Case Report

# Unusual Presentation of Lipofibromatosis-Like Neural Tumor in an Adult: A Case Report

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## Abstract

Lipofibromatosis-like neural tumor (LPF-NT) is a rare variant of lipofibromatosis. Standard lipofibromatosis tumors show a predilection for the distal extremities of male children or young adults and are typically painless, slow-growing, subcutaneous or deep soft tissue masses. We present a case of a 50-year-old male with a slowly expanding, right foot mass. Physical examination revealed a painful, non-tender firm mass on the right medial foot. Magnetic imaging studies revealed a poorly defined soft tissue mass extending through subcutaneous tissue up to the dermis. Histologic examination revealed a spindle cell neoplasm. Immunohistochemistry showed co-expression of S100 protein, CD34 and TRK. In addition, the lesion was found to be positive for the *LMNA-NTRK1* fusion by next-generation sequencing. These findings were supportive of a diagnosis of LPF-NT. At 3-month post-excision, the patient had no pain and repeat imaging indicated no evidence of tumor. The authors recommended including LPF-NT in the differential diagnosis of masses or lesions that are fibro-fatty tumors.

**Keywords:** Adult, foot, immunohistochemistry, infiltrative, lipofibromatosis, NTRK

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**Submitted:** 25-Jan-2021 **Revised:** 07-Jul-2021 **Accepted:** 28-Jul-2021 **Published:** 21-Aug-2021

## INTRODUCTION

Lipofibromatosis-like neural tumor (LPF-NT) is a rare variant of LPF that primarily affects the pediatric population.[1,2] Although a few cases of LPF-NT involving the foot have been documented in children, it has not been previously described in the foot of a middle-aged adult. Here, we present a case of a 50-year-old male with an enlarging right foot mass, ultimately diagnosed as LPF-NT based on histological examination, immunohistochemistry and next-generation sequencing.

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| Quick Response Code: | Website: www.sjmms.net |
| | DOI: 10.4103/sjmms.sjmms_63_21 |

## CASE REPORT

A 50-year-old male was referred for the evaluation of a mass in the right foot. He had recalcitrant, intermittent right ankle pain for several years that worsened after an injury to his foot. Multiple visits to healthcare providers eventually concluded to relating the pain to the injury; however, when the pain did not subside, the primary care physician referred the patient to an orthopedic surgeon. Magnetic resonance imaging (MRI) of the right ankle demonstrated a 3.9 × 2.4 × 2.3 cm soft tissue mass located



**How to cite this article:** Zarak MS, Sliker T, Javadi T, Ullah A, Heneidi SG, Biddinger P, *et al*. Unusual presentation of lipofibromatosis-like neural tumor in an adult: A case report. Saudi J Med Med Sci 2021;9:267-70.

along the medial aspect of the first metatarsal. The mass was poorly defined and soft tissue component extended through the subcutaneous tissue up to the dermis. The mass differed from the surrounding fat with an infiltrative appearance [Figure 1].

Upon presentation, the patient had no systemic symptoms or ongoing musculoskeletal pain. His past medical history included hypertension, hyperlipidemia and oral tobacco use. On physical examination, the patient was an obese Caucasian male in no distress. A firm, non-tender mass was palpated on the mediodorsal foot centered on the first metatarsal, without discoloration. Chronic venous changes were noted just proximal to the mass. Motor movements were intact, distal pulses were present, and the patient was otherwise unremarkable.

An ultrasound-guided core needle biopsy of the mass was performed. Histology revealed a spindle cell neoplasm with fascicular proliferation of relatively plump, bland, fibroblastic to somewhat neural-appearing cells growing in an infiltrative fashion throughout the connective tissue [Figure 2a-c]. There was no significant nuclear pleomorphism, mitotic activity or necrosis. Immunohistochemically, the neoplastic cells were positive for S100, CD34 and epithelial membrane antigen (EMA), and PAN-TRK was strongly positive with cytoplasmic staining [Figure 3a-c]. Tumor was negative for desmin, smooth muscle actin and pan-keratin. Next-generation sequencing showed *LMNA-NTRK1* fusion. The histopathologic analysis, distinct immunoprofile of S-100 protein and CD34 reactivity, and classic presence of *LMNA-NTRK1* gene fusion altogether displayed a pattern most consistent with a diagnosis of LPF-NT.

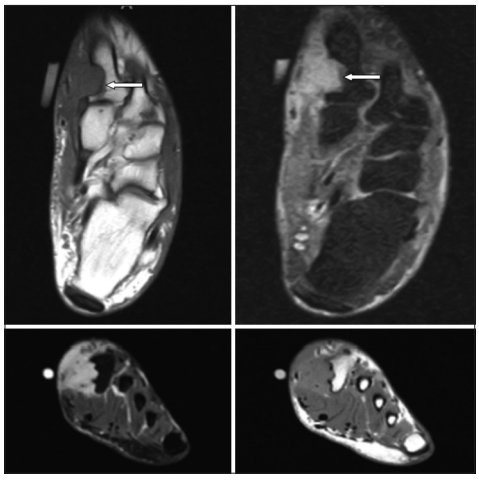

**Figure 1:** Magnetic resonance imaging showing poorly defined soft tissue mass extending into subcutaneous tissue

The patient agreed to proceed with surgical intervention. During surgery, the tumor was visualized to be centered between the tibialis anterior, while extending over to the extensor hallucis longus tendon and eroding into the bone just distal to the tarsometatarsal joint of the first metatarsal. The LPF-NT was completely excised, along with an infiltrated portion of the abductor hallucis muscle. On gross examination, the tumor consisted of a single piece of tan-white soft tissue with homogenous cut surfaces, measuring 6.0 × 3.5 × 1.0 cm. No hemorrhage or necrosis were appreciated on serial sections. There were no significant complications following the procedure.

At the 3-month follow-up, the patient had no pain, and repeat radiographs of the right foot and ankle indicated no evidence of tumor recurrence.

## DISCUSSION

Initially described in the year 2000, LPF is an uncommon, benign pediatric soft-tissue neoplasm that occurs in children.[1] LPF often presents as a painless, slow-growing and ill-defined mass. Grossly, it is firm in consistency and yellow or tan-white in color due to its dominant adipose nature.[2] LPF is composed of an admixture of abundant adipose tissue and spindled fibroblastic elements. The fibroblasts of this entity exhibit a spindled shape with ovoid nuclei, minimal cytologic atypia, and low mitotic activity. Immunohistochemical staining of this tumor is generally variable and nonspecific. The characteristic anatomic distribution and integral fat component of LPF

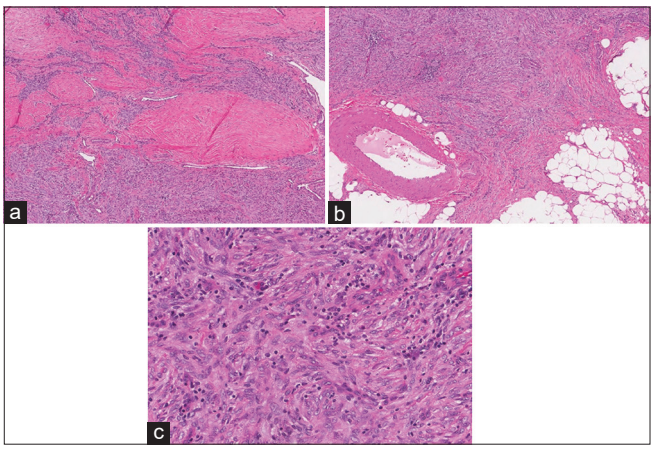


**Figure 2:** (a) Spindled neoplastic cells of lipofibromatosis-like neural tumor growing in a fascicular pattern, while infiltrating adjacent connective tissue (×100 magnification). (b) Lipofibromatosis-like neural tumor cells infiltrating throughout the surrounding subcutaneous adipose and connective tissue (×200 magnification). (c) Spindled fibroblasts showing mild nuclear hyperchromasia and atypia with scattered pleomorphism characteristic of lipofibromatosis-like neural tumor (×400 magnification; all H&E stain)

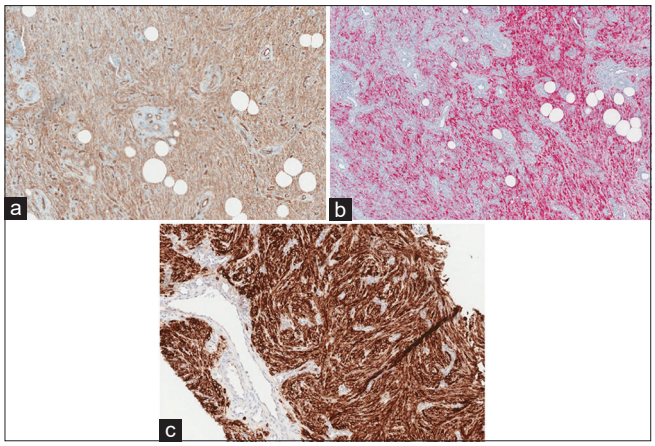


**Figure 3:** (a) Strong membranous CD34 positive tumor cells (×100) (b) Cytoplasmic S100 staining (×100) (c) Diffuse cytoplasmic Pan-TRK staining of core needle biopsy (×200 magnification; all immunohistochemical stains)

can help to distinguish it from other benign fibro-fatty pediatric tumors.[1]

In 2016, the term lipofibromatosis-like neural tumor (LPF-NT) was first coined for LPF tumors that showed reactivity to S-100 protein.[3] Microscopic features of LPF-NT include fibroblasts with mild nuclear hyperchromasia and atypia with scattered pleomorphism. These tumors tend to show infiltrative growth, entrapping muscle, nerves and adnexal structures. Immunohistochemically, LPF-NT shows co-expression of S-100 protein, CD34, and pan-Trk. On FISH analysis, LPF-NT typically contain *NTRK1* gene rearrangements, such as *TPR-NTRK1*, *TPM3-NTRK1*, and most commonly, *LMNA-NTRK1*.[3-7] While it is difficult to differentiate LPF and LPF-NT due to nearly identical clinical presentations and histopathologic features, S-100 protein reactivity and detection of *NTRK1* gene abnormalities are features almost exclusive to LPF-NT.[3]

Imaging features of LPF-NT have not been extensively documented in the literature.[5] It is not entirely specific and can overlap with that of other fibro-fatty tumors, including LPF.[2] Thus, histological examination is essential to differentiate and confirm the diagnosis.

LPF-NT usually arises in the distal extremities of children and young adults, with a higher prevalence in males than females across all age groups.[4,8] We have reported here the first case of LPT-NT presenting on the foot of a middle-aged adult confirmed by *LMNA-NTRK1* fusion.[5,9] In the literature, only nine cases of LPF-NT has been reported in adults: one in an older adult, where the tumor was in the left arm of a 61-year-old male,[9] and eight in younger adults, ranging from one in the right chest wall of a 22-year-old male to one in the scalp of a 38-year-old female.[3,4,9]

The limited cases of LPF-NT in adults emphasizes the importance of recognizing LPF-NT by its unique histologic features, which can facilitate early diagnosis and prompt treatment.[10] Further reports of LPF-NT among adults may also provide a better understanding of the gender specificity associated with this tumor.

## CONCLUSION

This case report highlights the unusual presentation of LPF-NT in adults. Based on this, the authors recommend including LPF-NT in the differential diagnosis of masses or lesions that are fibro-fatty tumors. A biopsy is helpful to follow the case accordingly, and surgical excision remains the choice of treatment.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

### Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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