Surgical treatment of common peroneal neuropathy in schwannomatosis:
illustrative cases

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BACKGROUND Neurofibromatosis syndromes such as neurofibromatosis type 1, neurofibromatosis type 2, and schwannomatosis often result in painful symptoms related to tumor burden.

OBSERVATIONS Painful symptoms classically associated with common points of peripheral nerve entrapment, such as common peroneal neuropathy at the fibular tunnel, may present in patients both with and without focal tumor involvement.

LESSONS Surgical decompression at the point of entrapment, with or without resection of tumor, may provide symptomatic relief. Examples of surgical decompression at the point of entrapment, both with and without resection of tumor, are presented.

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KEYWORDS schwannomatosis; common peroneal nerve; peroneal tunnel syndrome; double-crush syndrome; peripheral nerve entrapment

Schwannomatosis is the least common of the neurofibromatosis syndromes, affecting approximately 1 in 126,000 people.1 It is characterized by multiple schwannomas in the absence of vestibular nerve involvement and is clinically and biologically distinct from neurofibromatosis types 1 and 2.2 For patients with schwannomatosis, pain is the most common presenting symptom leading to diagnosis and is a leading cause of disability, and nearly 70% of patients report suffering from chronic pain.3 Chronic pain in schwannomatosis is often multifactorial but dominated by neuropathic pain related to schwannomas, with the overall tumor burden significantly associated with the severity of patient-reported pain.4 However, despite the relationship of tumor burden to overall pain and the frequent correlation of specific tumors to localizing painful symptoms, focal tumor burden does not always correlate with a patient’s specific painful symptoms.5,6 Surgical treatment of painful symptoms in schwannomatosis often focuses on the resection of symptomatic tumors.5,7,8 However, when considering surgical treatments in this patient population, particularly for localizing neuropathic pain, it is critically important to consider other etiologies, such as entrapment neuropathies, in addition to focal symptomatic tumors. Here, we present cases detailing the surgical treatment of two patients with an established diagnosis of schwannomatosis and painful common peroneal neuropathy due to entrapment at the fibular tunnel. The cases illustrate examples of how schwannomatosis may lead to an entrapment neuropathy due to either a small, focal tumor within the nerve or mild thickening of the nerve at a point of nerve constriction (such as the fibular tunnel), leading to painful neuropathy. These patients underwent decompression of the common peroneal nerve at the fibular tunnel with removal of any identifiable focal tumor; both obtained a good clinical result with symptomatic relief and no neurological detriment.

Illustrative Cases

Case 1

History, Physical Examination, Imaging Findings

A 46-year-old man presented with a past medical history of schwannomatosis, chronic lower back pain, and multifocal neuropathic pain associated with multiple nerve tumors and the sequelae of prior surgical treatments for painful schwannomas. He had undergone more than 10 prior resections of painful nodular tumors over the previous 30 years. Each of these resected tumors was a benign...
At his presentation to the multidisciplinary neurofibromatosis clinic at the MD Anderson Cancer Center, the patient noted multiple sites of pain, but his most bothersome symptom was a focal area of severe pain affecting the anterolateral right lower leg, from just below the knee to just above the ankle joint (Fig. 1). This pain was intermittent, present for more than 1 year, and rated at a severity of 8 of 10 on the visual analog scale (VAS). It was sharp and burning in character, without specific aggravating or alleviating triggers and without any radiating pain proximal or distal to the area. Previous treatments of his chronic right leg pain included laminectomy for resection of a right L5–S1 schwannoma, lumbar epidural steroid injections, lumbar sympathetic nerve blocks, and comprehensive medical pain management with multiple neuromodulatory medications.

On physical examination, he had no neurocutaneous markings or skin changes, no palpable nodules along the major nerves of the upper or lower limbs, and normal muscle bulk in the legs. His neurological examination showed normal ankle dorsiflexion, eversion and inversion of the foot, extension of toes, and ankle plantarflexion. He also exhibited no loss of sensation in the lower limbs. He did have a positive Tinel’s sign just below the right fibular head. The patient’s clinical examination and history appeared most consistent with a painful neuropathy of the common peroneal nerve. Review of multiple prior magnetic resonance imaging (MRI) studies of his spine and lower extremities revealed numerous nerve sheath tumors consistent with his diagnosis of schwannomatosis, but none were located within the right distal thigh or proximal right lower extremity to explain his focal pain (Fig. 2 left). After a discussion of treatment options, including decompression of the common peroneal nerve at the fibular head, spinal cord stimulation, and resection of nerve sheath tumors within the proximal sciatic nerve, he underwent decompression of the common peroneal nerve in conjunction with resection of several other disparate painful, nodular schwannomas, including a large tumor arising from an intercostal nerve on the right chest wall.

**Operation**

The patient was positioned in a left lateral decubitus position to facilitate resection of a schwannoma arising from the right sixth intercostal nerve in addition to decompression of the right common peroneal nerve. The latter was addressed through a 4-cm diagonal incision just below the fibular head. The nerve was easily identified, coursing around the anterolateral aspect of the fibular head. We inserted a #4 Penfield dissector into the fibular tunnel to follow the course of the nerve distally and found that the nerve was tightly compressed within the tunnel. The nerve was diffusely thickened but without focal nodularity or evidence of schwannoma (Fig. 3 left). We cut the overlying ligamentous and fascial band and, in this fashion, completely freed the nerve from further pressure in this location. The articular branch was identified and preserved. Direct intraoperative ultrasound showed no hypoechoic foci, confirming the absence of occult tumor within the diffusely enlarged nerve.

**Postoperative Course**

After surgery, the patient had complete and immediate resolution of the right anterolateral leg pain (0 of 10 on the VAS) without sensory or motor deficits. At his last follow-up 2 years after the surgery, he remained free of his prior lateral right lower leg pain.
Case 2
History, Physical Examination, Imaging Findings
A 59-year-old woman with a past medical history of dermatomyositis, lymphocytic colitis, and schwannomatosis presented with chronic abdominal pain and neuropathic pain affecting her right face and right lower leg. The patient had undergone prior resection of multiple schwannomas from the right arm and left upper thigh. She developed bothersome pain affecting the anterolateral right lower leg, starting just below the knee and radiating down the tibia. The pain in her right lower leg was similar in character to pain relieved by prior resection of schwannomas and was inadequately controlled with medical management. On physical examination, the patient had a small superficial palpable schwannaoma on the right anterior lower leg and normal muscle bulk in her legs. Ankle dorsiflexion, eversion and inversion of the foot, extension of toes, and ankle plantarflexion all showed full strength. Sensation was intact in the right leg, and Tinel’s sign was positive on the anterior aspect of the fibula just below the fibular head. As in case 1, the patient’s clinical examination and history suggested a painful common peroneal neuropathy. MRI revealed a contrast-enhancing nerve sheath tumor 3 mm in diameter, located in the vicinity of the fibular head and anatomically consistent with her focal pain syndrome (Fig. 2 right). The patient underwent decompression of the common peroneal nerve with resection of a small schwannoma arising from a single fascicle within the common peroneal nerve (Fig. 3 right). Operative details and postoperative course are summarized below.

Operation
The patient was positioned supine with a roll placed underneath her right hip, internally rotating the right leg and providing easy access to the anterolateral aspect of the right lower leg. In addition to the lower extremity surgery, the patient also underwent resection of two schwannomas of the anterior chest wall. As in case 1, a 4-cm diagonal incision at the junction between the fibular head and fibular shaft exposed the common peroneal nerve just proximal to the fibular tunnel. Opening of the fascia overlying the tunnel revealed a focal, round irregularity in the nerve consistent with the tumor seen on MRI at the proximal segment of the fibular tunnel. To protect the nerve, we inserted a #4 Penfield dissector into the tunnel and cut the fascial bands above the dissector to expose the nerve as it coursed distally. The tumor capsule was incised and dissected off the tumor to enable a subcapsular removal, and single entering and exiting fascicles to and from the tumor were identified. The fascicles were coagulated and cut, and the tumor was gently elevated en bloc.

Postoperative Course
The patient was admitted overnight for pain control and perioperative intravenous antibiotics. She had prompt and significant improvement of the right anterolateral leg pain and no sensory or motor deficits. She remained without recurrence of pain at the last follow-up 18 months after surgery.

Discussion
Observations
Surgical treatment of pain in patients with neurofibromatosis/schwannomatosis syndromes is often complicated by challenging diagnostic dilemmas. Combinations of simultaneous, related peripheral nerve and spinal nerve tumors, or multiple tumors along the course of a single peripheral nerve can make it difficult to define the symptomatic lesion. Additionally, recurrent or refractory pain may arise from a combination of tumor burden, sequelae of prior treatments, and/or additional diagnoses such as an intrinsic or entrapment neuropathy.

The etiology of a painful focal neuropathy in the presence of a readily identifiable, isolated lesion (such as a tumor) appears intuitive; however, in cases without a focal lesion, the etiology is less clear. Hypertrophy of nerves may be diffuse or segmental, and it is often seen in patients with neurofibromatosis type 1 and occasionally in those with schwannomatosis. It is important to note that the absence of tumor by palpation or by ultrasonography does not completely exclude the possible presence of one or more occult tumors within a segment of thickened nerve. In case 2, biopsy of the nerve was not done because of a concern that it would cause injury to nerve fascicles, local fibrosis, and neuroma formation that could cause pain in the future. In neurofibromatosis type 2, a peripheral polyneuropathy causing axonal sensory dysfunction is well described and can cause focal thickening, both in the dorsal root ganglia and in more distal segments of peripheral nerves, due to small endoneurial tumorlets and diffuse proliferation of Schwann cells and/or perineurial
cells. Although a similar phenomenon is likely in schwannomatosis, it has not been described to date, to the best of our knowledge.

In addition to neuropathy from isolated, severe lesions affecting the involved peripheral nerve, some authors have proposed that symptomatic peripheral neuropathies may also result from a combination of less severe multifocal lesions, with or without additional systemic disease (like diabetes mellitus) affecting the function of the nerve. Upton and McComas first proposed such a “double-crush” phenomenon as it related to cervicothoracic spine pathology with concomitant carpal or cubital tunnel syndrome in 1973, and numerous other authors have since added clinical evidence supporting such a phenomenon. The notion that a similar double crush applies for simultaneous focal neuropathies in the lower extremities is also well supported. In essence, each of the cases we describe here is likely an example of double crush in the context of schwannomatosis, and it is certainly conceivable that exactly analogous clinical scenarios may arise in patients with neuroﬁbromatosis type 1 as well. It is difficult to know whether the nerve enlargement (whether caused by hypertrophy or schwannoma) is sufﬁcient to cause a ﬁbular tunnel syndrome in a tunnel of normal caliber or whether the additional presence of ligamentous thickening may contribute to the insufﬁciency of the tunnel’s cross-sectional area relative to that of the nerve traversing it.

Lessons
Management of chronic pain in patients with neuroﬁbromatosis syndromes represents a signiﬁcant clinical challenge but remains a central aspect of their medical care. Our cases demonstrate examples of common peroneal neuropathy due to entrapment in the ﬁbular tunnel in patients with schwannomatosis: one with a small tumor (3-mm diameter) and one without an identiﬁable tumor. Common peroneal neuropathy is the most common mononeuropathy of the lower extremity. Most often associated with an entrapment syndrome at the ﬁbular head, common peroneal neuropathy has a variety of etiologies, including signiﬁcant weight loss, external compression, posture-related stretch injury, trauma, and local mass effect from benign or malignant sporadic tumors. For appropriately selected patients with such entrapment, surgical decompression of the common peroneal nerve yields symptomatic (motor and/or pain) improvement in up to 80%–90% of patients.

Both of the patients presented here had a good clinical result. However, the effectiveness of surgery in patients with schwannomatosis may be less assured than in the general population. It has been reported that nearly 30% of surgical treatments for pain in a schwannomatosis cohort saw no signiﬁcant improvement. Although the incidence of entrapment neuropathies and the overall effectiveness of a peroneal tunnel release in patients with neuroﬁbromatosis syndromes remain unclear, this report does offer examples of marked and sustained improvement in patient symptoms from decompression and resection and from decompression alone. Entrapment neuropathies, such as common peroneal entrapment at the ﬁbular head, both with and without an identiﬁable tumor, should not be discarded in developing a differential diagnosis for a painful extremity in patients with neuroﬁbromatosis and may be amenable to surgical treatment. Although the observations made here are limited to patients with a neuroﬁbromatosis syndrome, the lesson that very small mass lesions at points of nerve entrapment may lead to signiﬁcant symptoms is readily applicable to patients without an underlying neurocutaneous syndrome.

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