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Neuromuscular choristoma and circumferential nerve territory desmoid-type fibromatosis: imaging findings supporting a nerve-driven mechanism

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OBJECTIVE Neuromuscular choristoma (NMC) is a rare developmental malformation of peripheral nerve that is frequently associated with the development of a desmoid-type fibromatosis (DTF). Both NMC and NMC-DTF typically contain pathogenic *CTNNB1* mutations and NMC-DTF develop only within the NMC-affected nerve territory. The authors aimed to determine if there is a nerve-driven mechanism involved in the formation of NMC-DTF from the underlying NMC-affected nerve.

METHODS Retrospective review was performed for patients evaluated in the authors' institution with a diagnosis of NMC-DTF in the sciatic nerve (or lumbosacral plexus). MRI and FDG PET/CT studies were reviewed to determine the specific relationship and configuration of NMC and DTF lesions along the sciatic nerve.

RESULTS Ten patients were identified with sciatic nerve NMC and NMC-DTF involving the lumbosacral plexus, sciatic nerve, or sciatic nerve branches. All primary NMC-DTF lesions were located in the sciatic nerve territory. Eight cases of NMC-DTF demonstrated circumferential encasement of the sciatic nerve, and one abutted the sciatic nerve. One patient had a primary DTF remote from the sciatic nerve, but subsequently developed multifocal DTF within the NMC nerve territory, including 2 satellite DTFs that circumferentially encased the parent nerve. Five patients had a total of 8 satellite DTFs, 4 of which abutted the parent nerve and 3 that circumferentially involved the parent nerve.

CONCLUSIONS Based on clinical and radiological data, a novel mechanism of NMC-DTF development from soft tissues innervated by NMC-affected nerve segments is proposed, reflecting their shared molecular genetic alteration. The authors believe the DTF develops outward from the NMC in a radial fashion or it arises in the NMC and wraps around it as it grows. In either scenario, NMC-DTF develops directly from the nerve, likely arising from (myo)fibroblasts within the stromal microenvironment of the NMC and grows outward into the surrounding soft tissues. Clinical implications for patient diagnosis and treatment are presented based on the proposed pathogenetic mechanism.

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KEYWORDS desmoid-type fibromatosis; neuromuscular choristoma; nerve territory; NMC-DTF; oncology

Neuromuscular choristoma (NMC) is a rare developmental malformation in which skeletal muscle is aberrantly located within peripheral nerve fascicles. NMC typically involves major nerves.[1–5] The clinical features of NMC may be subtle and are often underrecognized and overlooked.[6] NMC is associated with nerve territory findings that can help establish the diagnosis. Patients with NMC frequently present with neuropathy and undergrowth, such as a shortened cavovarus foot, limb length discrepancy, or joint dysplasia. Our group has previously reported that NMC is frequently associated with the development of a desmoid-type fibromatosis (DTF).[7] NMC-DTF occurs in as many as 80% of patients[7] and has been identified in those with recognized[7] or initially unrecognized NMC.[6] Similar to sporadic DTF, NMC-DTF is a locally aggressive, (myo)fibroblastic neoplasm. Although it does not undergo malignant transformation, NMC-DTF is locally infiltrative, frequently involving neurovascular

ABBREVIATIONS DTF = desmoid-type fibromatosis; LN = lipomatosis of nerve; NMC = neuromuscular choristoma.

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TABLE 1. Patient demographics and radiological characteristics of NMC-DTF

Pt No.	Age (yrs), Sex	Potential Trigger Factor for DTF	Site of Primary DTF Mass	NMC on MRI at Site of Primary DTF	Primary DTF Pattern	Focality	Site of Satellite DTF Mass	Satellite DTF Abutting or Circumferentially Involving Parent Nerve
1	15, F	Surgery, common peroneal nerve decompression (3 mos before)	Distal sciatic & proximal tibial/common peroneal nerve	Yes	Circumferential	Uni	NA	NA
2	34, F	Spontaneous	Proximal sciatic nerve	Yes	Circumferential	Multi	Gastrocnemius muscle	Circumferential
3	20, M	Spontaneous	Distal sciatic/tibial nerve	Yes	Circumferential	Uni	NA	NA
4	51, M	Biopsy (3 yrs before)	Proximal sciatic nerve	Yes	Circumferential	Uni	NA	NA
5	18, M	Biopsy (5 mos before)	Proximal sciatic nerve	Yes	Circumferential	Multi	Main sciatic nerve (distal to primary NMC-DTF)	Abutting
6	14, M	Biopsy (2.5 yrs before)	Mid sciatic nerve	Yes	Abutting sciatic nerve	Multi	Main sciatic nerve (proximal to primary NMC-DTF)	Abutting
7	11, M	Biopsy (6 mos before)	Proximal sciatic nerve	Yes	Circumferential	Uni	NA	NA
8	16, M	Spontaneous	Sciatic nerve	Yes	Circumferential	Multi	2 DTFs: gastrocnemius muscle & pes anserinus tendons	Gastrocnemius muscle, abutting; pes anserinus tendons, no contact
9	20, F	Biopsy (5 mos before)	No nerve seen, potential intramuscular branch	No	Gluteal mass remote from sciatic nerve	Multi	3 DTFs: proximal sciatic nerve, distal sciatic nerve, common peroneal nerve	Proximal sciatic nerve, circumferential & distal sciatic nerve, abutting; common peroneal nerve, circumferential
10	13, F	Spontaneous	Proximal sciatic nerve	Yes	Circumferential	Uni	NA	NA

Multi = multifocal; NA = not available; Pt = patient; Uni = unifocal.

structures.[8–13] Similar to sporadic DTF, both NMC and NMC-DTF typically contain pathogenic-activating mutations in *CTNNB1*, the gene encoding beta-catenin.[14–16]

The radiological features of NMC are fusiform fascicular enlargement, less than 50% intralesional fat, and signal characteristics similar to skeletal muscle on pre- and postcontrast MRI.[17] The 50% intralesional fat rule should be applied to the portion of the lesion with soft-tissue elements rather than the entire lesion.[17,18] NMC can be misinterpreted or misdiagnosed as lipomatosis of nerve (LN), also known as lipofibromatous or fibrolipomatous hamartoma;[19–21] however, LN is composed of greater than 50% fat. LN, in contrast to NMC, is typically associated with neuropathy, nerve territory bone and soft-tissue overgrowth (such as macrodactyly), and lipomas.[22]

Our group has observed that NMC-DTF arises consistently within the NMC-affected nerve territory and has direct contact with the NMC itself.[6,23] This nerve territory concept has treatment implications.[23] We recently evaluated a patient who presented with NMC-DTF and observed that imaging studies of the NMC-DTF showed circumferential encasement of the NMC-affected sciatic nerve, prompting an evaluation of the imaging features of all available cases of NMC-DTF to characterize these imaging features in relation to the underlying sciatic nerve.

Methods

After obtaining IRB approval, a retrospective review was performed for any patient evaluated in our institution during the last 20 years with a diagnosis of NMC-DTF in the sciatic nerve or sciatic nerve territory. We selected the sciatic nerve as the simplest model to verify our hypothesis. The sciatic nerve is the most commonly affected site for NMC, and in our experience, for NMC-DTF as well. Moreover, the sciatic nerve is a large single peripheral nerve that is easier to evaluate on MRI examinations than other sites, such as the brachial plexus, which is the second most common site for NMC-DTF. The diagnosis was established based on a confirmatory biopsy of NMC and/or NMC-DTF in patients with clinical and radiological features of NMC-DTF. Only patients with available MRI were included in the study. Serial MR images were reviewed when available. Some patients also underwent ^{18}F-FDG PET with CT (FDG PET/CT) studies when available, but this was not an inclusion criterion. Many of these

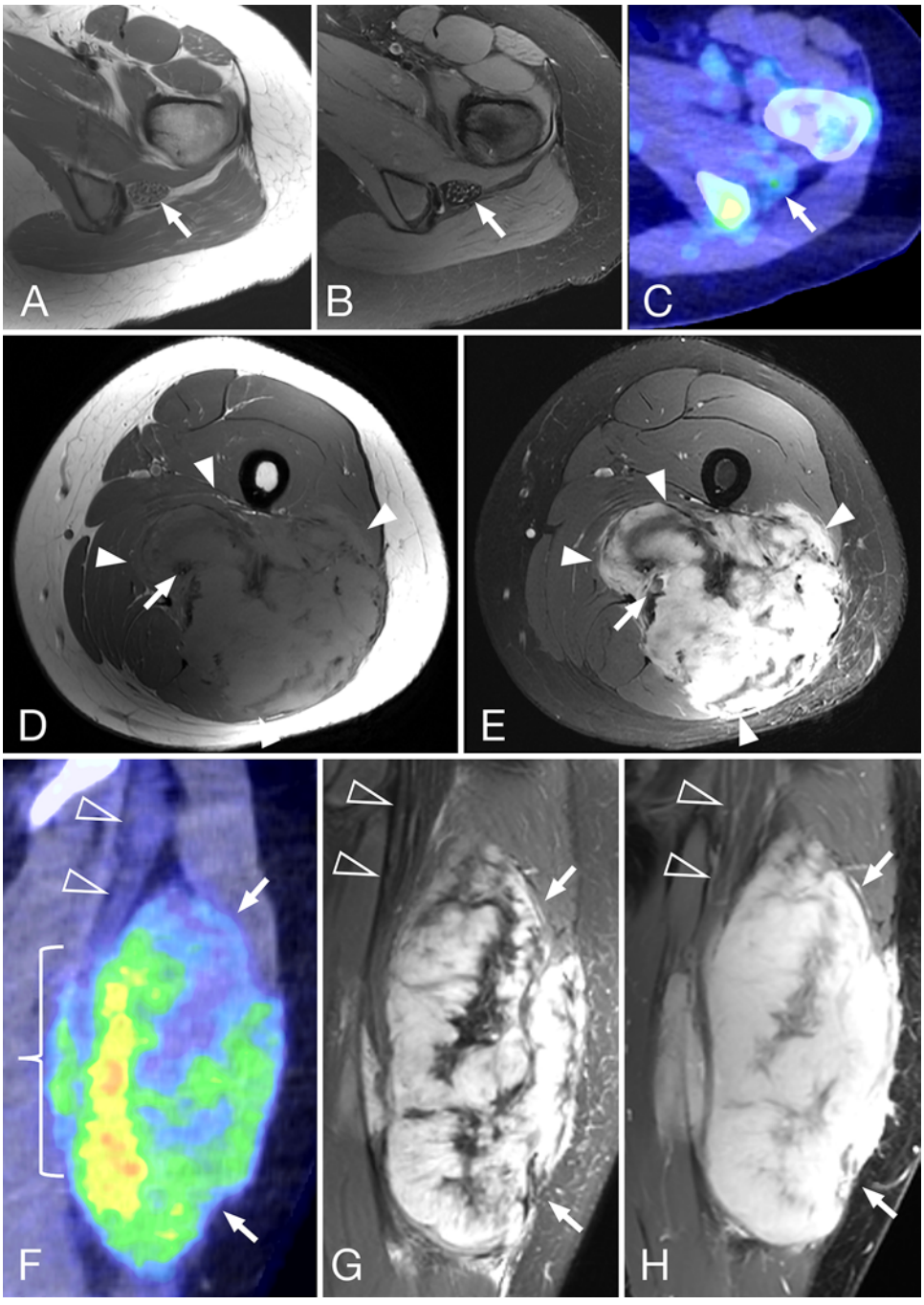

FIG. 1. Patient 10. NMC-DTF with circumferential involvement of the sciatic nerve. A 14-year-old girl presented with a 1-year history of a progressive posterior left-thigh mass. The mass was first noted several months after a horseback jump resulted in a fall on her thighs. She described consistent discomfort with occasional radiating paresthesias into her foot with prolonged sitting or long walking. The mass was firm and nonmobile. Her neurological examination was normal. The left leg was 0.5 cm shorter than the right (hip to ankle). Axial T1-weighted (**A**) and T2-weighted fat-saturated (**B**) MR images at the level of the buttock demonstrated an abnormality of the left sciatic nerve (*arrows*). The nerve demonstrated diffuse fascicular enlargement with a paucity of intraneural fat, consistent with an NMC. There were areas of decreased T1 and T2 signal within the proximal sciatic nerve, which may have represented developing fibromatosis. A corresponding axial fused FDG PET/CT image (**C**) demonstrated low-level FDG uptake within the sciatic nerve at this level (*arrow*). Axial T1-weighted (**D**) and T2-weighted fat-saturated (**E**) MR images at the mid-thigh showed a large heterogeneous DTF mass (*arrowheads*) completely encasing the sciatic nerve (*arrows*). Coronal oblique fused FDG PET/CT (**F**), T2-weighted fat-suppressed MR (**G**), and postgadolinium fat-suppressed MR (**H**) images demonstrated fascicular thickening of the proximal left sciatic nerve (*arrowheads*), which was surrounded by an FDG avid (standardized uptake value [SUV] max 5.4) heterogeneously T2 hyperintense, enhancing mass (*arrows*) within the proximal thigh. The segment of the sciatic nerve associated with the mass showed areas of increased FDG activity (*bracket*, F). Figure is available in color online only.

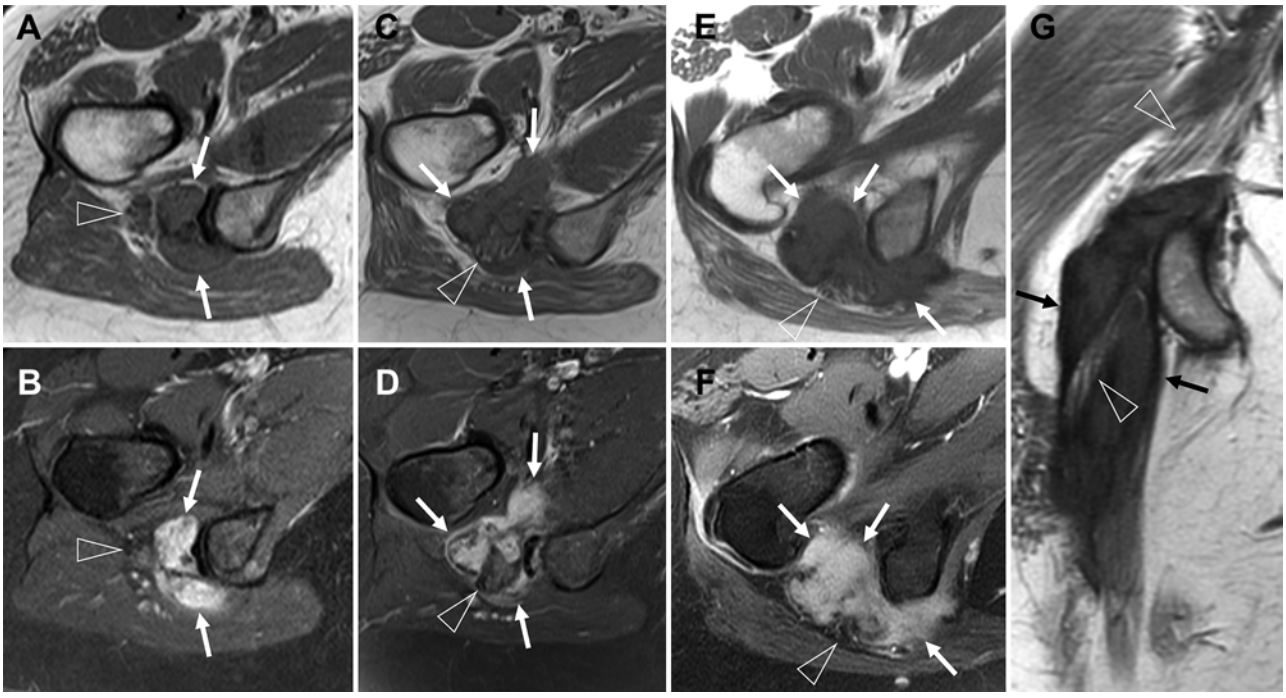

FIG. 2. Patient 2. Evolution of an NMC-DTF over time. A 35-year-old woman presented with right lower-extremity pain and a posterior thigh mass. She had mild pes cavus. Her right foot was 0.5 cm smaller than the other side. There was a positive Tinel's sign in the proximal third of the thigh. Discrete motor testing other than the heel and toe rise was essentially normal. There was decreased sensation in the dorsum of the foot. Sequential axial T1-weighted and fat-saturated postgadolinium MR images from 2012 (**A and B**), 2013 (**C and D**), and 2014 (**E and F**) demonstrated progressive DTF formation associated with a right sciatic nerve NMC at the level of the ischial tuberosity. On the baseline examination, DTF formation (*arrows*) was limited to the medial aspect of the sciatic NMC (*arrowheads*), with progressive DTF enlargement and infiltration along the entire anterior aspect of the NMC on follow-up examinations. Coronal T1-weighted MR image from 2014 (**G**) demonstrated a DTF (*arrows*) encircling the proximal sciatic NMC (*arrowheads*), with both proximal and distal extension.

patients have been previously included in other NMC or NMC-DTF studies by our group.[7,23–25]

MRI and FDG PET/CT studies were reviewed by two board-certified musculoskeletal radiologists (B.M.H. and S.M.B.) by consensus. The pattern and focality of the NMC-DTFs were analyzed. The pattern (circumferential around the parent nerve, abutting/not circumferential, or remote from an identifiable nerve) was determined based on the location of the NMC-DTF and relationship to the NMC-affected nerve. The focality (unifocal or multifocal) was determined by the number of identified NMC-DTFs, with ≥ 2 defined as multifocal NMC-DTF: primary was the largest lesion, and satellite was either a smaller separate DTF at the time of initial imaging or a new DTF that developed on follow-up imaging. Clinical variables were obtained from medical records including age, sex, NMC and NMC-DTF location, and potential trigger factors for NMC-DTF formation.

Results

We identified 10 patients with NMC of the sciatic nerve and NMC-DTF of the sciatic nerve or sciatic nerve territory (Table 1). NMC-DTF occurred in 6 males and 4 females, with a mean age at diagnosis of 21 (range 11–51) years. Six patients developed DTF after an NMC-related procedure or event (5 with fascicular biopsy and 1 common peroneal nerve neurolysis) and 4 had no history of traumatic or iatrogenic trigger for the DTF. On MRI, all NMC-DTFs were present at or distal to the NMC lesions identified by morphological changes. Four patients underwent serial MRI. FDG PET/CT images were available in 3 patients. On all PET/CTs, the segment of sciatic nerve NMC surrounded by DTF showed low-level FDG uptake, which while hypometabolic relative to the DTF itself, was appreciably increased above the perineural soft tissues. Segments of NMC proximal to and uninvolved by DTF also showed low-level increased FDG activity compared with background soft tissue. The pattern of FDG activity in all DTF masses was heterogeneous.

Patterns of DTF Development in NMC

In 8 of the 10 patients, circumferential DTF encasement of the sciatic nerve NMC was observed (Fig. 1). In patients with serial imaging, DTF enlargement and progression along the nerve territory was observed on consecutive follow-up examinations (Fig. 2). Patient 6 presented with a DTF abutting, but not encasing, the sciatic nerve (Fig. 3). Patient 9 presented with a DTF within the gluteal musculature that was separate from the sciatic nerve, and not associated with a visible nerve branch (Fig. 4).

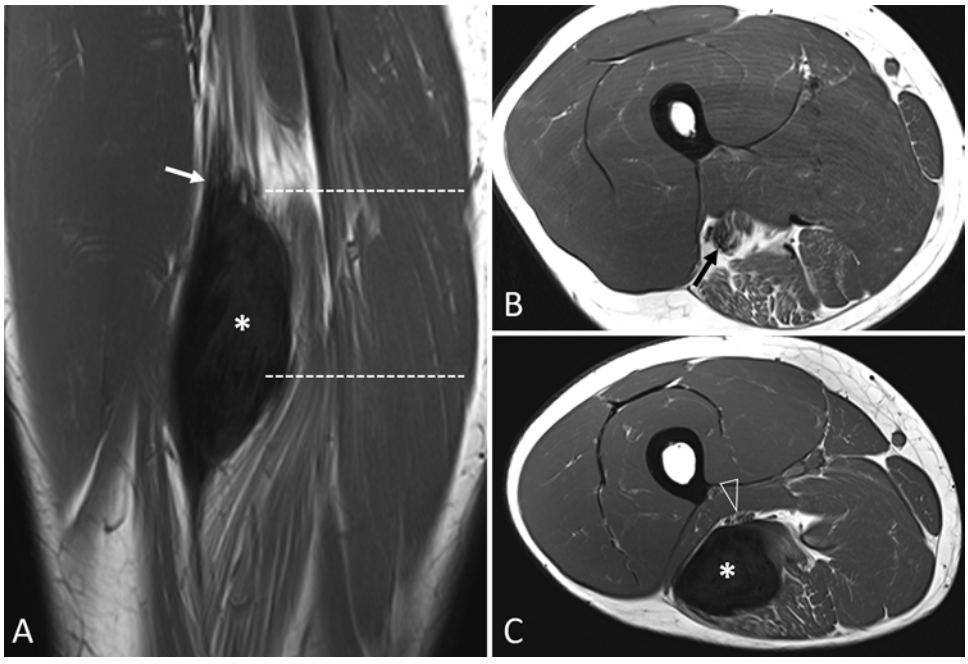

FIG. 3. Patient 6. NMC-DTF involving the sciatic nerve and likely a hamstring branch. A 14-year-old boy presented with a 1-cm shorter right leg, positive Trendelenburg sign, and weakness in the tibial-innervated muscles. He had a cavus foot with normal sensation and no pain. A coronal T1-weighted MR image of a DTF (*asterisk*) involving the right sciatic nerve (**A**) showed a T1 hypointense fibromatosis interdigitation with the sciatic nerve bundles along the proximal margin of the mass (*arrow*). Corresponding axial T1-weighted MR images at the levels denoted by the *dashed lines* in panel A demonstrated a T1 hypointense signal between enlarged, T1 isointense sciatic NMC nerve fascicles (**B**, *arrow*). More distally, the DTF (*asterisk*) appears adjacent to, but separate from, the sciatic NMC (*arrowhead*) in the expected location of a hamstring nerve branch (**C**).

Five patients had multifocal DTF, with a total of 8 satellite DTF lesions. Patients 2 and 8 had a DTF in the gastrocnemius muscle. The satellite DTF in patient 2 within the gastrocnemius muscle circumferentially involved the tibial nerve. In patient 8, a DTF in the gastrocnemius muscle abutted the tibial nerve. A second, more distal DTF in patient 8 was located medially along the pes anserinus tendons. Interestingly, patient 9 developed a satellite DTF along the proximal sciatic nerve 1 year after resection of the gluteal DTF and also developed recurrence within the operative bed. Follow-up imaging in patient 9 demonstrated the development of two additional DTFs, one abutting the distal sciatic nerve and one circumferentially encasing the common peroneal nerve. The local recurrence within the gluteal musculature eventually progressed to involve the entire proximal sciatic nerve and lumbosacral plexus in a circumferential fashion (Fig. 4). The remaining satellite DTF lesions all occurred along the sciatic nerve NMC, and all abutted the NMC without circumferential encasement.

Discussion

Our group has previously reported imaging features of NMC-associated DTF, including the observation that DTF associated with NMC arises solely within the NMC-affected nerve territory and that it typically shows direct contact with the NMC itself.[23] The present study expands upon the imaging features of this clinicoradiological pattern that further support a nerve-driven mechanism. In all cases, the MR images demonstrated NMC in the sciatic nerve (some of which extended proximally into the lumbosacral plexus) beginning in the buttock region. The primary DTF was located in the thigh with circumferential encasement of the sciatic nerve in 8 cases and abutted the sciatic nerve in 1 case. Of the 8 satellite DTFs, 7 abutted or encased the sciatic nerve or sciatic nerve branches.

We recognize that the presence of the circumferential pattern in these cases likely evolves over time and may not be identified on early imaging studies. Nevertheless, there are a few possibilities to account for the circumferential growth pattern: the NMC-DTF develops outward from the NMC in a radial fashion from abnormal fibroblasts, or it arises from the epineurium or immediate perineural tissue around the NMC and wraps around it as it grows (Fig. 5). In either scenario, DTF likely develops from (myo)fibroblasts within the stromal microenvironment of the NMC and grows outward into the surrounding soft tissues, supporting an NMC nerve-driven process. While we must consider that the NMC-DTF could arise more peripherally in the soft tissues of the NMC-affected territory and grow toward the NMC, we consider this less likely for the following reasons: 1) most NMC-DTFs show direct contact with the NMC irrespective of NMC-DTF size and even with multifocal NMC-DTFs (which arise along nerve segments); 2) NMC-DTFs typically develop after the NMC, and as mentioned, universally arise within the NMC-affected nerve territory; and 3) NMCs

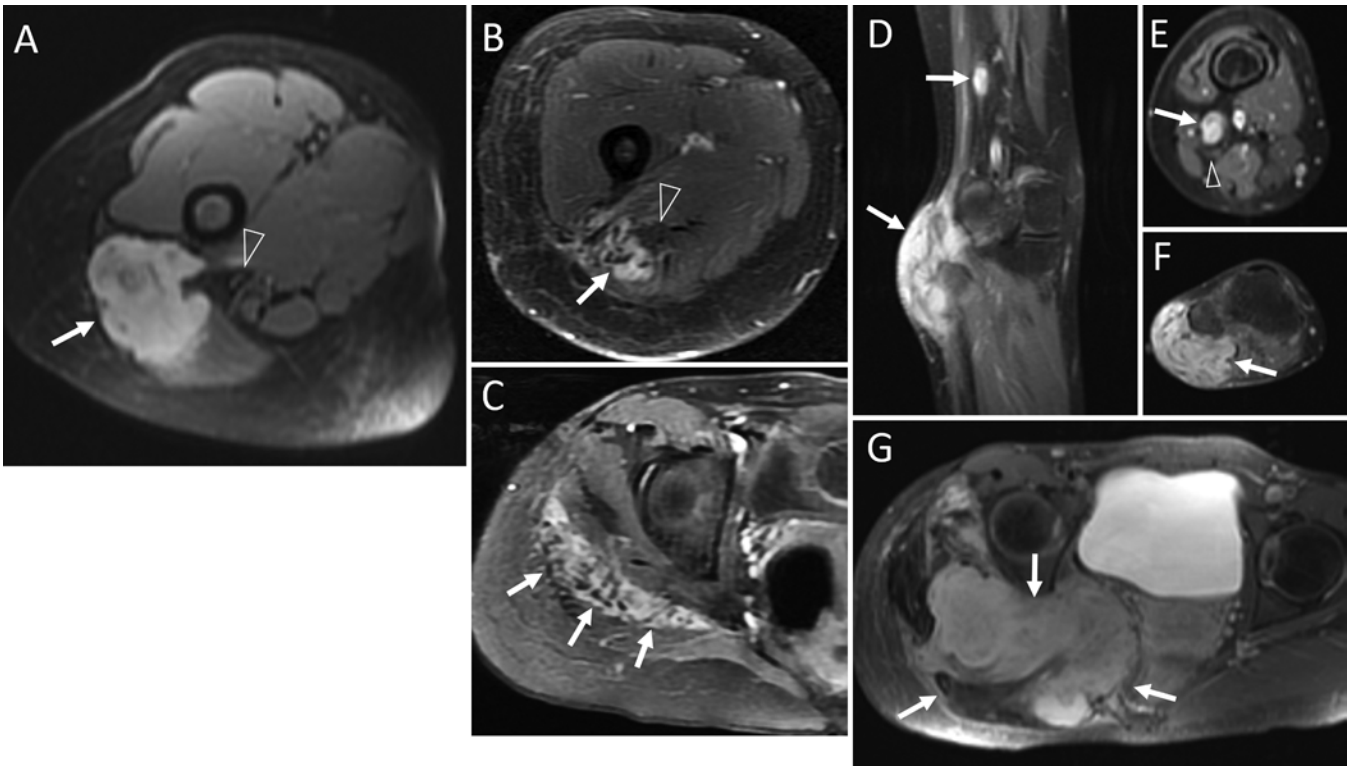

FIG. 4. Patient 9. Multifocal satellite DTFs abutting and circumferentially involving the right sciatic NMC territory nerves. A 20-year-old woman initially presented with a right gluteal DTF that was resected. Axial T2-weighted fat-saturated MRI from 2006 (**A**) demonstrated a hyperintense intramuscular mass (*arrow*) that appeared separate from a right sciatic nerve NMC (*arrowhead*). Axial T1-weighted fat-saturated postgadolinium MR images from 2008 (**B and C**) showed a satellite DTF (*arrows*) abutting the sciatic nerve NMC (*arrowhead*) distal to the resected gluteal DTF (B), and a locally recurrent DTF extending proximally within the right gluteal musculature (C). Coronal and axial T1-weighted fat-saturated postgadolinium MR images from 2012 (**D–G**) demonstrated a new satellite DTF (*upper arrow* in D, *arrow* in E) abutting the distal sciatic nerve NMC (*arrowhead*, E) and another satellite DTF circumferentially involving the common peroneal nerve (*lower arrow* in D, *arrow* in F). Significant progression of the proximal DTF was also observed, with diffuse involvement of the gluteal musculature, circumferential involvement of the sciatic nerve and lumbosacral plexus, and extension into the pelvis (*arrows*, G).

and NMC-DTFs typically harbor identical pathogenic-activating *CTNNB1* mutations. Finally, we have recently observed that NMCs show low-level FDG uptake that may reflect a population of activated *CTNNB1*-mutated (myo)fibroblasts in the stromal microenvironment of the NMC.[23] Similarly, in the current series, FDG PET/CT demonstrated mild diffuse increased uptake throughout the NMC, and the NMC encased by DTF demonstrated hypometabolism relative to the DTF, but increased FDG uptake relative to background soft-tissue uptake. Together, the imaging findings and pathologic and molecular genetic data support our hypothesis that NMC-DTF arises from *CTNNB1*-mutated NMC (myo)fibroblasts.

For the two cases in this series without circumferential growth of the DTF along the sciatic nerve NMC, 1 DTF broadly abutted the sciatic nerve and appeared to interdigitate with sciatic nerve fascicles (patient 6). The other case (patient 9) initially presented with an intramuscular DTF within the gluteal musculature, separate from the sciatic NMC. Interestingly, both of these patients later developed satellite DTFs abutting the sciatic nerve, and patient 9 also developed a satellite DTF encasing the proximal sciatic and common peroneal nerves. We hypothesize that DTFs without circumferential encasement of the parent nerve likely develop from and circumferentially involve an NMC-affected branch of the parent nerve. This hypothesis is supported by two prior observations: 1) we previously reported a case of NMC with clear involvement of both the parent and nerve branches due to intraoperative observation of skeletal muscle and contractility of both the parent nerve and its branch (see attached video in Hébert-Blouin et al.[7]); and 2) we have reported a case of occult NMC identified only retrospectively in an NMC-DTF initially believed to be sporadic DTF. In this case, the focus of the NMC identified within the NMC-DTF was a very small nerve twig with pathologic confirmation as an NMC, providing further support that NMC can extend into branches of a parent nerve.[6] In these cases of noncircumferential growth of the NMC around the parent nerve, we propose that the underlying pathogenetic mechanism for NMC-DTF formation is identical to those with a circumferential growth pattern of the parent nerve, that is, *CTNNB1*-mutated (myo)fibroblasts in the stroma of nerve branch NMC or in its immediate microenvironment. While we cannot prove our hypothesis

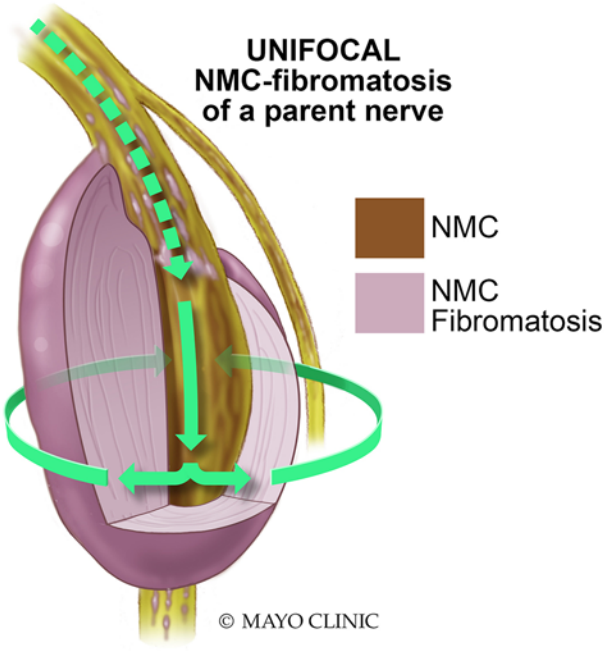

FIG. 5. Illustration of the nerve-driven pathogenetic mechanism for NMC-DTF formation (*green arrows*) from an underlying NMC of the parent sciatic nerve. By permission of the Mayo Foundation for Medical Education and Research. All rights reserved. Figure is available in color online only.

of direct nerve-derived DTF from an NMC-affected nerve segment, the imaging findings do support an intimate relationship between the nerve and the NMC-DTF. The occurrence of DTF arising apart from the parent nerve in the nerve territory appears analogous to the well-known finding of intramuscular schwannomas, which arise from small nerve branches that may be impossible to confidently identify by MRI, or even intraoperatively during resection.

In addition to our cases, we have identified evidence for the circumferential pattern in other NMC-DTF cases in the literature. These cases were described as "encompassing," "enveloping," "involving," etc., the parent nerve.[26–30] For example, in the paper by Wadhwa and colleagues,[26] a case was presented with an enlarged proximal right sciatic nerve and fibromatosis "encasing the right sciatic nerve and infiltrating the gluteal muscles" (Fig. 5 in that paper). The imaging features are remarkably similar to those seen in many of the cases in this series, such as patient 2 (Fig. 2), and we believe that this case and others like it represent NMC-DTF. Two other papers describing alternate pathologies leading to DTF also have similar MR images: Lee et al.[19] described a case of LN, and Woo and Win[31] described a case of myofibromatosis, both of which we believed was NMC.[20] These cases further support our proposed mechanism. Finally, we have observed that NMC-DTF in the brachial plexus shows the same mechanism, although it is more complicated to delineate the pattern in this location due to the complex anatomy, with multiple parent nerves and nerve branches within a relatively limited space.

NMC, and by association NMC-DTF, are rare entities, and their rarity hinders study of any causal relationship. While the molecular genetic data describing shared pathogenic *CTNNB1* mutations in NMC and NMC-DTF provide strong evidence that the two entities are linked, it is unclear if or how the NMC itself triggers the formation of NMC-DTF.[32] In this paper, we describe a novel radiological pattern of circumferential encasement of the NMC-DTF around the NMC-affected nerve in these patients, which we argue provides additional support of the direct relationship between NMC and NMC-DTF. Specifically, we propose that these imaging findings underlie a nerve-derived mechanism of NMC-DTF formation. This proposed mechanism has several clinical implications.

First, diagnostic biopsies from any position along the NMC-affected nerve are not recommended. In patients with NMC, the risk of NMC-DTF development is high, and both the MR and PET/CT imaging features of affected nerves and the cases with multifocal NMC-DTF suggest that NMC-DTF can develop anywhere along the affected nerve.[33] We suspect that "primed" *CTNNB1*-mutated (myo)fibroblasts are present throughout the NMC and/or nerve-adjacent soft tissues along the entire nerve, and thus advocate for a clinicoradiologic-based diagnosis of NMC.

Second, NMCs are difficult to resect with nerve-sparing or aggressive techniques given concerns for function and propensity for recurrence; even extremity amputation may not cure NMC-DTF. If we consider that the entire nerve contains NMC, any proximal residual NMC-affected nerve stump and its surrounding soft tissues likely harbor a *CTNNB1* mutation[14,25] and could represent a source for future development of NMC-DTF.[34,35] Systemic and nonsurgical treatment should be considered for the present until pending future treatment developments.

Third, given the observation of NMC-DTF multifocality and the development of NMC-DTF distal to nerve regions with the most characteristic imaging features of NMC, imaging the entire NMC-affected nerve should be considered at the time of diagnosis as well as serial imaging at follow-up for early detection of NMC-DTF.[23]

Limitations of the Study

We recognize several limitations of this study. MRI and PET/CT have inadequate spatial resolution to unequivocally characterize the pattern of NMC-DTF or its association with the nerve in small sciatic nerve branches, although the location of the NMC-DTF may still suggest circumferential encasement of a small nerve branch. While it is reasonable to suppose that the NMC-DTFs occurred along the expected course of a branch, without enough imaging resolution, this is a hypothesis rather than a data-supported assertion. Serial imaging was not available in all patients, and more frequent imaging over a longer period may offer an opportunity to delineate the imaging features of subclinical or early NMC-DTF, its relationship to NMC, as well as its growth patterns over time. While this series describes the imaging features of the association between the NMC-affected nerve and NMC-DTF based partly on our prior observation that NMC and NMC-DTF share identical pathogenic *CTNNB1* mutations, we cannot perform *CTNNB1* mutational testing of (myo)fibroblasts in the stroma of NMC or its immediate microenvironment

due to limited tissue access and current inability to test for mutations with single-cell resolution. Furthermore, we acknowledge that other mechanisms may underlie the imaging findings of NMC and NMC-DTF. Further studies with larger series and serial imaging are needed to better understand why some patients with NMC do not develop NMC-DTF, and ultimately to inform strategies for both prevention and early detection of NMC-DTF.

Conclusions

Based on clinical, radiological, and existing molecular genetic data, we propose that a nerve-driven pathogenetic mechanism underlies the intimate relationship between NMC and the development of an NMC-DTF. This proposed mechanism expands upon the previously described clinicoradiological nerve-territory pattern of NMC-DTF. Clinical implications for the diagnosis and treatment of NMC and NMC-DTF are presented based on our new proposed mechanism. Careful identification and evaluation of these patients with long-term follow-up, including serial MRI, will lead to further advances and answers to the many unresolved questions about NMC and NMC-DTF.

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Disclosures

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Author Contributions

Conception and design: Spinner, Maldonado, Broski, Carter, Howe. Acquisition of data: Spinner, Maldonado, Broski, Marek, Howe. Analysis and interpretation of data: Spinner, Maldonado, Broski, Carter, Howe. Drafting the article: Spinner, Maldonado, Broski, Carter, Howe. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Spinner. Administrative/technical/material support: Spinner, Howe. Study supervision: Spinner.

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