Ultrasonographic findings in nevus lipomatosus cutaneous superficialis: What differentiates this tumor from other soft tissue tumors?

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Abstract

Nevus lipomatosus cutaneous superficialis is a rare, benign hamartoma characterized by mature adipocyte proliferation in the dermis. It is frequently difficult to distinguish clinically from soft tissue tumors, including lipoma, neurofibroma, venous malformation, and angiolipoma. Notably, the classical form, which shows multiple and sometimes enlarged nodules, is difficult to differentiate from liposarcoma based on clinical examination, computed tomography, and magnetic resonance imaging findings. Therefore, to ascertain the utility of ultrasonography in diagnosing nevus lipomatosus cutaneous superficialis, sonographic examinations were performed on eight patients with nevus lipomatosus cutaneous superficialis. All patients had ill-defined hyperechoic masses in the dermis or from the dermis to the subcutis, and the posterior echoes were attenuated in seven patients. Color Doppler sonography revealed no blood flow to the lesions. Ultrasound images were created using the reflections of ultrasound waves at interfaces with different acoustic impedances. Therefore, it is assumed that, in nevus lipomatosus cutaneous superficialis, the ultrasound beam is scattered by ectopic mature adipocytes intermingled with collagen bundles, which are shown as hyperechoic masses. Furthermore, the scattering of the ultrasound beam is thought to reduce tissue penetration, which may attenuate the posterior echo.

Keywords

Lipoma, Liposarcoma, Nevus lipomatosus cutaneous superficialis, Ultrasonography, Venous malformation

1 INTRODUCTION

Nevus lipomatosus cutaneous superficialis (NLCS), first described by Hoffman and Zuhrelle in 1921, is a rare, benign cutaneous hamartoma characterized by the presence of mature ectopic adipocytes in the dermis.[1,2] It is clinically classified into classical (multiple) and solitary types.[2] The classical type is characterized by multiple soft, non-tender, pedunculated, or sessile yellowish or skin-colored papules, nodules, or plaques. Lesions typically occur at birth or in the two to three decades of life. They frequently develop in the lower back, buttocks, and upper thighs.[3] The solitary type manifests clinically as solitary, soft, dome-shaped, or sessile skin-colored papules or nodules. Lesions generally develop in adults and can occur anywhere on the skin.[4]

NLCS is frequently difficult to distinguish clinically from other elevated soft tissue masses, such as lipomas. Particularly, the classical type manifests as multiple large tumors, resulting in a clinical suspicion of a life-threatening liposarcoma. Therefore, imaging studies are important for preoperative examination or follow-up without resection; however, only a few case studies have described the imaging findings of magnetic resonance imaging (MRI) and computed tomography (CT) owing to the rarity of NLCS.[5–7] Although ultrasonography, a common non-invasive modality, has been shown to be highly useful for assessing soft tissue masses, few ultrasonographic features of NLCS have been reported. Therefore, in this study, we performed an ultrasonographic analysis of eight patients with pathologically proven NLCS and summarized their features.

2 METHODS

2.1 Patients

This study included eight patients with histologically diagnosed NLCS after surgical

resection at the Nara Medical University Hospital between 2010 and 2021. This retrospective study was approved by the Research Ethics Committee of Nara Medical University (approval number: 2236). Informed consent was obtained using the opt-out method.

2.2 Sonographic examination

Sonographic examinations were performed using a LOGIQ E9 diagnostic ultrasound device (GE Healthcare, Hino, Japan), with linear probes at frequencies of 18 MHz (L8-18i), 15 MHz (ML6-15), or 9 MHz (L2-9VN). Eight patients underwent grayscale and color Doppler sonography. A radiologist and two dermatologists retrospectively reviewed the images. The sonograms were analyzed for location, margins, echo texture, echogenicity, and vascularity. However, elastography was not performed in this study.

3 RESULTS

3.1 Clinical features of the solitary form

The clinical data are summarized in Table 1. The eight patients comprised two males and six females (mean [range], 53.5 [32–72] years). According to the clinical classification of NLCS, one patient had the classical form, and seven had the solitary form. All seven patients with the solitary form had a solitary, soft, dome-shaped papule or nodule with a maximum diameter of 5–35 mm (Figures 1a and 2a). Three of these patients had tumors on the extremities, and four had tumors on the trunk. Five patients demonstrated onset at 20–70 years of age, and two had an unknown onset.

3.2 Clinical features and MRI findings of the classical form

A 33-year-old male patient with classical-form NLCS presented with multiple soft nodules

within an area of approximately 14 × 10 cm on the right lumber region for the past 17 years (Figure 3a). MRI revealed the presence of a fat-containing mass with high signal intensity on T2-weighted images and decreased signal intensity on T1-weighted images (Figure 3b). The mass showed a heterogeneous internal signal that was slightly enhanced with a contrast agent, suggesting that it was a well-differentiated liposarcoma.

3.3 Ultrasonographic findings

Table 1 shows the ultrasonographic features of NLCS. Grayscale sonography revealed that the masses were located only in the dermis in four cases and extended from the dermis to the upper subcutaneous fat layer in four cases (Figures 1b, 2b, and 3c). All lesions had ill-defined margins with the adjacent dermis and were internally heterogeneous and hyperechoic. The posterior echo was attenuated in seven cases as follows: two, three, and two cases were weakly, moderately, and intensely attenuated, respectively. Color Doppler sonography showed absent blood flow in all lesions.

3.4 Histopathological examination

In all cases, a group of ectopic mature lipocytes was irregularly scattered within the dermis, leading to a diagnosis of NLCS (Figures 1c, d, 2c, and d). The adipocytes within the dermis were continuous, with the fat layer of the subcutaneous tissue. In five cases, aggregates of mature adipocytes were observed around the eccrine glands. In the classical form, which was suspected on MRI to be a well-differentiated liposarcoma, mature adipocytes also proliferated between the collagen fibers of the papillary dermis and adipose tissue without atypical lipoblasts (Figure 3d).

4 **DISCUSSION**

Histopathologically, NLCS shows ectopic proliferation of mature adipocytes in the reticular dermis, which may extend into the papillary dermis. Adipocytes usually form small aggregates around the blood vessels and/or eccrine glands. However, they can also appear as isolated adipocytes between collagen bundles. Adipocytes may be connected to the underlying subcutaneous fat or separated by connective tissue, such as collagen.[8] The pathogenesis of NLCS is unknown, and several hypotheses have been proposed. Hoffman and Zurhelle speculated that dermal fat deposition is caused by the degeneration of collagen and elastic fibers.[9] It has also been hypothesized that ectopic adipocytes originate from the vascular wall of the dermis or that they are true nevi resulting from the localized ectopic development of adipose tissues.[9,10]

We described the sonographic characteristics of eight patients with NLCS in this study. The typical sonographic finding was an ill-defined hyperechoic mass with posterior echo attenuation in the dermis, which was depicted as a dermal-to-subcutaneous hyperechoic mass in patients with a large mass. In ultrasound, images are created using the reflections of ultrasound waves at interfaces with different acoustic impedances. Therefore, it is assumed that in patients with NCLS, the ultrasound beam is scattered by ectopic mature adipocytes intermingled with collagen bundles, which are shown as hyperechoic masses. Furthermore, the scattering of the ultrasound beam is thought to reduce tissue penetration, which may attenuate the posterior echo.

The differential clinical diagnoses of NLCS include lipoma, cutaneous neurofibroma, venous malformation, and angiolipoma (Table 2). Lipoma is a common subcutaneous tumor comprising adipose cells and often encapsulated by a thin fibrous tissue layer (Figure 4a). On ultrasonography, lipoma appeared as a well-defined, homogeneous, spindle-shaped, and isoechoic mass containing linear echogenic lines in the subcutaneous layer (Figure 4b).[11]

Lipoma and NLCS differ in terms of several features, including location, echogenicity, margin, echo texture, and presence of posterior echo attenuation, and they can be easily differentiated on ultrasonography. Cutaneous neurofibromas appeared as a well-defined hypoechoic mass within the dermis (Figures 4c and d), whereas NLCS appeared as an ill-defined hyperechoic mass in the dermis.[12,13] Venous malformation showed heterogeneous, hypoechoic structures compared to the surrounding subcutaneous tissue and may contain anechoic tubular structures representing vascular channels within the mass (Figures 4e and f).[14] Low-velocity Doppler flows are obvious within the anechoic vascular channels, which is useful for distinguishing between venous malformation and NLCS.[15] Subcutaneous angiolipoma was depicted as an oval-shaped hyperechoic mass with well-defined borders (Figures 4g and h).[11,15] NLCS can be distinguished from angiolipoma by the location and presence of posterior echo attenuation.

In our present case of classical-form NLCS, the clinical and MRI findings suggested a diagnosis of liposarcoma, which is histopathologically classified into the following four types: well-differentiated, myxoid, dedifferentiated, and pleomorphic. Of these, the most common type is well-differentiated liposarcoma, which accounts for approximately half of all cases of liposarcoma.[16] Moreover, because the tumor comprises abundant adipose tissue, CT and MRI may show findings similar to those of NLCS. However, as liposarcomas frequently recur with inadequate resection, it is necessary to differentiate well-differentiated liposarcoma from the classical-form NLCS to provide appropriate treatment. Shimamori et al. have identified several sonographic findings that are characteristic of well-differentiated liposarcoma.[17] Well-differentiated liposarcomas are depicted as relatively hyperechoic, heterogeneous tumors with an irregular shape from the subcutaneous tissue to the muscle and frequently localized more deeply than lipomas (Figure 4i and j). In contrast, NLCS occurs primarily in the dermis, and the location of the mass can easily differentiate NLCS from a

well-differentiated liposarcoma.

A limitation of our study was its small sample size because it was conducted at a single center, and NLCSs are rare. Due to the small sample size, these eight cases have not covered NLCS's potential features, particularly those complicated by inflammation. An inflammatory process following lesion torsion may result in different NLCS features, such as an acute enlargement of the lesion and serous fluid collection around the lesion, as well as separation of the epidermis from the dermis layer.[18,19] Moreover, in this study, we did not perform elastography, which is used to assess the stiffness or elasticity of various tumors. Therefore, to establish the ultrasound characteristic of NLCS, it would be useful to accumulate more cases, including those with inflammation, as well as data from analyses using various techniques, such as elastography.

In this study, we demonstrated the ultrasonographic features of eight cases of NLCS. We conclude that ultrasonography is useful in differentiating NLCS from cutaneous neurofibroma and venous malformation, as well as lipoma and liposarcoma comprising adipose tissues.

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Figure legends

Figure 1

Case 1: Solitary form of nevus lipomatosus cutaneous superficialis in a 70-year-old female patient.

(a) A soft papule of 7 mm in diameter on the left upper arm (black arrow).

(b) Sonographic examination reveals an ill-defined hyperechoic mass in the dermis (white arrowheads).

(c, d) Histological examination showing the proliferation of ectopic mature adipocytes within the dermis, part of which is continuous with the subcutaneous fat layer [hematoxylin and eosin stain, original magnification ×10 (c), ×50 (d)].

Figure 2

Case 2: Solitary form of nevus lipomatosus cutaneous superficialis in a 32-year-old female patient.

(a) A soft dome-shaped nodule of 1.5 cm in diameter on the left buttock.

(b) Sonographic examination revealed an ill-defined hyperechoic mass in the dermis with strong posterior echo attenuation.

(c, d) Histological examination showed the proliferation of ectopic mature adipocytes from the reticular dermis to the subcutaneous layer [hematoxylin and eosin stain, original magnification ×5 (c), ×10 (d)].

Figure 3

Case 4: Classical form of nevus lipomatosus cutaneous superficialis in a 33-year-old male patient.

(a) Multiple soft nodules observed within an area of approximately 14 × 10 cm on the right lumber region.

(b) Magnetic resonance T1-weighted image showed a partially low-signal mass with heterogeneous internal signal (a white arrow).

(c) Sonographic examination revealed ill-defined hyperechoic masses in the dermis and subcutaneous fat layer with moderate posterior echo attenuation.

(d) Histological examination showed the proliferation of ectopic mature adipocytes from the papillary dermis to subcutaneous tissue among collagen bundles (hematoxylin and eosin stain, original magnification ×5).

Figure 4

Clinical findings and sonographic images of lipoma, neurofibroma, venous malformation, angiolipoma, and well-differentiated liposarcoma diagnosed at our institution.

(a,b) Lipoma. A soft elevated nodule on the right mandible of a 57-year-old male patient (black arrow) (a). Lipoma is depicted as a spindle-shaped, isoechoic, homogeneous mass containing linear echogenic lines in the subcutaneous layer (b).

(c,d) Cutaneous neurofibroma. A soft nodule of 1.5 cm in diameter on the posterior right thigh of a 73-year-old male patient (black arrow) (c). Cutaneous neurofibroma is depicted as a well-defined hypoechoic mass in the dermis (d).

(e,f) Venous malformation. A nodule of 2 cm in diameter on the left upper eyelid of a 58-year-old female patient (black arrows) (e). The venous malformation is depicted as a heterogeneous, hypoechoic mass in the subcutaneous layer containing anechoic tubular structures representing internal vascular channels (f).

(g,h) Angiolipoma. A soft mass on the right upper extremity of a 63-year-old male patient (g). Angiolipoma is depicted as an oval-shaped, hyperechoic tumor in the subcutaneous layer (h).

(i,j) Liposarcoma. An elevated mass of approximately 11 cm in size on the left breast in an 83-year-old male patient (black arrows) (i). Well-differentiated liposarcoma is depicted as a relatively hyperechoic, heterogeneous tumor, with an irregular shape from the subcutaneous tissue to the muscle (j).

Table 1. Clinical and sonographic features of eight patients with nevus lipomatosus cutaneous superficialis

Case	Sex/Age	Clinical pattern	Region	Size	Location	Echogenicity	Margin	Echo texture	Posterior attenuation	Doppler flow
1	F/70	solitary	upper extremity	6 mm	in the dermis	hyperechoic	ill-defined	heterogeneous	none	none
2	F/32	solitary	buttock	18 mm	in the dermis to the subcutis	hyperechoic	ill-defined	heterogeneous	strong	none
3	F/66	solitary	lower extremity	9 mm	in the dermis	hyperechoic	ill-defined	heterogeneous	weak	none
4	M/33	classical	lumber lesion	multiple nodules over 14×10-cm area	in the dermis to the subcutis	hyperechoic	ill-defined	heterogeneous	moderate	none
5	M/66	solitary	lower extremity	30 mm	in the dermis to the subcutis	hyperechoic	ill-defined	heterogeneous	moderate	none
6	F/44	solitary	abdomen	5 mm	in the dermis	hyperechoic	ill-defined	heterogeneous	weak	none
7	F/45	solitary	chest	25 mm	in the dermis to the subcutis	hyperechoic	ill-defined	heterogeneous	moderate	none
8	F/72	solitary	chest	9 mm	in the dermis	hyperechoic	ill-defined	heterogeneous	strong	none

Table 2. Ultrasonographic findings of diseases that are clinically difficult to differentiate from nevus lipomatosus cutaneous superficialis

Disease	Location	Echogenicity	Margin	Echo texture	Vascularity	Additional characteristics
Nevus lipomatosus cutaneous superficialis	in the dermis (to the subcutis)	hyperechoic	ill-defined	heterogeneous	no vascular signal	with posterior echo attenuation
Lipoma	in the subcutis	isoechoic	defined	homogeneous	no vascular signal	a spindle-shaped mass containing linear echogenic lines in the mass
Cutaneous neurofibroma	in the dermis	hypoechoic	defined	homogeneous	internal	
Venous malformation	in the subcutis	hypoechoic	defined	heterogeneous	internal	contain anechoic tubular structures representing vascular channels
Angiolipoma	in the subcutis	hyperechoic	defined	heterogeneous	peripheral	an oval-shaped mass
Well-differentiated liposarcoma	in the subcutis to the muscle	hyperechoic	defined	heterogeneous	internal	frequently localized more deeply than lipomas