Surgical treatment of multiple neurofibromas of the ulnar nerve in segmental neurofibromatosis

Case report

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The case of an 18-year-old man with numerous neurofibromas along his left ulnar nerve is described. The patient had a painful mass in the medial third of the internal aspect of his left forearm, and two additional symptomatic painful masses were identified during clinical examination: one in the distal portion of the retroepitroclear groove and another near the Guyon tunnel in the wrist. The main symptom was neurogenic pain; however, sensory and motor disturbances were also present. No other stigma of neurofibromatosis (NF) was found, and no cases of NF were known in the patient’s family. During surgery many neurofibromas were found; the three painful neurofibromas and some of the other larger lesions were microsurgically excised. The patient’s symptoms fit the criteria for segmental NF or NF5. This is a very rare form of NF characterized by lesions located in a particular area of the body.

Key words: segmental neurofibromatosis • neurofibromatosis Type 5 • neurofibroma • neuropathic pain • ulnar nerve

Since the initial description of neurofibromatosis (NF) made by von Recklinghausen, numerous data have led to the conviction that under the generic term “neurofibromatosis” are included different diseases.9,12–14 According to Riccardi,14 there are at least seven types of NF (NF1–NF7), with an additional category reserved for cases not otherwise specified (NF-NOS). Segmental NF, or NF5, is an unusual form characterized by cutaneous lesions and neurofibromas that are localized to a particular region of the body.12 Cases of NF5 with an isolated deep noncutaneous involvement are even more rare. Because the natural history and genetics of these rare types of NF may be very diverse and are not completely understood, reports of new cases are of interest. Moreover, surgical treatments of nerve tumors in these patients have specific difficulties. In this report, we present the case of a patient with NF5 restricted to the ulnar nerve, who underwent successful neurosurgical treatment.

Case Report

History. This 18-year-old left-handed man noticed a lump in the ulnar aspect of his left forearm when he was 13 years of age. Two years afterward, he began to complain of dysesthesia in the cubital portion of the hand and, later, loss of strength in the same hand. The lump grew, and shortly before admission, the patient developed spontaneous and mechanically provoked pain on the cutaneous distribution of the ulnar nerve.

Examination. Physical examination disclosed an incipient ulnar claw with atrophy of the hypothenar muscles and the first interdigital area and paresis of the abductor muscle of the little finger, first palmar interosseous muscle, and adductor muscle of the thumb. There was hypesthesia in the cutaneous area of the ulnar nerve in the hand. A mass was evident in the medial third of the ulnar side of the patient’s forearm. This lesion was extremely painful to mechanical stimulation, including any light touch. However, careful examination revealed two other painful masses along the trajectory of the ulnar nerve: one in the distal portion of the retroepitroclear groove and another near the Guyon tunnel in the wrist. An intense Tinel’s sign was positive all along the route of the ulnar nerve. The patient did not complain of any other symptoms, and his cognitive status was normal. He had no other lesions or cutaneous stigmas. An ophthalmological examination...
failed to disclose Lisch nodules. There was no evidence of osseous abnormalities, and the results of blood cell count and blood chemistry studies were normal. His blood pressure and findings on chest x-ray films and electrocardiography were normal. There was no family history of NF stigmas. No preoperative neuroimaging studies were performed. A neurophysiological study showed moderate-to-severe axonotmesis of the left ulnar nerve, with the lesion located at the level of the elbow.

Operation. During surgery, the left ulnar nerve was exposed from the elbow to the wrist (Fig. 1). Many tumors were discovered lying on the ulnar nerve. Using microsurgical techniques, the three painful lesions identified in the neurological examination were excised. Some of the largest additional lesions were removed, the selection criteria in this case being their easy resectability. Every tumor grew as an individual spherical structure from one or more fascicles of the nerve. The largest lesion measured approximately 3 cm in diameter. With the aim to preserve nerve function, many small lesions were not removed. Some nerve fascicles harbored several individual tumors. There were no extraneural tumors. An anterior transposition of the ulnar nerve in the elbow was performed at the end of the microsurgical procedure. The histological examination revealed neurofibromas.

Postoperative Course. After surgery, the patient’s pain disappeared and he returned to his previous occupation. A magnetic resonance (MR) imaging study revealed no lesions in the brain or in the cervical, thoracic, or lumbar spine. The MR images of the major nerve plexuses demonstrated two small nodular lesions located in the inferior aspect of the axillary portion of the left brachial plexus. Two years after surgery, the patient’s clinical and neurological status remains unchanged.

Discussion

Neurofibromatosis is one of the most frequently occurring genetic diseases, and it is the most common among the group of phakomatoses. Currently it seems clear that NF is heterogeneous with respect to both phenotypical and genotypical aspects. Riccardi proposed a clinical classification into eight types. Neurofibromatosis Type 1 (von Recklinghausen’s disease) and NF2 (acoustic or central NF) are the most common and genetically are the best differentiated forms. The gene locus for NF1 is found on the proximal long arm near the centromere of chromosome 17 (chromosome band 17q11.2), and the gene locus for NF2 is found on the distal long arm of chromosome 22 (chromosome band 22q11.2). Approximately 90% of all cases of NF are attributable to NF1, which affects approximately one of every 3500 individuals, whereas NF2 occurs in approximately one of every 50,000 individuals.

Type 5 or Segmental NF

Segmental NF or NF5 is a rare disorder characterized by cutaneous or deep NF lesions that are localized to a particular region of the body. The concept of segmental NF was introduced by Crowe in 1956. The criteria for diagnosis of segmental NF included: unilateral neurofibromas limited to one or adjacent nerves and café-au-lait spots or areas of pigmentation limited to the involved region. These authors presumed that the genetic factor involved in the pathogenesis of this nonfamilial form of NF would be a somatic mutation. In his classification, Riccardi claims that the NF5 phenotype is characterized by a distribution of lesions that is not as random as that found in NF1. The genetic basis of the disease might represent a postzygotic somatic mutation, which would explain why the disease is restricted to a unilateral anatomical area and is not inherited. This description of NF5 led to the report of new cases of segmental NF with some phenotypical differences, introducing the concept of heterogeneity into NF5. This concept moved Roth, et al., to divide NF5 into four clinical subcategories: 1) true segmental NF, which strictly adheres to Riccardi’s criteria; 2) localized cases with underlying deep systemic involvement; 3) hereditary segmental, localized cases with genetic transmission of the disease or with an increased susceptibility to somatic mutation at the locus of the disease; and 4) bilateral segmental NF. The first NF5 subcategory is by far the most
Segmental neurofibromatosis

Review of reported cases of surgically treated tumors of the major peripheral nerves in patients with NF5*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Affected Area</th>
<th>Lesions</th>
<th>Nerve(s) Involved</th>
<th>Preop/Postop Pain</th>
<th>Motoneuronal/ Sensory Symptoms</th>
<th>Tumor Type (recurrence, FU)</th>
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<td>yes</td>
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* A case of NF5 involving the sciatic nerve was reported by Segal; however, no clinical data were presented. Two additional cases have been reported by Donner, et al., although they are included in a large surgical series of peripheral nerve tumors. In each reported case a mass was evident. Abbreviations: FU = follow up; ? = probable.

The mean age of patients with NF5 at clinical presentation is 28 years, although cases of very late onset have been described.3,15 The incidence is higher in women, and most patients do not have a familial history of NF. In that surgical series only two patients with neurofibromas or a plexiform neurofibroma in an unilateral and ipsilateral to the side of disease.6 Deep regional lesions include multiple neurofibromas, plexiform neurofibroma, or osseous and muscle hypertrophy.3,6 A few patients with NF5 present with Lisch nodules, all of which are unilateral and ipsilateral to the side of disease.6 Deep regional lesions include multiple neurofibromas, plexiform neurofibroma, or osseous and muscle hypertrophy.3,6 Our case fits the criteria for NF5 (subcategory 2 of Roth’s classification)3,15 because the patient had multiple documented neurofibromas restricted to the left ulnar nerve, without cutaneous lesions or other clinical manifestations of NF and no familial history of disease.

Neurosurgical Treatment of Nerve Tumors in NF5

From a neurosurgical standpoint, patients with NF5 present symptoms and signs of chronic peripheral neuropathy, harboring one or more masses along the trajectory of the affected nerve (Table 1). A very important feature is the complaint of progressive, severe, and chronic neuropathic pain. The association of this clinical picture with the complaint of progressive, severe, and chronic neuropathic pain. The target sign has been claimed to be a diagnostic characteristic of benign peripheral nerve tumors, but unfortunately, there are no pathognomonic findings on MR imaging.16 Diagnosis of plexiform neurofibromas is based on their anatomical extension, which involves the nerves, plexuses, and soft tissues that are more infiltrative and heterogeneous than nodular neurofibromas.

The most characteristic peripheral nerve tumor in NF is the neurofibroma, although schwannomas grow on cranial nerves or dorsal root nerves in patients with NF2. In a review of 288 primary benign tumors of major peripheral nerves, Donner and colleagues found 197 neurofibromas, 85 schwannomas, and six plexiform neurofibromas. Eighty neurofibromas and all plexiform neurofibromas were diagnosed in patients with von Recklinghausen’s disease, but only one schwannoma was found in a patient with NF. In that surgical series only two patients with neurofibroma met the criteria for NF5.2

Neurofibromas are benign encapsulated tumors that can be completely removed using microsurgical techniques, although as intrafascicular tumors, their removal requires the division of one or more nerve fascicles. However, Donner and colleagues have shown perioperatively that these fascicles do not usually transmit nerve action potentials, and therefore, their division does not produce a demonstrable postoperative loss of function. We did not use any intraoperative neurophysiological monitoring in our patient, but despite the sacrifice of some nerve fascicles for tumor removal, his neurological deficits did not become worse and his pain disappeared. Two types of plexiform neurofibromas are distinguished by Riccardi.15 Diffuse plexiform neurofibroma involves large portions of the nerve trunk that grow intra- and extrafascicularly. This tumor cannot be radically removed, the rule being recurrence. The second type is the nodular plexiform neurofibroma that grows in clusters or strings along the nerve trunk and can be excised. Patients with NF5 may have multiple neurofibromas, as was the case in our patient, or diffuse plexiform neurofibromas.11

Only a few cases of neurosurgical treatment of major nerve trunk tumors in NF5 have been reported (Table 1).
Indication for surgery is pain in most cases, as it was in our patient. In all reported cases the patient suffered pain, and a common observation after surgery was pain relief. However, some authors advise of the danger of postoperative severe neuropathic pain following removal of peripheral nerve tumors. Kline and Hudson reported resolution or improvement in pain in 74% of patients with von Recklinghausen’s disease after removal of benign tumors; however, 16% of patients who had no preoperative pain developed pain after surgery. One patient with NF5 experienced improvement in pain but developed postoperative dysesthesia. The sensory and/or motor deficits are usually present preoperatively in patients with NF5, but they may worsen postoperatively because of nerve manipulation, despite the use of microsurgical techniques and intraoperative electrophysiological monitoring or because of the need for division of some functional fascicles, which has to be performed for multiple tumor removal.

Conclusions

In patients with NF5 and multiple neurofibromas the suggested surgical technique would be planned following these principles: removal of all painful nerve masses identified in the neurological examination; removal of all big lesions that are easily resectable without compromising nerve function and based on anatomical and/or neurophysiological criteria; and finally, decompression of the nerve by using standard surgical procedures in peripheral nerve surgery, such as a wide surgical exposure, nerve transposition, external neurolysis, and/or freeing the nerve from ligament, muscle, or aponeurotic bands. Thus, in cases of multiple neurofibromas, it is worth leaving in place all small tumors that later can be selectively resected if there is documented growth, pain, or new neurological deficit. Moreover, NF5 has a favorable histological grading. However, NF5 has a favorable histological prognosis, and there is only one reported case of malignant degeneration.

However, patients with NF5 who harbor plexiform neurofibromas have a poor prognosis, the rule being recurrence of tumor and, therefore, of clinical symptoms (Table 1). In these cases a radical surgical removal would require sacrifice of a major nerve trunk, resulting in a severe neurological deficit.

Genetic counseling should be offered to relatives and patients with NF5. Most cases and subcategories of NF5 are nonfamilial, but some patients with NF5 have affected relatives. Genetic counseling has been summarized by Huet, et al., as follows. If there are no Lisch nodules, the risk of genetic transmission is very low, but in cases in which ipsilateral Lisch nodules are present, the risk could be high, although it is not well established. Finally, if there are bilateral Lisch nodules, this is not a case of true NF5 and the risk approaches that of NF1.

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References