Unrecognized neuromuscular choristoma with recurrent desmoid-type fibromatosis and Marjolin ulcer: expanding the spectrum of neuromuscular choristoma sequelae within the nerve territory? Illustrative case

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BACKGROUND Neuromuscular choristoma (NMC) is a rare congenital lesion in which muscle tissue is admixed with nerve fascicles within a peripheral nerve. Patients commonly present in early childhood with neuropathy, plexopathy, or chronic undergrowth in the distribution of the affected nerve.

OBSERVATIONS The authors present the case of a 35-year-old man with unrecognized neuromuscular NMC of the sciatic nerve, which resulted in recurrent, multicentric NMC-associated desmoid-type fibromatosis (NMC-DTF) within the nerve territory in association with a Marjolin ulcer, a cutaneous malignancy.

LESSONS Based on anatomical and pathophysiological findings described in this case report, the authors support the association between NMC-DTF and Marjolin ulcer.

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KEYWORDS neuromuscular choristoma; fibromatosis; NMC-DTF; Marjolin ulcer

Choristomas are lesions in which normal tissue is found in abnormal locations. Neuromuscular choristoma (NMC), previously known as benign Triton tumor, is a rare congenital lesion in which muscle (most commonly mature skeletal) tissue is admixed with nerve fascicles within a peripheral nerve. Patients with NMC often present with progressive weakness, dysesthesias, and neuropathic pain. Patients commonly present in early childhood with neuropathy or plexopathy and undergrowth in the distribution of the affected nerve.1,2

We recently evaluated a patient found to have an unrecognized NMC of the sciatic nerve, which resulted in recurrent, multicentric NMC-associated desmoid-type fibromatosis (NMC-DTF) within the nerve territory in association with a Marjolin ulcer—a cutaneous malignancy (of which squamous cell carcinoma is the most common) that occurs in the setting of previously injured skin (such as from prior surgery or radiation), longstanding scars, burns, chronic wounds, and neuropathies, such as from diabetes or leprosy. We explore the possible interrelationship between NMC and the Marjolin ulcer due to the associated neuropathy and compressive NMC-DTF.

Illustrative Case

During the peak of the coronavirus disease 2019 (COVID-19) pandemic, we were asked to review clinical records, including imaging and pathological slides from a 35-year-old man treated at an outside institution, with a history of a recurrent DTF and a nonhealing ulcer in the left posterior thigh. When he was 16 years old, he had presented with a mass in the posterior thigh for which he underwent resection; external pathology reports rendered a diagnosis of DTF. (Slides were not available for review; biopsy of the lesion was performed at an overseas institution.) Local recurrence of the pathologically confirmed DTF led to re-resection 1 year after the first, with a resultant peroneal nerve palsy, and the patient subsequently underwent radiotherapy (unknown dose). Eleven years after
the re-resection, he spontaneously developed a nonhealing ulcer in the posterior thigh, which, after another 6 years, had increased in size (5 × 8 cm). The patient developed consistent pain with occasional radiating paresthesias into the foot. There was no documentation of interval imaging studies or treatment, but electrodiagnostic studies at the time demonstrated a complete longstanding, axonal, left common peroneal nerve lesion. Reinterpretation of magnetic resonance imaging studies done approximately 2 years earlier demonstrated diffuse abnormality of the left sciatic nerve with fusiform enlargement involving the extrapelvic sciatic nerve extending from the sciatic notch to the common peroneal and tibial nerves in the popliteal fossa, consistent with the radiological features of an NMC. Muscular denervation and atrophy were present involving the posterior thigh and anterior and deep posterior compartments of the proximal leg (Fig. 1). There were several perineural masses with heterogeneous T1- and T2-weighted signal consistent with NMC-DTF, including a 5.1 × 4.8-cm mass encasing the sciatic nerve in the proximal thigh (Fig. 1), a 5.0 × 4.2 × 9.2-cm lesion encasing the tibial neurovascular bundle within the popliteal fossa (Fig. 2), as well as a 2.4 × 2.3 × 7.6-cm mass along the posteromedial aspect of the proximal tibia. There were additional areas of linear T1/T2 hypointensity extending along nearly the entire length of the sciatic nerve in the thigh (Fig. 2). The appearance was consistent with extensive multifocal NMC-associated DTF. In addition, there was a large skin ulceration measuring 2.8 × 4.5 × 7.0 cm overlying the thigh-region NMC-DTF. In the proximal thigh, the sciatic nerve was only 7 mm from the skin (Fig. 3). In the spring of 2021, fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) demonstrated faint uptake in the sciatic nerve within the thigh, low-level uptake within the perineural NMC-DTF within the thigh and proximal leg with a maximum standardized uptake value (SUVmax) ranging from 2.1 to 2.7 (Fig. 2), and intense uptake along the area of ulceration, SUVmax 12.0 (Fig. 3). The intense FDG uptake along the superficial aspect of the ulcer was strikingly different from the
low-level uptake within the thigh and proximal leg, and greater than what would be expected with inflammatory uptake related to a nonhealing ulcer. This raised concern for malignancy. The FDG-PET abnormalities in the sciatic nerve, the masses, and the ulcer were discrete but contiguous in the thigh (Figs. 2 and 3). Excisional skin biopsy from the ulcerated region revealed invasive, well-differentiated squamous cell carcinoma (reviewed at our center with agreement). While there was no evidence of NMC or NMC-DTF, the biopsies sampled only the superficial soft tissues. Recommendations were made for either local treatment such as cryoablation or high-frequency ultrasound with magnetic resonance guidance, or systemic therapy such as sorafenib or doxorubicin-based chemotherapy.

**Discussion**

**Observations**

In sum, based on the constellation of clinical, imaging, and pathologic findings, we believe that this patient had an NMC of the sciatic nerve with longstanding and recurrent NMC-DTF, and that the cutaneous invasive squamous cell carcinoma (Marjolin ulcer) may have developed secondary to these lesions.

**Lessons**

Several relevant points need to be highlighted. (1) Occult cases of NMC have been identified in patients with neuropathy and in those with “sporadic” DTF.\(^3\) Based on our previous observations and the imaging findings, we believe that this case represents another example of unrecognized NMC with (recurrent) NMC-DTF. We have previously recommended not biopsying suspected cases of NMC given the pathognomonic clinicoradiologic features (and the potential for inducing DTF with biopsy or surgery).\(^3\) (2) The finding of nerve-territory NMC-DTFs,\(^4,5\) whether unicentric or multicentric, has been established in patients, with the NMC-DTFs developing either spontaneously or after iatrogenic injury (e.g., biopsy, resection of the NMC).\(^6,7\) (3) To our knowledge, this is the first case of NMC and NMC-DTF associated with an invasive squamous cell carcinoma/Marjolin ulcer within the nerve territory. We posit that the Marjolin ulcer was likely related to the repetitive micro- or macro-trauma/compression of the sciatic NMC or the NMC-DTF on the (previously operated and irradiated) skin and the chronic neuropathy and ulceration. We recognize that the posterior skin of the thigh is within the nerve territory of the lumbosacral plexus/sciatic NMC and are aware of the relationship between NMC and nerve-territory skin and soft tissue abnormalities (keloid and hypertrophic scar) following biopsy or surgery in patients.\(^4\) It is intriguing to speculate whether the skin in the NMC-affected territory harbored a CTNNB1 mutation, similar to those seen in NMC/NMC-DTF\(^8,9\) and, if present, whether this may have contributed to the development of the invasive squamous cell carcinoma within the ulcerated skin.

While the novel findings and possible association are apparent and important, the limitations underlying the observations are readily acknowledged. Because of the nature of the chart review, we did not perform a clinical examination and thus could not document any occult evidence of nerve-territory undergrowth, such as cavus foot or shortening of the limb. There was no histological diagnosis or molecular testing of the previously unrecognized NMC and, despite our attempts, we were unable to obtain tissue from the NMC-DTF or the Marjolin ulcer for genetic testing. We have previously described that NMC and NMC-DTF lesions share the same mutations in CTNNB1 (encoding beta-catenin)\(^8,9\) and that they tend specifically to harbor CTNNB1 p. S45 mutations, which have been associated with more aggressive behavior in DTF.\(^10\) Molecular studies may have provided insight into the relationship of the NMC-DTF, the Marjolin ulcer, and the background tissue within the NMC-affected nerve territory.

In conclusion, there are anatomical and pathophysiologic reasons to support an association between NMC-DTF and development of a Marjolin ulcer in this patient. We believe that the finding of the Marjolin ulcer, while unusual, may be an important sequel of NMC/NMC-DTF, particularly in a patient with longstanding NMC-DTF.

**References**


Disclosures
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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