudinal study of intraneural perineurioma—a benign, focal hypertrophic neuropathy of youth. **Brain** **132**:2265–2276, 2009
9. Saporta MA: Charcot-Marie-Tooth disease and other inherited neuropathies. **Continuum (Minneapolis)** **20** (5 Peripheral Nervous System Disorders):1208–1225, 2014
10. Spinner RJ, Carmichael SW, Wang H, Parisi TJ, Skinner JA, Amrami KK: Patterns of intraneural ganglion cyst descent. **Clin Anat** **21**:233–245, 2008
11. Thawait SK, Chaudhry V, Thawait GK, Wang KC, Belzberg A, Carrino JA, et al: High-resolution MR neurography of diffuse peripheral nerve lesions. **AJNR Am J Neuroradiol** **32**:1365–1372, 2011
12. Woertler K: Tumors and tumor-like lesions of peripheral nerves. **Semin Musculoskelet Radiol** **14**:547–558, 2010

Disclosure

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, Restrepo, Amrami. Acquisition of data: Spinner, Amrami. Analysis and interpretation of data: Restrepo, Amrami. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Study supervision: Spinner, Amrami.

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