ORIGINAL RESEARCH PAPER

Orthopaedics

LIPOFIBROMATOUS HAMARTOMA OF PERIPHERAL NERVE- A RARE AND CHALLENGING ENTITY

KEY WORDS: Hamartoma, Median nerve, Macrodactyly, debulking

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ABSTRACT

Lipofibromatous Hamartoma (LFH) is rare condition involving diffuse peripheral nerve infiltration by normal appearing fibrous and adipose tissues. The cause and pathophysiology of LFH remains unclear however commonly proposed etiologies are congenital malformation and trauma. LFH affect the median nerve mainly but also buccinators, sciatic, superficial peroneal, posterior interosseous nerve, radial nerve, ulnar nerve, even the entire brachial plexus. Patients present with gradually enlarging non-tender lesions in the affected nerve distribution. Patient complains of numbness and tingling sensation. Motor deficits are a late finding. The majority of cases are diagnosed within the first three decades, with a mean age of 22.3 in remote cases and 22.0 in subjects presenting with macrodactyly. There are numerous overlapping clinical features with other conditions like klippal-Trenaunay-Weber syndrome, Hypertropic mononeuritis and congenital lymphedema. Upper extremity morphology includes mass, hypertrophy, macrodactyly, syndactyl, radial or ulnar deviation of phalanx , neurological symptoms including dysesthesia, paresthesia, motor deficits, cafe-au- lait spots, port wine stains, neurofibromatosis. On physical examination, the mass is soft, firm, nonfluctuant, mobile, minimally tender. Neurological deficits associated with LFH are hypesthesia, decreased grip, pinch, opposition strength and paraesthesia, yielding positive Tinel's and phalen's test. Tumors mimicking LFH of the median nerve include ganglion cyst, Déjerine Sottas disease, Klippel-Trénaunay-Weber syndrome, lipoma, and traumatic neuroma, neurofibroma and schwannoma. MRI, CT, Nerve Conduction Study, Electromyogram gets us closer to the diagnosis. Biopsy and histopathological examination are the only definitive means of LFH diagnosis. Care must be taken to rule out potentially malignant tumors. Treatment goals for LFH are symptom prevention, symptomatic relief, function, and aesthetics. Conservative approach can be offered to patients who present with an asymptomatic swelling without severe neurological impairment. There are two options of surgery. One is staged debulking and other Epiphysiodesis in a growing child. For cosmetic reasons, surgical debulking can only be undertaken if the risk of nerve damage is minimal. Digital amputation is usually reserved for severe cases refractory to debulking procedures.

INTRODUCTION

Lipofibromatous Hamartoma (LFH) is a rare condition involving diffuse peripheral nerve infiltration by normal-appearing fibrous and adipose tissues. There have been few published cases involving the median nerve since Mason's first report in 1953 [1]. In 1965, Emmett described this excessive tissue growth as a hamartoma[2]. It was not until 1969 that Johnson and Bobfigli introduced the term LFH to describe the characteristic histological findings[3] accurately. Other names for describing LFH, including fibrolipomatous hamartoma, fibro lipoma, lipofibroma, fibrofatty proliferation, macrodystrophia lipomatosa, and intraneural lipoma[4-6]. The term macrodystrophia lipomatosa describes LFH associated with macrodactyly, where overgrowth of all mesenchymal elements is present in the affected digits[7]. Some authors classify this variation as LFH with or without macrodactyly[8,9]. However, the lack of a single descriptive name has complicated the diagnosis of this condition.

The cause of LFH remains obscure; however, commonly proposed etiologies are congenital malformation[4,10-14] and trauma[9,15]. LFH preferentially affects the median nerve, although reports include the buccinators, sciatic, plantar, superficial peroneal, and posterior interosseous nerves[16-20]. LFH may affect the radial nerve and branches in the upper extremity, ulnar nerve and branches, and even the entire brachial plexus[21-23]. Patients often present a progressively enlarging mass in the median nerve territory between the distal forearm and fingers, with nerve compression and carpal tunnel syndrome. In one instance, LFH of the median nerve was found at an unusual location in the elbow, presented with thumb paresthesia[24].

No gold standard has been clearly established for diagnosing and treating LFH. Historically described approaches include complete Excision of the enlarged median nerve and branches, often resulting in debilitating consequences to sensory and motor functions of the hand[25].

This study reviews the presentation, diagnostic modalities, treatment options, and outcomes of median nerve LFH to formulate a systematic approach to evaluating and managing the condition.

Data Sources

A literature search including Embase, Current Contents, Medline, Google Scholar and Science Citation Index yielded original publications from January 1946 to August 2021 using

fibrolipomatous hamartoma and fibrolipoma macrodystrophia lipomatosa hamartoma, lipofibroma, intraneural lipoma was done. The relevant references were taken from the selected articles.

Etiology

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

Clinical Feature

Patients typically present with gradually enlarging non-tender lesions in the affected nerve distribution. The clinical features of median nerve LFH notably overlap with carpal tunnel syndrome. Patients usually complain of numbness and tingling along the volar aspect of the hand and the wrist. Motor deficits are a late finding. The genetic origin of LFH with or without macrodactyly has been suggested in earlier studies, but results have been mixed. The majority of cases are diagnosed within the first three decades, with a mean age of 22.3 in remote cases and 22.0 in subjects presenting with macrodactyly[26 art1 14]. Silverman and Enzinger studied twenty six cases combined effecting lower and upper extremity LFH, seven with macrodactyly while nineteen have no macrodactyly. Comparing their work and further studies, it was concluded that the cases with macrodactyly had a ratio of 1: 2 male to female and a 1:1 ratio in cases without[27 art1 14,15]. The numerous overlapping clinical features of Klippel-Trenaunay-Weber syndrome, hypertrophic mononeuritis, hereditary hypertrophic interstitial neuritis of Dejerine-Sottas, and congenital lymphedema [28 art1 10] further complicate the scenario.

Upper extremity morphology includes mass, hypertrophy, macrodactyly, syndactyly, radial or ulnar deviation of the phalanx, neurological symptoms including pain/dysesthesia, paresthesia (numbness, tingling, pins, and needles), motor deficits (weakness, impaired function), decreased sensibility, others including café-au-lait spots, port-wine stains, neurofibromatosis.

Personal or family history of patients with LFH includes trauma to the affected area, surgery of the involved area, Klippel-Trénaunay-Weber syndrome. Family with LFH or macrodactyly and neurofibromatosis.

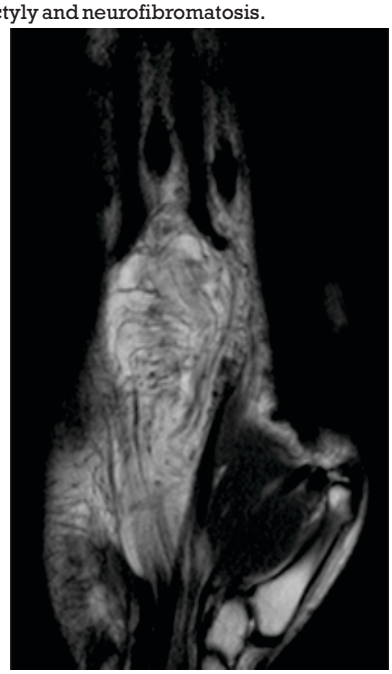
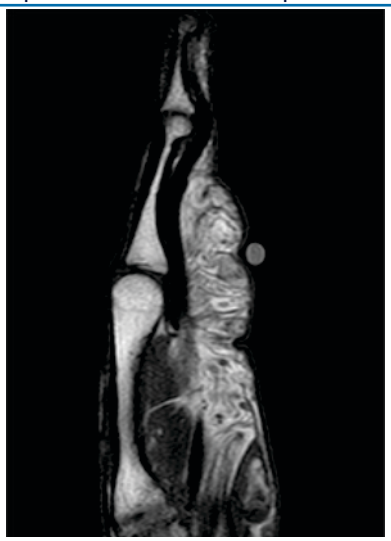


Fig 1A



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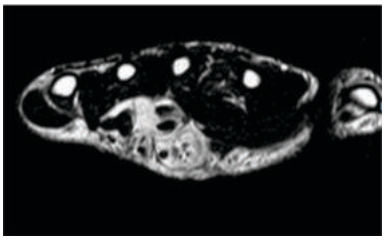

Fig 1C

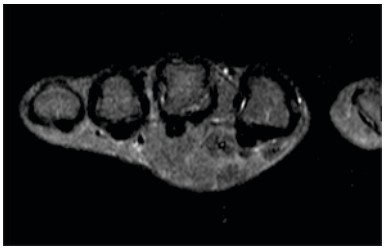

Fig 1D

Fig1 (A, B, C, and D). T2 W coronal, T1 W Sagittal, T2W axial, and STIR axial images to reveal Grossly thickened median nerve with lipomatous tissue (T1W/T2W hyperintense, suppressed on STIR images) interdigitating between prominent fascicles with a coaxial cable like appearance, extending from carpal tunnel to proximal middle finger (radial aspect).

On physical examination, the mass is commonly described as soft, firm, nonfluctuant, mobile, and minimally tender—Macrodactyly, when present, follows the course of the median nerve[29 art2 57]. Syndactyly has also been reported to be associated with LHF.[30 art2 32 58 59] radial or ulnar deviation of the affected digit is associated with macrodactyly and results from the asymmetrical lengthening of the radial and ulnar aspects of the involved digits. There was one report of "syndromic" presentation with a "monstrous" enlargement of the entire right upper extremity, clinodactyly, and syndactyly [31 art 2 32]. One female patient reported port-wine stains on the neck, chest, and arm. [32 art 2 60]

Some reports describe neurological deficits associated with LFH, such as hypesthesia, decreased grip, pinch, opposition strength, and paresthesia, yielding positive Tinel's and Phalen's tests.[33 art 2 3, 4, 8, 14,15,25,26,29,31-38,40,47,50]. Functional impairment is caused by either mass effect or muscle weakness. Many patients who present with impaired hand function experienced asymptomatic swelling months to years before the consultation.

Differential Diagnosis

There is no single consensus on the management of LFH. However, various features of LFH on physical examination, diagnostic imaging, and histology can facilitate its recognition. Benign tumors mimicking LFH of the median nerve include ganglion cyst[art 2 42], DéjerineSottas disease (Charcot-Marie-Tooth type III)[art 2 13,43,44], Klippel-Trénaunay-Weber syndrome[art2 7,45], lipoma[art2 13,46,47], and traumatic neuroma (spindle and terminal neuromas)[art2 48]. Tumors with malignant potentials, such as neurofibroma[art2 48-50] and schwannoma[art2 48,49,51], may also be similar. Finally, it is important to exclude malignant conditions like liposarcoma[art2 52] and malignant peripheral nerve sheath tumors[art2 48 53]. Macroscopically, neurofibromatosis is difficult to distinguish from LFH with macrodactyly because neither is encapsulated, and both may present with mesenchymal overgrowth following a nerve distribution.[art2 7,54]. However, the lack of neurocutaneous manifestations and family history differentiates LFH from neurofibromatosis type I (von Recklinghausen disease).[art2 49,55] Magnetic resonance imaging (MRI) is used to distinguish plexiform neurofibroma from LFH, wherein signals depict neural overgrowth in the place of fat.[art2 56] The two can be further distinguished on histology: LFH is predominantly associated with the proliferation of fibrofatty tissue, which infiltrates between nerve fibers, whereas neurofibromatosis is associated with tumefaction. Klippel-Trénaunay-Weber syndrome is not usually linked to LFH. The two conditions have been reported together on only two occasions.

Management

There are no known laboratory abnormalities associated with LFH. Common imaging modalities used include radiography, ultrasound, and MRI. The X-ray may show soft tissue swelling in the affected area with or without macrodactyly. In LFH with macrodactyly, there may also be bony hypertrophy with osteoarthritic changes.[art2 4,7,13, 25, 36, 37] ultrasound depicts a fusiform mass with longitudinal nerve bundles[34-38] and alternating hypoechoic and hyperechoic bands.[art2 34,38,47,48] MRI of LFH shows a fusiform or hourglass-shaped enlargement of the median nerve on the coronal section, with a displacement of the flexor retinaculum and adjacent tendons on transverse views.[art 2 21,56,67,75,78] In the transverse section, this soft tissue mass has a round or oval contour or may appear multilobulated. T1- and T2-weighted images show characteristic findings of low-intensity serpentine nerve bundles embedded within abundant hyperintense adipose material, with fine fibrous tissue septa coursing along the median nerve.[art2 15,21,28,34,38,47,48, 52, 57] LFH of the median nerve with or without macrodactyly has pathognomonic MRI appearances that are "coaxial cable-like" on the axial plane and "spaghetti-like" on coronal or sagittal cuts. [art2 38, 48, 71, 78, 90, 96] Computed tomography (CT) depicts a discus-shaped bulging mass in the carpal tunnel, displacing the flexor retinaculum and tendons.[art2 33, 50,75] The mass density shows fibroblastic components.

Nerve conduction studies (NCS) and Electromyogram (EMG) on the median nerve yield abnormal results, showing decreased sensory and motor conduction, fibrillations in distal muscles, signs of chronic denervation, and findings consistent with compressive neuropathy.[art2 8,13,15,29,31-34,37,38,40,50,54,61,63]

Biopsy and histopathological examination are the only definitive means of LFH diagnosis. Histological analysis shows interlacing collagen, fibroblasts, mature adipocytes, and occasional capillaries, which separate nerve fascicles and infiltrate the space between the epineurium and the perineurium.[art2 24,54,70] The nerve sheath may be thickened and fibrotic. Nerve fibers appear normal, and there are no mitotic figures, inflammation, or myelin degeneration. [art2 3,8,15,73,81]

We suggest an approach to diagnosing LFH of the median nerve that focuses on the presenting symptom of an isolated palmar mass. This is the initial complaint in 88% of patients. Routine nerve biopsy, although diagnostic, is not recommended because it may cause functional sequelae. MRI, conversely, offers pathognomonic features that confidently identify the lesion, bypassing the need for additional invasive techniques. Moreover, care must be taken to rule out alternative diagnoses of potentially malignant tumors. Characteristics suggestive of malignancy may include a rapidly growing firm mass and invasion into adjacent structures. Signs of central hemorrhage or necrosis, which appear as inhomogeneous enhancements on MRI, raise suspicion of malignant peripheral nerve sheath tumors. Still, these may also be present in benign neurofibromas and schwannomas.[art2 48,53] Family history is essential in the case of neurofibromatosis-1 because the disease may have associations with malignant peripheral nerve sheath tumors, Klippel-Trénaunay Weber syndrome, and schwannomas. Histological findings are limited to perineural and endoneural fibrosis with axons normal in size or atrophic and fatty infiltration around the nerve branches.

Treatment Plan

Treatment goals for LFH with or without macrodactyly are 4-fold: symptom prevention, symptomatic relief, function, and aesthetics. There is no definitive cure for LFH of the median nerve, and patient management varies case by case. Traditionally, complete tumor excision was performed to eliminate the risk of malignancy. Patients would often be left with devastating sensory and functional impairments and painful neuroma formation.[2, 11,18] Excision of the hamartomatous nerve and the overlying skin it innervates have been proposed to minimize sensory loss[2,26] This procedure has demonstrated superior results in children, possibly due to the younger population's increased neuroplasticity.[2] Interestingly, two authors reported a Martin Gruber anastomosis discovered intraoperatively, and this preserved the patients' hand function following aggressive resection of the median nerve main trunk.[2,10]

Medical Management

Treatment of LFH is based on the clinical symptoms of the patients. While some present with no neurologic or functional complications, others might have. In cases presenting with neurologic deficits, the role of surgery and medical management is still reserved. Current treatment has shifted toward a more conservative approach. Expectant management can be offered to patients who present with an asymptomatic swelling without severe neurological impairment. However, spontaneous regression is uncommon, and the lesion may continue to enlarge, eventually progressing to compressive neuropathy.

Indications for Surgery

Indications for surgical intervention vary case by case. Due to the intimate nerve involvement, neurologic morbidity is often anticipated. For cosmetic reasons, surgical debulking can only be undertaken if the risk of nerve damage is minimal. However, in advanced nerve involvement, indications for intervention are progressive and unrelenting neurological deficits. LFH primarily affects the median nerve in 66 to 80% of cases, causing motor deficits, sensory loss, and pain in the affected nerve distribution.[1,2] There have been cases of LFH affecting the brachial plexus, ulnar, radial, peroneal, and plantar nerves.[1,11,14] There is no explanation of why the median nerve is most commonly affected. The anatomical distribution along the nerves helps distinguish LFH from other hand tumors as LFH only involves the nerve. In addition, on physical exam, there are soft, palpable nodules along the nerve.

Surgical Management

Since the first description in the literature in the 1950s, there has been no single consensus on the surgical treatment of LFH; however, surgeons have adopted a case-by-case approach. The problems which complicate the management are threefold, each with multiple surgical options. The first problem being the management of carpal tunnel syndrome. Some advocate that carpal tunnel decompression should be undertaken to relieve paresthesias; some strictly consider waiting for the tumor to be symptomatic before surgical intervention. In cases of associated macrodactyly, three options exist. The first includes staged debulking, the second is a epiphysiodesis/ epiphysectomy, and the third is no treatment. In terms of debulking, in a study of eight cases, three patients reported a reduction in size from one to three-year follow-up, four patients had no significant change in two to seven years, and merely one case reported an increase in tumor mass following surgical intervention.[1,10]

In a considerable number of cases, both Excision and or neurolysis of the main trunk of the median nerve can end in abnormal two-point tactile discrimination and a loss of sensory distribution postoperatively in adult patients. Furthermore, the median nerve's micro-dissection has led to ischemic complications in one reported case and has been unsuccessful in others [1,20,21]. One case of successful median nerve excision in the presence of a Martin-Gruber anastomosis.[1,22,23]. Amadio reported cases of marked debulking of tissue followed by distal digital nerve excision as nerves affected by LFH had shown decreased EMG function as in our case presentation. Since there is considerable cutaneous overlap in hand, Amadio suggests debulking followed by a rotation of the excess skin from the dorsal to the volar aspect of the affected digits to restore sensation.[1,24] Though this does not fully restore the dermatomal sensation distribution, it offers a degree of sensation that would be lost with either no treatment or nerve Excision minus the dorsal to volar rotation. Open carpal tunnel release was performed to decrease motor and sensory impairments, provide symptomatic relief from median compressive neuropathy, and even prophylactically in asymptomatic patients demonstrating "marked enlargement" of the median nerve.[2, 51] Recently, a successful endoscopic carpal tunnel release has been reported.[2,107] Division of the flexor retinaculum with concurrent forearm fascial release yielded positive results.[2] Several authors describe decompression and debulking of the neural sheath.[2,3,9,11,] Microsurgical dissection generated disappointing results, although hand function was improved in some cases[2,12,30,] Intrafascicular dissection with nerve graft improved hand function in 1 patient[2,] Surgery performed on 14 patients with macrodactyly for functional and cosmetic concerns included digital amputation (8 cases)[2,26,], epiphysiodesis (4 cases)[2,26], and wedge osteotomy (3 cases)[2 25,]. Digital amputation is usually reserved for severe cases refractory to debulking procedures. In the growing child, epiphysiodesis can be performed to limit longitudinal growth, but this does not prevent circumferential expansion. Tan et al. have suggested that middle phalangectomy with arthroplasty may result in a functional joint.[2]

Follow Up

In 116 cases (64%), follow-up was reported, ranging from 3 weeks to 26 years.[2,]. Symptomatic relief was most successful in patients undergoing carpal tunnel release, and neurological symptoms improved after surgical decompression. However, long-term follow-up often showed a progressive decline in sensory and motor functions, regardless of treatment modality.[28,26,]

Summary

LFH of the median nerve is an uncommon condition, and only a few reported cases in the literature. About one-third of patients are associated with macrodactyly, with no gender predominance. Cases are often affected at or shortly after birth and usually present before thirty years. MRI is the single recommended diagnostic modality, with characteristic findings of fusiform median nerve swelling with bulging flexor retinaculum, displacing flexor tendons within the carpal tunnel. Biopsy, though diagnostic, is not routinely recommended owing to potential functional deficits. It shows normal-appearing nerve fibers embedded in abundant mature adipocytes with interlacing fibrous septa. Invasive diagnostic procedures are not warranted in the presence of pathognomonic MRI findings. Options have to be tailored according to individual preferences. Carpal tunnel decompression can relieve neurological symptoms with or without neurolysis and carpal tunnel release for large tumors. Digital amputation, middle phalangectomy with arthroplasty, wedge osteotomy or epiphysiodesis can be justified in cases of macrodactyly.

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