UCLA
UCLA Previously Published Works

Title
Case report 828

Permalink
https://escholarship.org/uc/item/2kp7b7ch

Journal
Skeletal Radiology, 23(2)

ISSN
0364-2348

Authors
Sullivan, Thomas P
Seeger, Leanne L
Doberneck, Susan A
et al.

Publication Date
1994-02-01

DOI
10.1007/bf00563213

Peer reviewed

Case report 828

Thomas P. Sullivan, M.D.[1], Leanne L. Seeger, M.D.[1], Susan A. Doberneck, M.D.[2], Jeffrey J. Eckardt, M.D.[3]

[1] Department of Radiological Sciences, UCLA School of Medicine, Los Angeles, California, USA
[2] Department of Pathology and Laboratory Medicine, UCLA School of Medicine, Los Angeles, California, USA
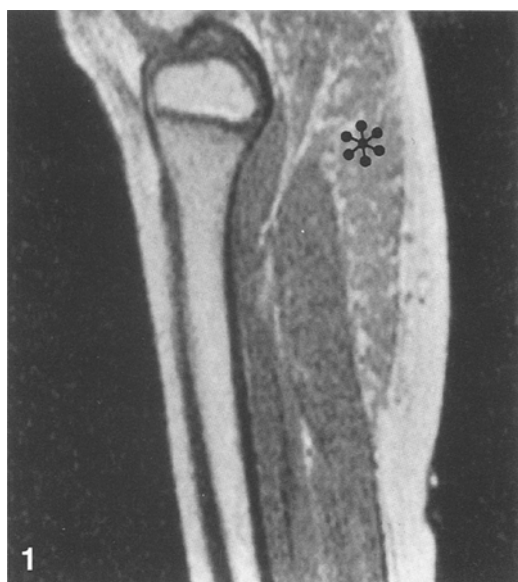[3] Department of Orthopedic Surgery, UCLA School of Medicine, Los Angeles, California, USA

Fig. 1. Sagittal T1-weighted magnetic resonance (MR) image (SE 750/30) demonstrates inhomogeneous intermediate and high signal involving the entire length of the medial head of the gastrocnemius muscle (*)
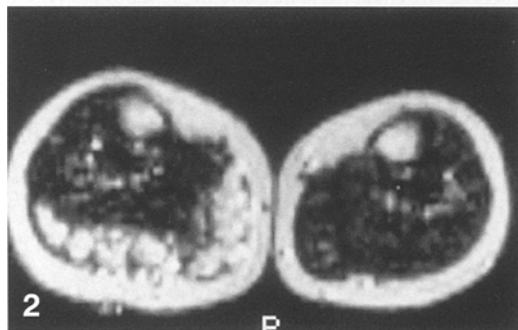
Fig. 2. Axial T2-weighted MR image (SE 2000/85). At the level of the mid calf, the abnormality is confined to the medial and lateral head of the gastrocnemius muscle. The muscle is diffusely enlarged as compared to the normal left side

Clinical information

This 5 year-old boy presented with a 6-month history of weakness in the right leg, complaints of falling down when running, and the recent onset of pain in the proximal part of the right calf. His right calf had been noted to be larger than his left since the age of 2 years, and had been gradually increasaing in size to the time of presentation.

Physical examination revealed a uniformly firm, mildly enlarged right calf. There was no significant medical history, and a review of systems was otherwise negative.

Radiographs were not obtained. Magnetic resonance imaging (MRI) demonstrated uniform but inhomogeneous signal intensity replacing the medial and lateral heads of the gastrocnemius muscle, and the muscle was diffusely enlarged. The mass showed intermediate to high signal intensity in T1-weighted images and high signal intensity with T2-weighting (Figs. 1, 2).

The lesion was surgically excised.

Correspondence to: L.L. Seeger, Department of Radiological Sciences, UCLA School of Medicine, 200 Medical Plaza, Suite 165-59, Los Angeles, CA 90024-6952, USA

Diagnosis: Plexiform neurofibroma of the tibial nerve invading the medial and lateral gastrocnemius muscles and plantaris muscle (Fig. 3)

The differential diagnosis for this lesion centers on processes which can be both long-standing (and thus most likely benign) and infiltrative. The lesion appeared to be somewhat tubular and serpiginous, findings which are characteristic of a vascular malformation such as hemangioma. The signal characteristics on the MR scan offered little assistance in the diagnosis, but the high signal intensity on the T1-weighted images, which further increased with T2-weighting, suggested a high content of mucinous material.

Fig. 3. Posterior view of popliteal fossa demonstrating neurovascular anatomy and musculature. *T,* Tibial nerve; *CP,* common peroneal nerve; *Sm,* medial sural cutaneous nerve; *Sl,* lateral sural cutaneous nerve; *P,* plantar muscle; *Gm,* medial head of gastrocnemius muscle; *Gl,* lateral head of gastrocnemius muscle

Fig. 4. Plexiform neurofibroma extending into fat and skeletal muscle. The infiltrative pattern of this tumor is not indicative of malignancy but merely reflects the diffuse nature of the process. (H & E, × 12.5)

Fig. 5. Multiple, contiguous expanded nerve bundles cut in cross-section appear as small nodules at low power. (H & E, × 25)

Fig. 6. Distortion and expansion of a nerve branch by a proliferation of Schwann cells with elongated, dark nuclei interspersed with occasional thick wavy collagen bundles. Mitotic figures which are more indicative of malignancy are not seen. (H & E, × 100)
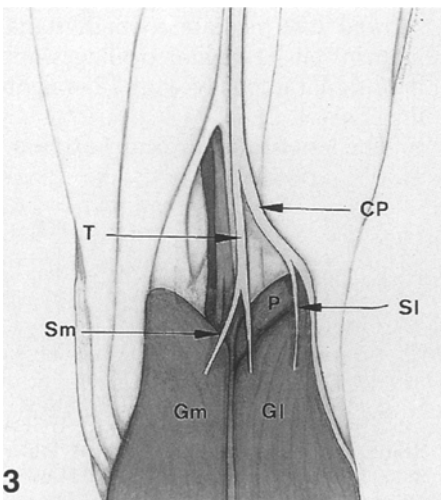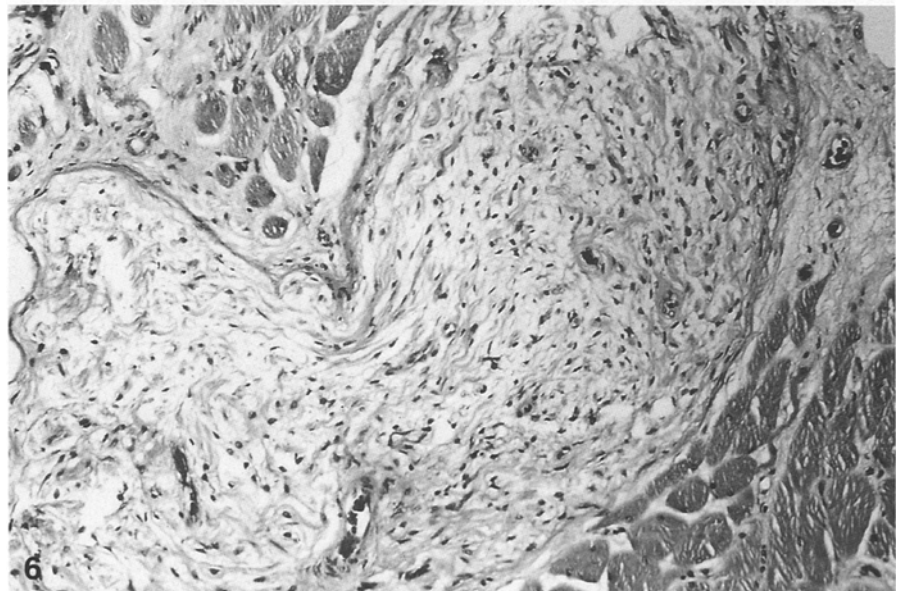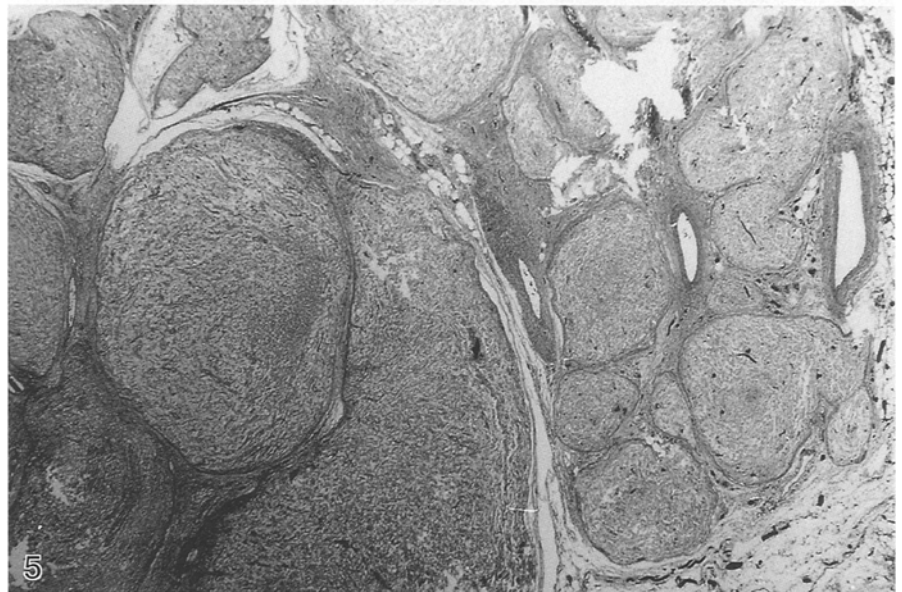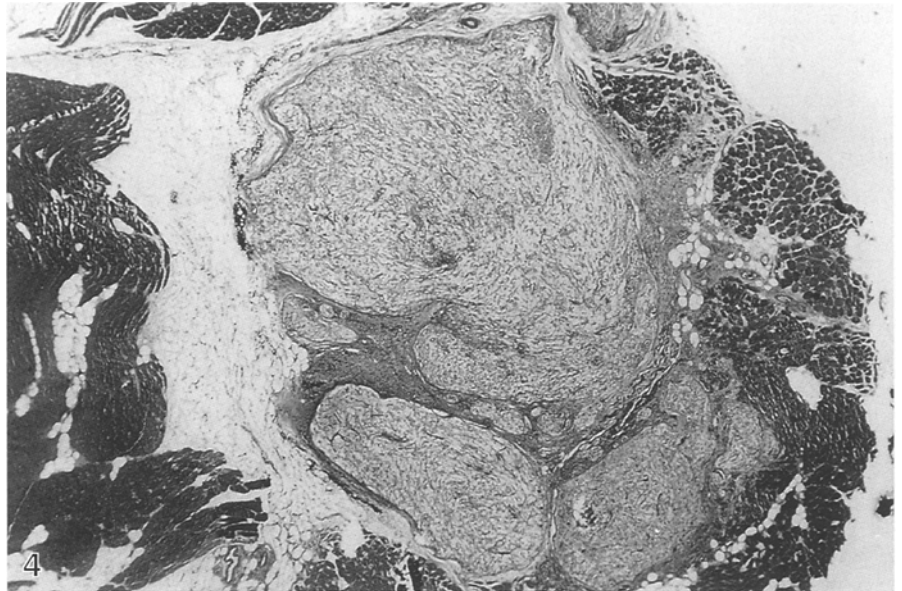
At surgery the tibial nerve was found to be four times its normal size, and many enlarged convoluted neural structures were present, exiting the tibial nerve and entering the medial and lateral heads of the gastrocnemius muscle and plantaris muscle. The sural nerve was also focally enlarged. A 15 × 7 × 2.7 cm medial gastrocnemius muscle mass with a central motor nerve of 0.7 cm diameter was resected, as well as a 15 × 7 × 3 cm lateral gastrocnemius and plantaris muscle mass and a 7 × 2 × 5 cm distal gastrocnemius muscle mass. A 17.5 cm segment of the lateral sural cutaneous nerve with a 2.9 × 1.8 × 1 cm fibroadipose tissue mass at its proximal end was also resected.

Pathological evaluation revealed a plexiform neurofibroma which was intimately associated with skeletal muscle, tendon, and adipose tissue. Grossly, the tumor was multilobulated and gray-white in color. It was circumscribed but not encapsulated. Normal nerve could be seen merging into the tumor mass. Microscopically, the tumor consisted of a convoluted, tortuous mass of nerve fibers cut in different planes of section which extended into fat and skeletal muscle (Figs. 4, 5). The nerve fibers were expanded and replaced by a proliferation of Schwann cells containing dark, wavy nuclei set in a mucinous matrix (Fig. 6). This matrix may have accounted for the high signal intensity seen on the T1-weighted images. Thick wavy collagen bundles were interspersed with the Schwann cells. There was no evidence of mitotic activity.

Detailed examination of the skin of the patient revealed multiple café-au-lait spots including the right cheek and under the chin, and the abdomen, chest, legs, back, and groin, the largest measuring 4 × 2.5 cm. Axillary freckles were also found. An MRI of the brain was performed which showed high signal intensity bilaterally along the optic tracts and into the lateral geniculate bodies with T2-weighted imaging. These areas did not enhance with intravenous contrast medium, and were felt to represent hamartomatous change. The patient was doing well 4 months after surgery.

Discussion

Neurofibromatosis, a phakomatosis or neurocutaneous syndrome, is a dysplasia of mesodermal and neuroectodermal tissue. It is one of the most common genetic disorders, with a frequency of approximately 1 in 3000 births [4]. It shows a slight male predominance [3] and demonstrates autosomal dominant inheritance with high penetrance [5]. The defect has been localized to the pericentromeric region of chromosome 17, and the resultant hyperplastic change of neural sheath cell elements is thought to result from more than one cell line (i.e., to be polyclonal) [1]. At least 50% of index cases result from new mutations [5].

Neurofibromatosis may be either peripheral (neurofibromatosis type I, or NF-1) or central (neurofibromatosis type II, or NF-2) [11]. Manifestations of NF-1, previously known as von Recklinghausen's disease, include congenital or developmental neurofibromas, "coast of California" café-au-lait spots, axillary or inguinal freckles, pigmented hamartomas of the iris (Lisch nodules), skeletal abnormalities, and optic gliomas. If one also considers the presence of an affected first-degree relative, the presence of two of these seven findings will establish the diagnosis of NF-1 (Table 1) [3–5, 12, 13]. Although neurofibromas are considered the hallmark of the disease, they often become evident after the café-au-lait spots and their presence is not necessary to make the diagnosis.

NF-2 rarely manifests peripheral lesions, but by definition includes intracranial or intraspinal tumors. The most common is the neurilemoma (schwannoma or peripheral glioma) of the eighth nerve [3, 14]. NF-1 is characterized by peripheral nerve sheath tumors which, in their benign form, may be either neurilemomas or neurofibromas. Neurilemomas are most often solitary, but may be multiple in patients with NF-1 and rarely undergo malignant transformation [8, 16]. Neurofibromas are multiple in patients with NF-1, and undergo malignant transformation to neurofibrosarcoma in approximately 2% of cases [4, 10]. The prognosis in patients with such sarcomas is poor [6]. Sarcomatous change is suggested by sudden enlargement or pain in a pre-existing neurofibroma [5, 9, 12].

Three types of neurofibromas are found in patients with NF-1. The most common is the localized neurofibroma, similar to the solitary neurofibroma in patients without NF-1 [5]. Least common is the diffuse neurofibroma, which occurs predominantly in children and young adults. This tumor is typically found in the region of the head and neck and presents as a plaque-like elevation. On microscopic examination, it is found along connective tissue septa and between fat cells, enveloping normal structures. Up to 10% of patients with diffuse neurofibromas have NF-1, but this tumor rarely undergoes malignant transformation [5].

The most *characteristic* lesion of NF-1 is the plexiform neurofibroma which may involve an entire extremity and is considered pathognomonic of the disease [2, 7]. In its most extreme form, the condition is known as *elephantiasis neuromatosa*. Plexiform neurofibromas appear grossly

Table 1. Diagnostic criteria for neurofibromatosis type 1. Two of the seven should be present for the diagnosis to be made

Finding	Incidence in NF-1
Neurofibroma (>2 or 1 plexiform type)	Hallmark
Café-au-lait spots	90%
(>6 in number, >5 mm in child or >15 mm in adult)	
Lisch nodules (>2 lesions by slit lamp examination)	90%
Axillary/inguinal freckles	66%
Osseous lesions (sphenoid dysplasia, cortical thinning)	40%
Optic glioma	12%
Affected first degree relative	50%

NF-1, Neurofibromatosis type 1

as ill-defined nodules which have been described as a "bag of worms". Microscopic examination may reveal cellular invasion of adjacent soft tissue. Malignancy is suggested by the presence of mitotic figures [5].

The MR appearance of neurofibroma is varied. Solitary neurofibromas appear as a well-defined mass, but the plexiform neurofibroma may show diffuse irregular infiltration into adjacent muscle and fat [17]. Both forms are usually isointense to muscle in T1-weighted images, but some may be hypo- or hyperintense to muscle. With T2-weighted imaging, both generally become hyperintense [15, 17]. In the solitary form, central inhomogeneity has been attributed to either hemorrhage or necrosis, or to variations in cellularity [9, 18].

Bone erosion has been reported with recurrent schwannoma and neurofibroma, and irregular bony destruction has been noted with malignant lesions. Most authors, however, agree that MRI is not capable of differentiating benign from malignant neural lesions [9, 17]. Neurofibrosarcoma has been described showing indistinct, infiltrative margins like the more aggressive but benign plexiform neurofibroma. Muscle atrophy distal to an enlarged nerve should suggest the diagnosis of a peripheral nerve sheath tumor [17]. This finding was not apparent in the case presented in this report.

In *summary*, a 5-year-old boy presented with a several-year history of swelling of his calf and muscular weakness. MRI demonstrated abnormal signal and diffuse enlargement of the gastrocnemius muscle. Pathological examination revealed plexiform neurofibroma, and the diagnosis of neurofibromatosis was subsequently made. The manifestations of neurofibromatosis and the peripheral nerve sheath tumors encounterd in this disease are discussed. Special attention is paid to the MR features of the plexiform neurofibroma which is characteristic of this disorder.

References

1. Barker D, Wright E, Nguyen L, et al. (1987) Gene for von Recklinghausen neurofibromatosis is in the pericentromeric region of chromosome 17. Science 236:1100
2. Burger PC, Vogel FS (1975) Surgical pathology of the nervous system. Wiley, New York, p 537
3. Canale DJ, Bebin J (1972) Von Recklinghausen's disease of the nervous system. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, vol 14. Elsevier, New York, p 132
4. Crowe FW, Schull WJ, Neel JV (1956) A clinical, pathological, and genetic study of multiple neurofibromatosis. Thomas, Springfield
5. Enzinger FM, Weiss SW (1988) Soft tissue tumors. Mosby, St Louis, pp 745–757
6. Guccion JG, Enzinger FM (1979) Malignant schwannoma associated with von Recklinghausen's neurofibromatosis. Virchow's Arch Pathol Anat 383:43
7. Harkin JC, Reed RJ (1969) Tumors of the peripheral nervous system. In: Firminger HI (ed) Atlas of tumor pathology. Armed Forces Institute of Pathology, Washington DC, 2nd series, fascicle 3
8. Izumi AK, et al. (1971) Von Recklinghausen's disease associated with multiple neurilemonas. Arch Dermatol 104:172
9. Levine E, Huntrakoon M, Wetzel LH (1987) Malignant nerve sheath neoplasms in neurofibromatosis: distinction from benign tumors by using imaging techniques. AJR 149:1059
10. Miller RM, Sparkes RS (1977) Segmental neurofibromatosis. Arch Dermatol 113:837
11. National Institutes of Health Consensus Development Conference (1988) Neurofibromatosis, Conference Statement. Arch Neurol 45:575–578
12. Resnick D, Niwayama G (1988) Diagnosis of bone and joint disorders, 2nd edn. Saunders, Philadelphia, p 4218
13. Riccardi VM (1981) Recklinghausen neurofibromatosis. N Engl J Med 305:1617
14. Rodriguez HA, Berthrong M (1966) Multiple primary intracranial tumors in von Recklinghausen's neurofibromatosis. Arch Neurol 14:467
15. Stark D, Bradley G (1992) Magnetic resonance imaging, 2nd edn. Mosby, St Louis, p 2179
16. Stout AP (1935) The peripheral manifestations of specific nerve sheath tumor (neurilemoma). Am J Cancer 24:751
17. Stull MA, Moser RP, Kransdorf MJ, Bogumil GP, Nelson MR (1991) Magnetic resonance appearance of peripheral nerve sheath tumors. Skeletal Radiol 20:11
18. Suh JS, Abenza P, Galloway HR, Everson LI, Griffith HJ (1992) Peripheral (extracranial) nerve tumors: correlation of MR imaging and histologic findings. Radiology 183:341