

LIPOFIBROMATOUS HAMARTOMA: A REVIEW ARTICLE

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Synonyms, Key Words, and Related Terms

Lipofibromatous Hamartoma, fibrolipomatous hamartoma, intraneural hamartoma, neural fibrolipomatosis, neural fibrolipoma, extraneural fibromas, neurofibromatosis, lipomas, intraneural lipomas, macrodystrophia lipomatosa, Klippel-Trenaunay-Weber syndrome, congenital lymphedema, hypertrophic mononeuritis, hereditary hypertrophic interstitial neuritis of Dejerine-Sottas syndrome.

INTRODUCTION

Lipofibromatous hamartoma (LFH) is a rare, fibrofatty benign tumor comprised of proliferation of mature adipocytes within peripheral nerves forming a palpable neurogenic mass. Although LFH was first described in English literature in 1953, there are fewer than 60 documented cases in recent medical literature.¹ It affects the median nerve in 66 to 80% of cases, causing pain, sensory and motor deficits in the affected nerve distribution. In the late 1950's and into the next decade, a number of authors reported cases of extraneural fibromas causing compression neuropathy of peripheral nerves; however, they were yet to be described in relation to one another.^{2,3,4,5,6,7,8,9}

In 1969, Johnson and Bonfiglio coined the term "lipofibromatous hamartoma", accurately describing the entity and its relation to carpal tunnel syndrome (CTS).¹⁰ While there is an unexplained predilection for the median nerve, cases of fatty infiltration of the brachial plexus, ulnar, radial, peroneal and plantar nerves have also been reported.^{11,14} To date, there are several terms used to describe this condition including fibrolipomatous hamartoma, intraneural hamartoma, neural fibrolipomatosis and neuralfibrolipoma.

The differential diagnosis includes ganglion cysts, vascular malformations, traumatic neuroma and lipomas.¹³ In 1994, Guthikonda et al. described four types of lipomatous masses which vary depending on their location within the parent

nerve: soft tissue lipomas, intraneural lipomas, macrodystrophia lipomatosa and lipofibromatous hamartomas.¹³

CLINICAL PROBLEM

Patients typically present with gradually enlarging non-tender lesions in the distribution of the affected nerve. Since LFH often involves the median nerve, the presentation of median nerve LFH shares considerable overlap with carpal tunnel syndrome. Affected individuals complain of numbness and tingling along the volar aspect of the wrist and hand. Motor deficits are a late finding.

FREQUENCY

Congenital origin of LFH with or without macrodactyly has been previously suggested, but results have been mixed. Most cases occur within the first three decades of life, with the mean age of 22.3 in isolated cases and 22.0 in cases with macrodactyly.¹⁴ Silverman and Enzinger reported 26 cases of upper and lower extremity LFH, 7 with macrodactyly and 19 without. Combining their work and subsequent studies, it was determined that there is a 2:1 female to male ratio of cases with macrodactyly and a 1:1 ratio in cases without.^{14,15} Complicating the scenario even further is the considerable overlap with Klippel-Trenaunay-Weber syndrome, congenital lymphedema, hypertrophic mononeuritis, and hereditary hypertrophic interstitial neuritis of Dejerine-Sottas.¹⁰

ETIOLOGY

Although there have been suggestions of a congenital origin to LFH, the etiology remains unclear. Cases arising from post-traumatic incidences have been reported, all showing the characteristic fatty infiltrate on biopsy. The pathophysiology of LFH is unknown.

INDICATIONS

Indications for surgical intervention vary case-by-case. Due to the intimate nerve involvement, LFH is often accompanied by a degree of neurologic morbidity. If the risk of nerve damage is low and nerve involvement is minimal, surgical debulking for cosmetic reasons can be undertaken. However, in the face of advanced nerve involvement, indications for intervention are progressive and unrelenting neurological deficits.

LFH most commonly affects the median nerve in 66 to 80% of cases, causing pain, sensory and motor deficits in the affected nerve distribution.² There have also been cases of LFH affecting the brachial plexus, ulnar, radial, peroneal and plantar nerves.^{11,14} There is no explanation of why the median nerve is most commonly affected. A fundamental knowledge of the anatomical distribution of nerves helps distinguish LFH from

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other hand tumors as LFH only involves the nerve. In addition on physical exam, there are soft, palpable nodules along the nerve.

WORKUP

LFH shares considerable gross overlap with neurofibromatosis, requiring both radiologic and microscopic investigation for accurate differentiation. The importance of this is apparent as LFH is a benign tumor, whereas neurofibromatosis can progress to frank malignancy. Thus, the treatment of the two entities differs vastly. The two are further differentiated as neurofibromatosis rarely occurs with macrodactyly, whereas LFH can be present with or without macrodactyly. Grossly, LFH tumors are irregular, yellow masses. Barsky reported isolated cases of macrodactyly in which there was not only fatty infiltration of the digital nerve, but marked overgrowth of all tissue types.¹⁶ Johnson and Bonfiglio were the first to propose a microscopic relationship between macrodactyly, neurofibromatosis and LFH, proposing that macrodactyly involves proliferation of all involved tissues, including skin and bone, and fatty enlargement between nerve fasciculi in the absence of thickening of the epineurium, perineurium and endoneurium. Neurofibromatosis includes a disorganized proliferation of the epineurium, perineurium and endoneurium in the absence of fatty infiltration. Finally, LFH involves disorganized overgrowth of epineurium, perineurium and endoneurium with fatty infiltration, no involvement of surrounding tissues and no inflammation.¹⁰

Although there is one reported case of atypical MR findings on LFH, this is in the distribution of the medial plantar nerve. Differentiation on the basis of MRI has now become relatively straight forward. Where LFH displays uniform fatty infiltration, intraneural lipomas show focal fatty masses separated from the individual nerve bundles.¹⁷ LFH differs from ganglion cysts, traumatic neuromas, macrodactyly, Dejerine-Sottas and plexiform neurofibromas because these show high intensity signals on T2-weighted imaging. Although both hemangiomas and LFH demonstrate high intensity signals on T1-weighted imaging, only hemangiomas have a markedly increased uptake on T2-weighted imaging as well.¹²

IMAGING STUDIES

The radiological appearance of LFH is now thought to be pathognomonic for the soft-tissue tumor. On MRI, serpiginous, low-intensity structures surrounded by fat, demonstrating high intensity on T1 and low intensity on T2 weighted images are the characteristic appearances. On the axial plane, the nerve fibers are often described as having a coaxial-cable like appearance, while on coronal sectioning, they are described as spaghetti-like. LFH demonstrates low signal on spin echo T1-weighted and fast spin echo T2-weighted images.¹⁷ Spin magnetic resolution of LFH shows a characteristic pattern of longitudinally oriented fibers with interspersed signal voids which represent nerve fascicles being infiltrated by fat.¹⁴ There are no known lab studies which aid in the diagnosis of LFH. Sonographic studies are now being used to further support the diagnosis of LFH but can not alone be reached for the diagnosis.²⁰

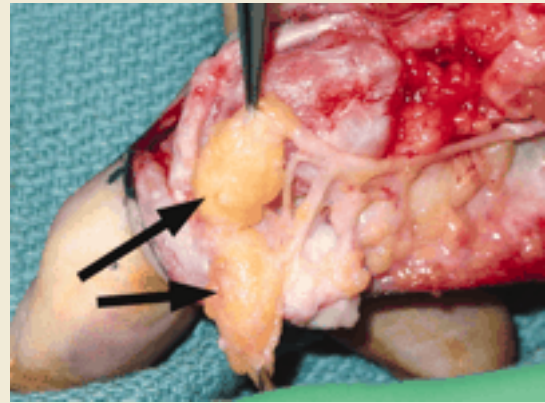


Figure 1: Intraoperative photograph shows a lipofibromatous hamartoma. This shows the typical gross appearance of LFH. Multiple soft, gray-yellow lobulated masses (arrows) are present within epineurial sheath of radial digital nerve of this right index finger. Epineurium of digital nerve displays extensive perineural fibrosis.¹⁸

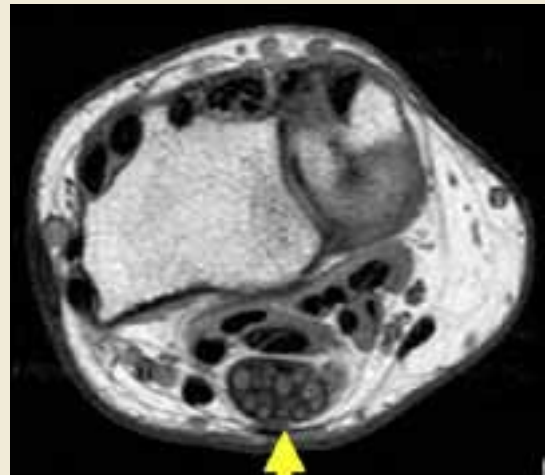


Figure 2: Axial T1-weighted imaging of the wrist through Gunyon's canal which is grossly distended with fat (arrowhead) and thickened fascicles of the ulnar nerve. The patient presented with paresthesia in the ulnar nerve distribution. EMG confirmed conduction delay.¹⁸



Figure 3: Axial T1-weighted section of arm showing LFH of the radial and median nerves (arrows).¹⁸

DIAGNOSTIC PROCEDURES

Prior to advancements in MRI, the diagnosis of LFH was strongly supported by imaging and confirmed by tissue biopsy. Sectioning of the involved nerve typically demonstrates nerve bundles that are entrapped within a fibrofatty-fusiform mass. LFH involves disorganized overgrowth epineurium, perineurium and endoneurium with fatty infiltration, no involvement of surrounding tissues and no inflammation.¹⁰ However, due to advancements in imaging modalities, the diagnosis is now made based on MRI.¹⁸

HISTOLOGIC FINDINGS

Histological findings are limited to perineural and endoneurial fibrosis with axons normal in size or atrophic and fatty infiltration around the nerve branches.¹⁹

TREATMENT

MEDICAL THERAPY

Treatment of LFH is based on symptoms of the condition. While some cases cause no neurologic or functional complications, others do. There is no role for medical management and surgery is reserved for those with neurologic deficits.

SURGICAL THERAPY

Since first appearing in the literature in the 1950's, there has been no widespread consensus on the surgical treatment of LFH; rather, surgeons have adopted a case-by-case approach. The problems which complicate the approach are threefold, each with multiple treatment options. The first problem to be addressed is the treatment of carpal tunnel syndrome. While it is widely accepted that carpal tunnel decompression should be undertaken for relief of paresthesias, some strictly consider waiting for the tumor to become symptomatic prior to surgery, mostly in younger children. In cases of associated macrodactyly, three options exist. The first includes staged debulking, the second is an epiphysiodesis/epiphysectomy and the third is no treatment. In terms of debulking, in a review of eight cases, three reported a decrease in mass size from one to three-year follow-up, four cases noted no change from two to seven years out and one case reported an increase in tumor mass following surgery.¹⁰

PREOPERATIVE DETAILS

INTRAOPERATIVE DETAILS

In many cases, both neurolysis or excision of the main trunk of the median nerve can lead to abnormal two-point tactile discrimination and a loss of sensory distribution post-operatively in adult patients. Furthermore, micro-dissection of the median nerve has led to ischemic complications in one

reported case and has been unsuccessful in others.^{19,20,21} One case reported success in median nerve excision in the presence of a Martin-Gruber anastomosis.^{22,23} Amadio reported cases of significant debulking of tissue followed by distal digital nerve excision as nerves affected by LFH have shown decreased EMG function as in our case presentation. Since there is considerable cutaneous overlap in the hand, Amadio suggests debulking followed by rotation of the excess skin from the dorsal aspect to the volar aspect of the affected digits to restore sensation.²⁴ While this does not fully restore the dermatomal distribution of sensation, it does offer a degree of sensation which would be lost with either no treatment or nerve excision minus the dorsal to volar rotation.

FOLLOW-UP

COMPLICATIONS

There have been mixed reports on the efficacy of nerve excision tumor debulking and microsurgical intraneural dissection.²⁵ Two studies described a complete loss of neurological function following complete excision, while there have been cases of children under 5 years of age where nerve excision and grafting have yielded favorable reports.^{24,26,27} In these cases, it was thought that children have a propensity for re-education of the sensory fibers which adults lack.

The outcomes and prognosis of surgical therapy on LFH has ranged from loss of sensory and motor function to full return of both motor and sensory function. It is thought that a number of factors affect prognosis: including the degree of involvement, the size of tumor burden, the age of the patient and the surgical technique.²⁴ As there have been no randomized controlled studies on the treatment of LFH, controversy still arises regarding the most optimal approach to the problem.

Due to the infrequency of this diagnosis, researchers have been unable to perform any randomized-controlled studies examining the treatment of LFH. As more cases of this are reported in the literature, further insight will be gained regarding the treatment of this condition.

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