A Rare Case of Segmental Neurofibromatosis Involving the Sciatic Nerve

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Abstract

Segmental neurofibromatosis (NF-5) is an extremely rare variant of neurofibromatosis involving a single extremity without pathologic features beyond the midline. A case of segmental neurofibromatosis involving the sciatic nerve and its branches is presented with a detailed description of the patient's preoperative findings plus postoperative course through 1-year follow-up. Clinical, histologic, and genetic findings are given along with a brief review of the literature on segmental neurofibromatosis. Last, treatment options and postoperative care recommendations are provided.

The deforming lesions of neurofibromatosis have been described throughout literature for the past 2 centuries. In 1856, Virchow depicted type 1 neurofibromatosis (NF-1) with its cutaneous manifestations and elephantiasis neuromatosa in his work "Krankhafte Geschwülste."[1] A total of 8 forms of neurofibromatosis have since been reported.[2] Segmental neurofibromatosis (NF-5) was first described by Crowe and colleagues[3] in 1956 and later defined by Riccardi[4] as limited café-au-lait spots and neurofibromas to a single area, such as an extremity. Its incidence is believed to be far lower than the 1 in 3000 people affected by NF-1.[1] Malignant transformation is a known complication of NF-1 but has not yet been reported with segmental neurofibromatosis.

Neurofibroma as defined in the *Atlas of Tumor Pathology* is a benign nerve sheath tumor composed of a variable mixture of schwann, perineural-like, and fibroblastic cells.[5] Neurofibromas may be classified grossly as localized cutaneous, diffuse cutaneous, localized intraneural, and plexiform. They may involve any peripheral nerves, including autonomic nerves.[5] Neurofibromas involved in NF-5 are often not categorized within the literature but are described grossly as intraneural neurofibromas. Grossly, they appear as diffuse fusiform expansions of the parent nerve. There is heterogeneity in both texture and color, and they often appear translucent on cut sections.[5]

To date, there have been scores of reports involving segmental neurofibromatosis but few involving the extremities. To our knowledge, segmental neurofibromatosis with involvement of the sciatic nerve has been reported only once by Sieb and Schultheiss.[6] We report a case of segmental neurofibromatosis involving approximately 3 dozen intraneural neurofibromas within the sciatic nerve and its branches from the gluteal fold distal to level of the proximal tibia. A discussion of the history, surgical management, and pertinent pathology will be presented. In addition, literature pertaining to the case will be presented. The authors have obtained the patient's informed written consent for print and electronic publication of the case report.

Case Report

A 44-year-old Caucasian female with no significant medical or family history presented with a chief complaint of severe right posterior thigh and knee pain. She stated that her first episode of posterior knee pain began approximately 10 years earlier with no inciting event and resolved spontaneously in 5 months. At that time, she was diagnosed with a popliteal cyst. Seven years later and 3 years prior to her presentation, she was involved in a motor vehicle accident, resulting once again in severe posterior right knee pain refractory to medication. The patient had been seen by multiple orthopedists within 1 month of the incident and had been diagnosed with a Baker's cyst, as confirmed with magnetic resonance imaging (MRI). She had undergone a diagnostic arthroscopy with synovectomy, which provided no relief. Over the next 3 years, until her evaluation at our institution, her

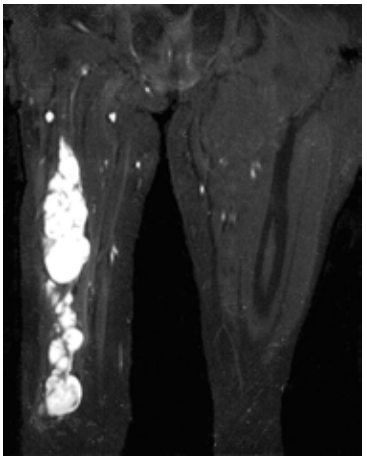

Figure 1. Coronal T_2-weighted magnetic resonance imaging of the affected thigh shows multiple cystic lesions about the sciatic nerve and its branches.

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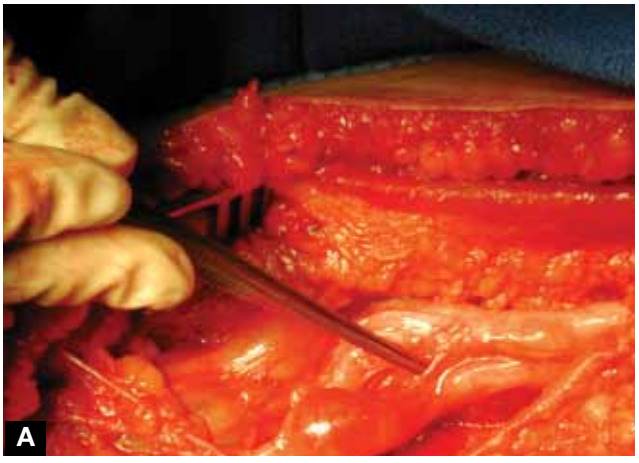

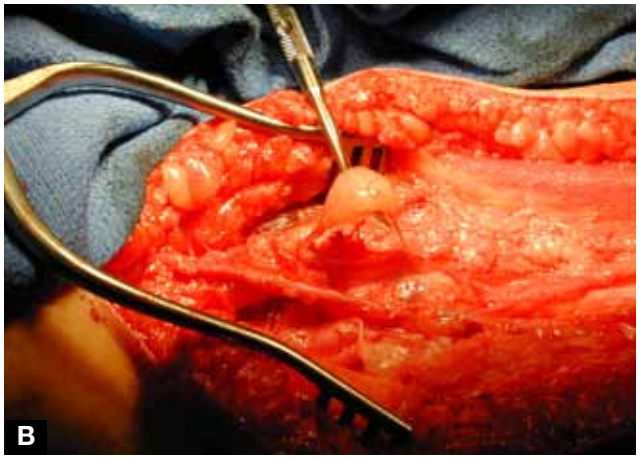

Figure 2. **(A)** Intraoperative view shows involvement of the sciatic nerve with multiple neurofibromas. **(B)** Fusiform eccentric neurofibroma encased with epineurium about the parent nerve. Nerve fascicles entering and exiting the nerve are appreciated.

pain worsened to the point that she had to use crutches secondary to extreme pain with weight-bearing to the right lower extremity. Narcotics provided minimal pain relief, and she developed a 30° flexion contracture as well as pain up the posterior aspect of her thigh. A recent MRI demonstrated, according to radiology, radiographic cysts beginning in the popliteal fossa and extending 20 to 25 cm proximal to the posterior knee (Figure 1). The patient had no constitutional symptoms and stated that she was in good health otherwise.

Examination of the right lower extremity demonstrated a 30° knee flexion contracture with no evidence of effusion or tenderness to the anterior aspect of the knee. Tenderness to palpation was present about the posterior thigh and popliteal fossa with multiple palpable mobile masses about the posterior aspect of the knee and thigh. The masses ranged from 0.5 cm to 4 to 5 cm in size. Pain increased with knee extension but not with hip motion. The patient had 5/5 motor strength throughout the lower extremity with full L2-S2 2-point discrimination. The Tinel sign about the posterior thigh and popliteal fossa was negative, and the Babinski sign was absent, with no clonus or hyperreflexia found on

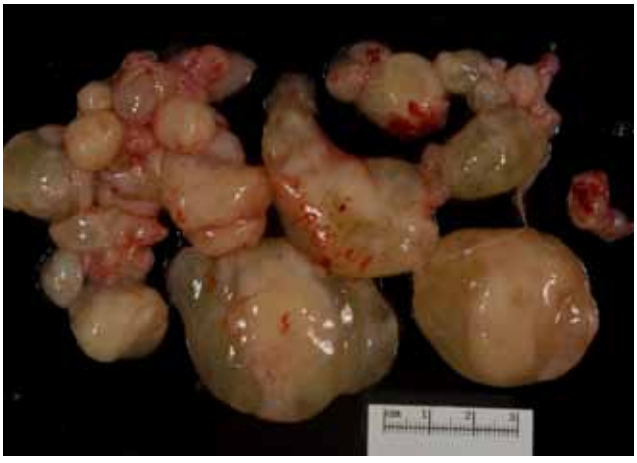

Figure 3. Gross photograph of multiple neurofibromas removed from the patient's thigh. The patient's symptoms were a result of the mass effect of these lesions.

exam. On further examination, the patient was found to have no freckling in the axilla or groin and no café-au-lait spots.

Anteroposterior and lateral radiographs of the femur and knee demonstrated no phlebolith, soft-tissue component, or any other significant pathology. T_2-weighted MRI showed a string of lesions, of varying size, about the midline of the posterior thigh and knee. There was no evidence of intra-articular knee pathology. It was explained to the patient that a biopsy of one of the smaller, more superficial lesions was to be performed. The working differential diagnosis included schwannoma, neurofibroma, malignant peripheral nerve sheath tumor, perineuroma, other nerve sheath tumors, and infection. Preoperative serology, which included white blood cell count, C-reactive protein, and erythrocyte sedimentation rate, demonstrated no systemic inflammatory response. An excisional biopsy was performed with a midline posterior incision of the thigh directly over a palpable mass. Frozen section demonstrated a benign nerve sheath tumor. Based on the findings of biopsy, the incision was extended distally with a S-pattern incision through the popliteal fossa. Lesions involved all branches of the sciatic nerve, such as the sural nerves, the common peroneal nerve, the tibial nerve, and the posterior cutaneous branches (Figure 2A). The lesions were fusiform eccentric masses encased in epineurium with nerve fascicles at each end (Figure 2B). Twenty-six lesions of varying size were excised. Multiple small lesions were not excised out of concern that the parent nerve would be further jeopardized.

Gross examination of the specimen revealed multiple irregular soft gelatinous-like pale tan tissue fragments measuring 12.5×9.6×4.3 cm in aggregate (Figure 3). On microscopic review, the lesions were seen as being composed primarily of schwann cells with ovoid to spindle nuclei. These cells were intermixed with dense

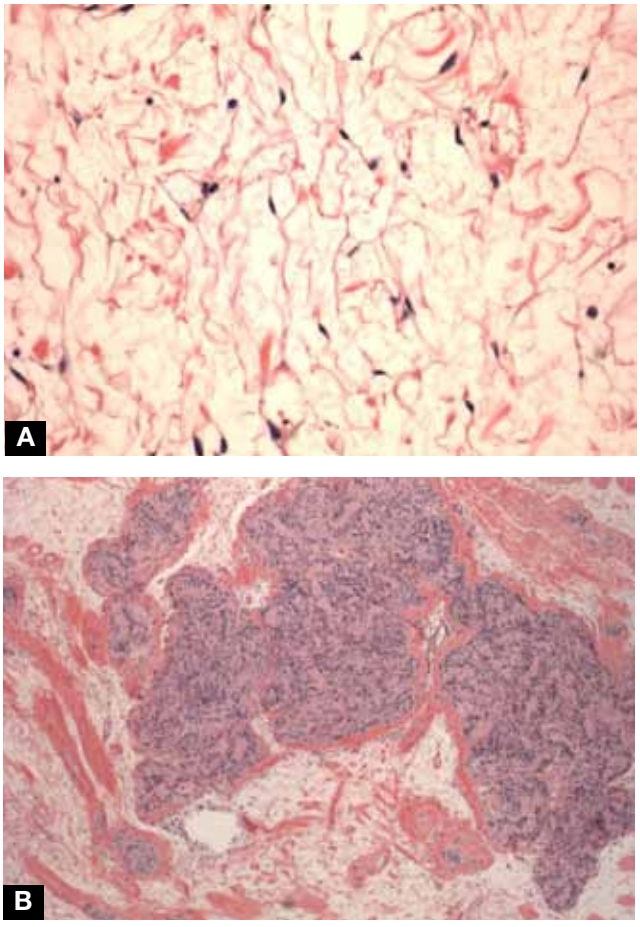

Figure 4. **(A)** Microscopic examination demonstrates collagen bundling interspersed with schwann cells, creating a "shredded carrot" appearance (hematoxylin-eosin, original magnification X 20). **(B)** High-power photomicrograph demonstrates histological finding similar to that of schwannomas in the setting of a neurofibroma. Characteristic Antoni A and B areas are displayed with Verocay bodies (hematoxylin-eosin, original magnification X 40).

foci of collagen bundles, imparting a "shredded carrots" appearance (Figure 4A). A minor schwannoma component was also present with characteristic Antoni A and B areas. Immunohistochemistry showed positivity for S-100 protein in schwann cells (Figure 4B). These features were consistent with neurofibroma.

Postoperatively the patient had remarkable pain relief with complete subsidence of pain in the following weeks. There was no neurologic deficit. The patient had begun physical therapy to improve knee motion and was ambulating without assistance. She was seen by a neurologist for further workup to exclude NF-1. MRI of the brain was negative, and no ophthalmologic evidence of NF-1 was present. At 1-year follow-up, MRI showed no evidence of recurrence.

Discussion

Neurofibromatosis and its many manifestations have been reported in some of the earliest modern medical literature. NF-1 or von Recklinghausen's disease results from a mutation on the long arm of the centromere of chromosome 17. With an incidence of 1:3000, this autosomal dominant disease has a penetrance of 100%, although approximately 50% of patients with NF-1 and type 2 neurofibromatosis (NF-2) represent new mutations. To diagnose NF-1, at least 2 of 7 distinctive criteria must be met. Other manifestations, such as astrocytomas, ganglioneuromas, and rhabdomysarcomas, have been reported.[1-4,7]

NF-2 or bilateral acoustic neurofibromatosis differs from NF-1 in that its hallmark is bilateral acoustic schwannomas. NF-2 has an autosomal dominance inheritance pattern with an incidence of 1:40,000. Similar to NF-1, NF-2 also has established diagnostic criteria as well as manifestations, such as meningiomas and cataracts, rarely seen in von Recklinghausen's disease.[1-4]

Segmental neurofibromatosis or NF-5, although extremely rare, remains an established disease, with most reports involving the head and trunk. In one of his earlier works, Riccardi[4] defined segmental neurofibromatosis as café-au-lait spots and neurofibromas limited to a single region of the body, most likely caused by a postzygotic somatic mutation. In his later works, Riccardi[2] stated that the key feature is restriction of café-au-lait spots with neurofibromas to the ipsilateral side of the body, with no crossing of the midline. He went on to state that the pathologic findings should be isolated to either an upper or lower extremity but not both. Unfortunately, these criteria do not account for the bilateral segmental NF cases reported, nor do they mention if the neurofibroma is grossly an intraneural or a plexiform neurofibroma, both of which have been reported in the setting of NF-5.[8]

Ilyas and colleagues[7] recently reported a case of NF-5 involving the presence of 12 painful subcutaneous masses identified about the right arm. Two café-au-lait spots were appreciated about the scapula. Excision of the most painful masses, involving the ulnar nerve, radial sensory nerve, and digital nerves, was performed. Pathologic examination demonstrated multiple neurofibromas. After appropriate screening, the patient was deemed to not have NF-1. Other reported cases have involved the upper extremity. Gonzalez and colleagues[8] reported on limited involvement to only the ulnar nerve, and Lallemand and Weller[9] reported on involvement of the posterior interosseous nerve with multiple intraneural neurofibromas.

Sieb and Schultheiss[6] reported on a 36-year-old woman with the complaint of right thigh pain and an imaging finding consistent with tumorous lesions about the sciatic, common peroneal, and tibial nerves. Similar to our report, their patient's symptoms initially eluded physicians. No evidence of neurofibromatosis was found preoperatively during workup. Excisions of the most accessible lesions were performed without jeopardizing the parent nerve. Neurofibromas were confirmed by pathology. Description of the neurofibromas was consistent with the intraneural type, but the type itself

was not clearly identified. Similar to other reports in the literature, later postoperative re-imaging of the patient identified additional tumors.[7] Although extremely rare, other reports of lower extremity involvement[10,11] exist, such as the case report by Kaplan[10] that involved the tibial nerve.

Grossly and histologically, our findings are consistent with those aforementioned within the literature. Our patient's neurofibromas were entirely of the intraneural subtype, with 1% to 2% demonstrating characteristics similar to those found in schwannomas. Ironically, these classic histologic patterns of Antoni types A and B have been reported to appear sporadically in the presence of known histologically established neurofibromas.[12,13] In the literature on NF-5, there is confusion as to exactly which types of neurofibromas are being presented. Although most authors have used the term *intraneural*, they have often grossly described the plexiform subtype.[14] Little to no mention of this discrepancy is made in the literature.

After making the diagnosis of segmental neurofibromatosis, the clinician must have a detailed discussion with the patient to address treatment options. Observation after biopsy is a plausible option that decreases the likelihood of nerve damage, but it does not address the inciting symptomatic pathology. Excision of the mass may alleviate the patient's symptoms, but it places the parent nerve at risk for damage.[2,7,14-17] In addition, future surgeries may be warranted to address the problem of recurrence. Malignant transformation can be assumed to be extremely rare, having not yet been reported in the setting of NF-5, but this too must be addressed when discussing options with the patient.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.