

SEGMENTAL NEUROFIBROMATOSIS OF THE HAND & UPPER EXTREMITY

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INTRODUCTION

Multiple tumors occurring in different peripheral nerves limited to a single body part are rare and have been associated with different syndromes based upon pathological criteria, including neurofibromatosis and schwannomatosis. Most cases of multiple neurofibromas involving cutaneous and peripheral nerves represent Neurofibromatosis type I and are associated with a well-described constellation of symptoms (See Table 1). (1) In contrast, segmental neurofibromatosis is a rare variant and presents with multiple plexiform neurofibromas limited to a single body part but without the typical characteristics of neurofibromatosis. We report our experience with a case of segmental neurofibromatosis of the upper extremity and detail the clinical appearance, genetic data, surgical management, and review the pathologic specimen.

CASE

The patient was a 20 year-old white female who was referred with multiple painful subcutaneous masses located on the volar and dorsal aspect of the right hand and forearm. Upon presentation to our service approximately twelve painful subcutaneous masses were identified from the hand to the elbow of her dominant right arm. No other masses were identified anywhere else on the body. Their size ranged from 5 to 15mm. The masses were not associated with any skin changes or pigmentation. Palpation revealed firm masses that were exquisitely tender and resulted in radicular pain with palpation. Neurologic examination of the upper extremity was normal globally including sensation in all dermatomes. Clinical examination under ambient and Wood lamp revealed only two faint café-au-lait spots below the right scapula. The patient had a normal steady gait, including toe and heel walking.

Imaging studies included an MRI that revealed numerous nodules involving the upper extremity that were well circum-

scribed, had a low signal on T1 and high signal on T2. They had an enhancement pattern that was inconsistent with ganglion cysts and were intimately related to different peripheral nerves.

Treatment was directed towards excision of the most painful lesions. The first lesion was the largest and involved the ulnar nerve at the wrist. It was found to be heterogeneous in nature without a well-defined cleavage plane and difficult to excise. Microsurgical dissection was required to separate the pathologic lesion from the splayed nerve fascicles. Upon removal it measured approximately 35mm x 10mm. (FIG 1) Next, attention was turned to the thumb and ring finger. There were an additional four lesions involving the radial sensory nerve over the thumb and both the ulnar and radial digital nerves of the ring finger (FIG 2), that were removed microsurgically. The lesions were also heterogeneous in nature and intertwined within the nerve fascicles. Post-operatively she experienced a significant improvement in pain and remarkably without any sensory loss.

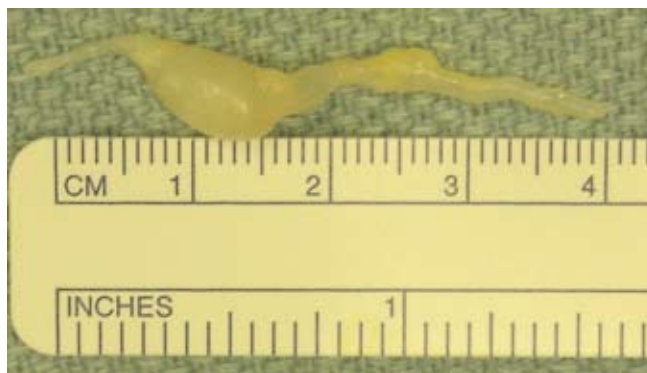


FIGURE 1. Gross specimen dissected from ulnar nerve at the wrist.

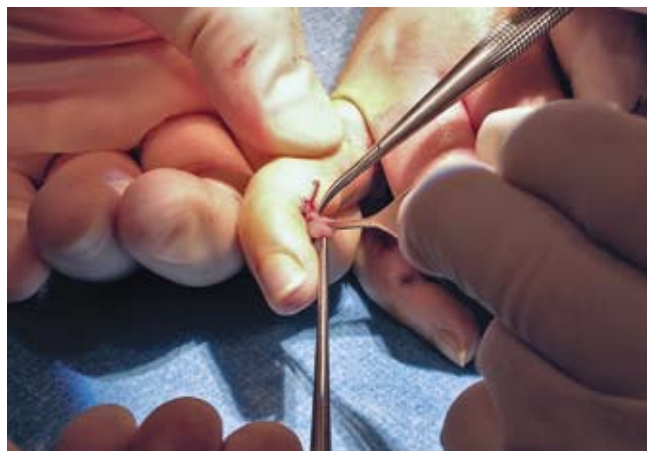


FIGURE 2. Lesion involving the radial digital nerve of the ring finger.

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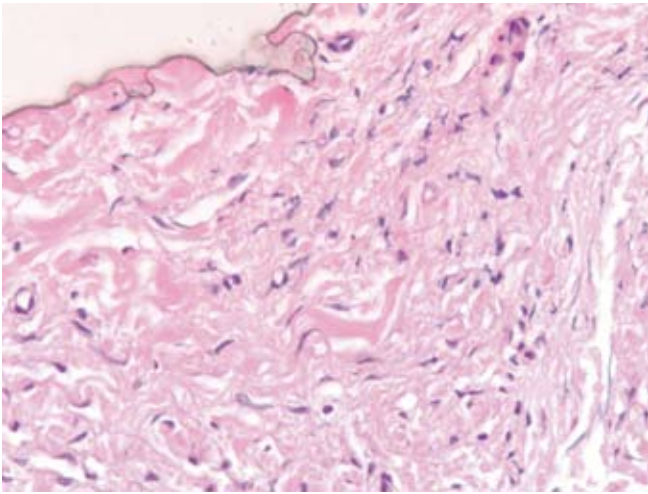


FIGURE 3. Histology at 40x magnification.

Pathologic examination of the specimen revealed a tan-gray smooth tissue with variable borders. The diagnosis was consistent with neurofibromas and contained loose fusiform cells in a fibrous stroma. (FIG 3)

DISCUSSION

The differential diagnosis of painful subcutaneous masses include: angioliipomas, leiomyomas, schwannomas, eccrine spiradenomas, and glomus tumors. Angioliipomas and leiomyomas are most common. Diagnosis requires an excisional biopsy.

Neurofibromatosis is an autosomal dominant disorder that affects the bone, the nervous system, soft tissue, and the skin. Up to eight different types of neurofibromatosis have been described. (2) Today, most investigators accept three main types of neurofibromatosis: Neurofibromatosis I (NF1), previously known as von Recklinghausen's disease; Neurofibromatosis II (NF2), also referred to as Central; and Segmental Neurofibromatosis (NF5). (3)

NF1 is the most common form and has an incidence of approximately 1 in 3000. It presents early in childhood and occurs equally in all genders and races. (4) Well-accepted criteria require the presence of 2 or more of 7 possible features to make the diagnosis. (see Table 1). (1) Its orthopaedic manifestations are usually limited and include: spinal deformity, tibial dysplasia, limb-length inequalities, and excessive bone and soft tissue growth. (3) Cutaneous and nervous manifestations can include plexiform neurofibromas.

TABLE 1. Diagnostic Criteria for NF1

1. Six or more café au lait macules of greater than 5-mm diameter in prepubertal individuals, or 15 mm diameter in postpubertal individuals.
2. Two or more neurofibromas of any type or 1 plexiform neurofibroma.
3. Freckling in the axillary or inguinal regions.
4. Optic nerve glioma.
5. Two or more iris Lisch nodules (iris hamartomas).

6. A distinctive osseous lesion such as a sphenoid wing dysplasia or thinning of long-bone cortex, with or without pseudarthrosis.
7. A first-degree relative (parent, sibling, or offspring) who meets the above criteria for NF1.

NF2 is much less common with an incidence of approximately 1 in 40,000. NF2 generally presents in young adulthood with hearing loss and is associated with bilateral vestibular schwannomas and multiple spinal schwannomas. (4) Diagnostic criteria requires the presence of eight or more nerve masses seen on imaging studies and the history of a first degree relative with NF2. (1) NF2 was recently separated from Multiple Schwannomatosis where the latter has a predilection for the development of tumors of nerve sheaths without the vestibular tumors that are diagnostic for NF2. (5,6)

Segmental Neurofibromatosis, is a term used to describe multiple neurofibromas limited to a single body region without the other characteristics of neurofibromatosis. It was originally described as NF5. (2) However, its original definition was too restrictive and required only unilateral features of NF1 including café au-lait spots, freckling and/or neurofibromas without crossing the midline. More recently it has been suggested that Segmental NF is related to mosaicism of NF1 or segmental hyper-expression of the condition as proven by mutation analysis. (7,8) The result is a limited form of neurofibromatosis without the other symptoms diagnostic for NF1. In our case, genetic consultation pre-operatively ruled out the diagnosis of NF1 by diagnostic criteria as well as Schwannomatosis by its number, varied location, and lack of central lesions.

In Segmental NF, skin lesions are limited to a single body part or limb. Café-au-lait spots or freckling may or may not be present. Systemic disease is uncommon. Unlike NF1, which has an incidence of 1 in 3000 births, and is one of the most common inherited diseases, segmental NF is extremely rare. (9) Epidemiological studies reveal that females are affected twice as often as males. (10) The age of onset falls into a bimodal distribution, with peaks at 10–30 years and 50–70 years. The right side of the body is more commonly affected than the left side (4:3), and approximately 6% of cases are bilateral. (11) Bilateral segmental NF is extremely rare with only 20 cases being reported in the literature. (12)

Histologically, neurofibromas are unencapsulated, poorly-circumscribed tumors that can incorporate all aspects of the nerve including the surrounding schwann cells and the axons within. Neurofibromas have a plexiform nature and infiltrate the nerve and can splay apart nerve fibers. They are often confused with schwannomas, which in contrast are globular well-circumscribed tumors of schwann cells that line nerves. In our case, the neurofibromas maintained its infiltrative nature resulting in splaying of fascicles within the peripheral nerve and deep to the schwann cell lining.

Review of the surgical literature on nerve tumors of the upper extremity reveals cases of multiple schwannomas affecting either a single peripheral nerve (13,14,15,16,17,18), the

brachial plexus (19), but not of segmental neurofibromatosis of the upper extremity. (20,21) The hand surgeon's role will be to aid in diagnosis and/or treat the painful lesions. Surgery is palliative and cannot provide a cure. Recurrence or the formation

of additional tumors is common as illustrated in our case. The hand surgeon may be the first to encounter such a patient and should direct them to a neurologist and/or geneticist to assist in diagnosis and education.

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