Dermatology Practical & Conceptual

Sonographic Characteristics of Leiomyomatous Tumors of Skin and Nail: a Case Series

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ABSTRACT

Introduction: The clinical appearance of the uncommon cutaneous leiomyomatous tumors (LMT) is nonspecific, leading to an extensive differential diagnosis. A non-invasive tool such as high-frequency ultrasound (HFUS) is required for characterizing LMTs in the clinical setting. Although the sonographic features of their uterine counterpart had been well reported, there are only scant reports on the use of ultrasound for studying leiomyomatous neoplasms of the skin and nail.

Objectives: To identify and well characterize common sonographic features of LMT.

Methods: A retrospective analysis of HFUS images of LMT in three different patients, two of them with multiple cutaneous leiomyomas and another with a subungual leiomyosarcoma.

Results: In all cases, several shared ultrasound characteristics were found. Moreover, we describe a new ultrasonographic sign in cutaneous leiomyomas called the "pine tree" sign, with other features not previously reported.

Conclusions: These ultrasonographic characteristics would strengthen the clinical diagnosis, assist with treatment management, and may help avoid serial biopsies in cases with multiple cutaneous lesions.

Introduction

Leiomyoma cutis was first described by Rudolf Virchow in 1854, yet their prevalence is still unknown [1]. These uncommon tumors are rarely detected outside the uterus or the gastrointestinal tract [1-4]. Furthermore, cutaneous leiomyosarcomas, the malignant form of these tumors, are even rarer, comprising only 4.0%-6.5% of all soft tissue sarcomas [5-10]. Superficial cutaneous leiomyomas are divided into 3 distinct variants based on the origin of the smooth muscle within the tumor. Angioleiomyoma, the most common form, originates from the tunica media of blood vessels; piloleiomyoma, which arises from the erector pili muscle of the pilosebaceous-unit; and genital leiomyoma, which derives from the network of smooth muscles in the external genitalia [2]. Leiomyosarcoma may also arise from a dermal component such as the erector pili muscle, or a vascular smooth muscle in the hypodermal tissue [3,5-7]. The origin of subungual leiomyomatous tumors is probably from the vascular smooth muscle at the subcutaneous layer since the erector pili muscle is missing in the nail bed [11,12]. To date, reports of digital cutaneous leiomyomas are scarce, and to the best of our knowledge, a presentation of leiomyosarcoma in the nail bed has not been previously reported [11-13].

The clinical appearance of cutaneous leiomyomatous tumors is nonspecific, and therefore, the differential diagnosis is broad, including other benign and malignant lesions, especially soft tissue tumors. Thus, a non-invasive tool to differentiate between these tumors is necessary. In recent years, high-frequency color Doppler ultrasound (HFUS) has been included in the dermatologic clinical practice tools arsenal [14]. This imaging technique provides relevant information about the nature of a lesion, its anatomical location and structures in its vicinity, and the degree of its vascularity. Although a definitive diagnosis of these smooth muscle tumors is made histologically with specific immune-histochemical stains, sonographic evaluation may be of great value for dermatologists and their patients, since the diagnosis may be determined on the spot, without risks or complications, and may potentially replace the need for a skin biopsy [4,7,8].

We herein report the common and unique ultrasonographic features of 3 patients with cutaneous smooth muscle tumors: 2 with sporadic multiple cutaneous leiomyomas and the third with a rare subungual leiomyosarcoma.

Objectives

The aim of our study was to identify and characterize shared sonographic features of the rare cutaneous leimyomatous tumors.

Methods

All patients were evaluated by dermatologists and underwent a high-frequency color Doppler ultrasound examination with a LOGIQ E9 XD Clear device (General Electric Health Systems) using linear and compact linear probes working with an upper frequency of 15 MHz and 18MHz, respectively. A copious amount of gel was used to contact the skin with the probe, and the protocol of the examination followed the published guidelines for performing dermatologic ultrasound examinations [15]. Our Institutional Review Board excludes the review of case series with five or fewer cases; however, according to the institutional protocol, the patients provided signed informed consent for the publication of their clinical and ultrasonographic data as well as their histological images. Moreover, ultrasound examinations followed the Helsinki principles of medical ethics.

Results

Case 1

A healthy 32-year-old male presented to our clinic with a 16-year history of tender and firm multiple erythematous nodules on the anterior-medial aspect of his left leg without a history of trauma or infection (Figure 1A). On sonography, several focal, deeply hypoechoic, solid, pseudo-nodular structures of different sizes located in the dermis and predominantly the hypodermis were detected. Some of these nodules showed an ill-defined area at the periphery with hypoechoic pseudo-tubular structures and a posterior acoustic reinforcement artifact. Some of these pseudo-tubules resembled branches of a pine tree and therefore named the "pine tree" sign. Few punctate hyperechoic spots were seen, but neither signs of gross calcifications with posterior acoustic shadowing artifact nor perilesional edema were detected. On color Doppler, low flow arterial and venous vessels were detected at the periphery and within these hypoechoic structures (Figure 1, B-D). The histology was compatible with cutaneous leiomyoma.

Case 2

A 36-year-old male presented at our clinic with a 9-year history of multiple, persistent, and slightly tender pink nodules on his trunk, right arm, and both legs (Figure 2A). The patient denied any systemic symptoms or relevant family history. Sonographic features uncovered multiple oval, round, and slightly lobulated deeply hypoechoic structures with somewhat heterogeneous areas of variable sizes, located in the dermis and hypodermis. These structures generated a posterior acoustic reinforcement artifact and presented some punctate hyperechoic spots (Figure 2, B-D). Neither signs of gross calcifications nor perilesional edema were detected. On

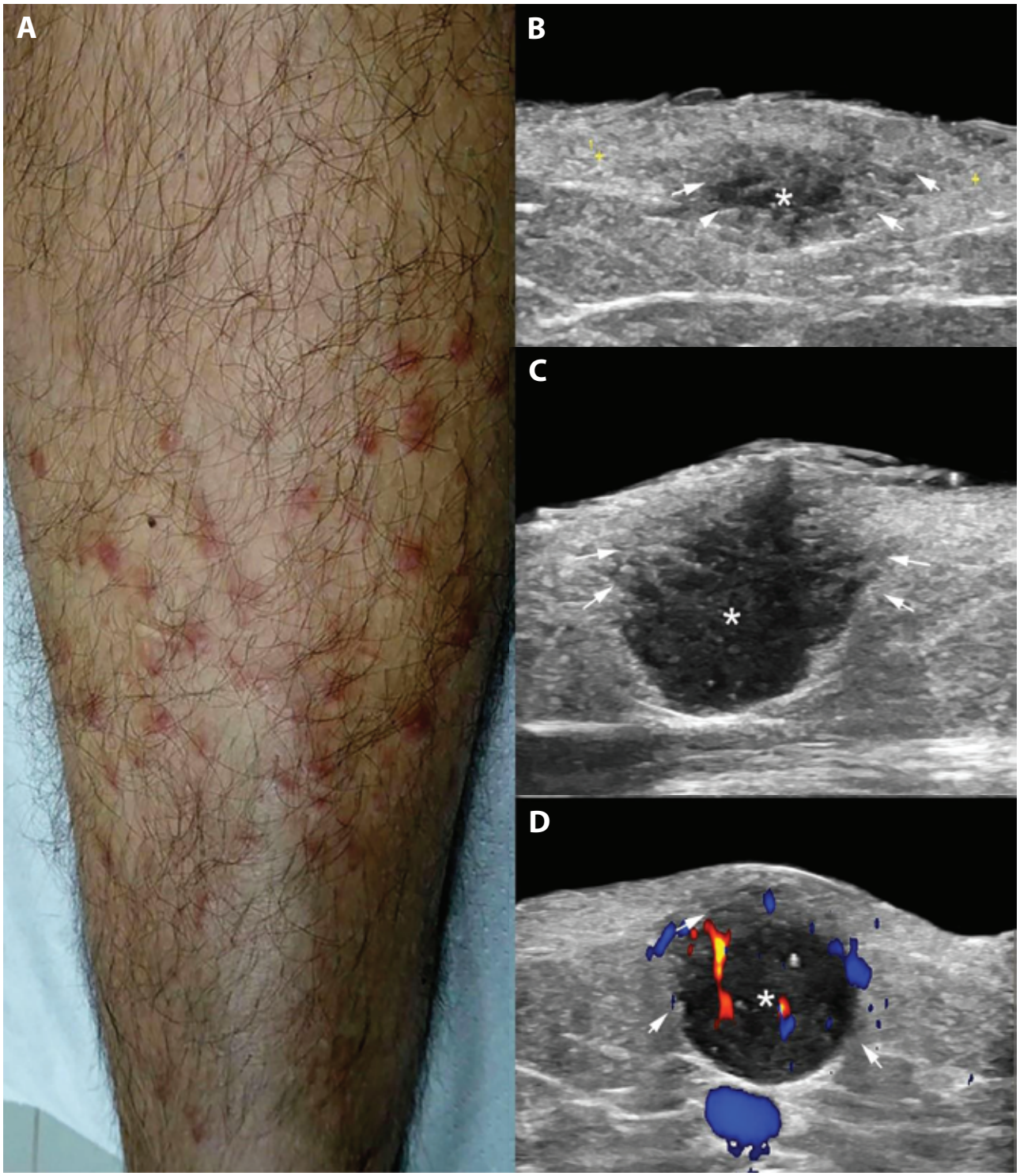

Figure 1. 32-year-old man with multiple cutaneous leiomyomas in case 1. (B and C grayscale; D, color Doppler). (A) Clinical photograph. (B) Dermal and hypodermal network (*) of hypoechoic bundles (arrows). (C) Dermal and hypodermal pseudo-nodular hypoechoic structure with peripheral bundles (arrows) that resembles a "pine tree". (D) dermal and hypodermal hypoechoic nodular structure with tiny peripheral bundles (arrows). Notice the moderate internal and peripheral vascularity.

color Doppler, lesional and perilesional low flow arterial and venous vessels were observed. Both clinically and ultrasonographically was compatible with cutaneous leiomyomatosis.

Case 3

A 31-year-old healthy female presented to the clinic with a two-year history of tender swelling at the nail region of her right first toe. Her physical examination revealed a firm, pink-colored, tender subungual nodule. On ultrasound, a hypodermal deeply hypoechoic solid structure involving the nail bed and the hyponychium was observed, adjacent to the bony margin of the distal phalanx (Figure 3A). Some punctate hyperechoic spots were detected inside the lesion. Increased thickness and decreased echogenicity of

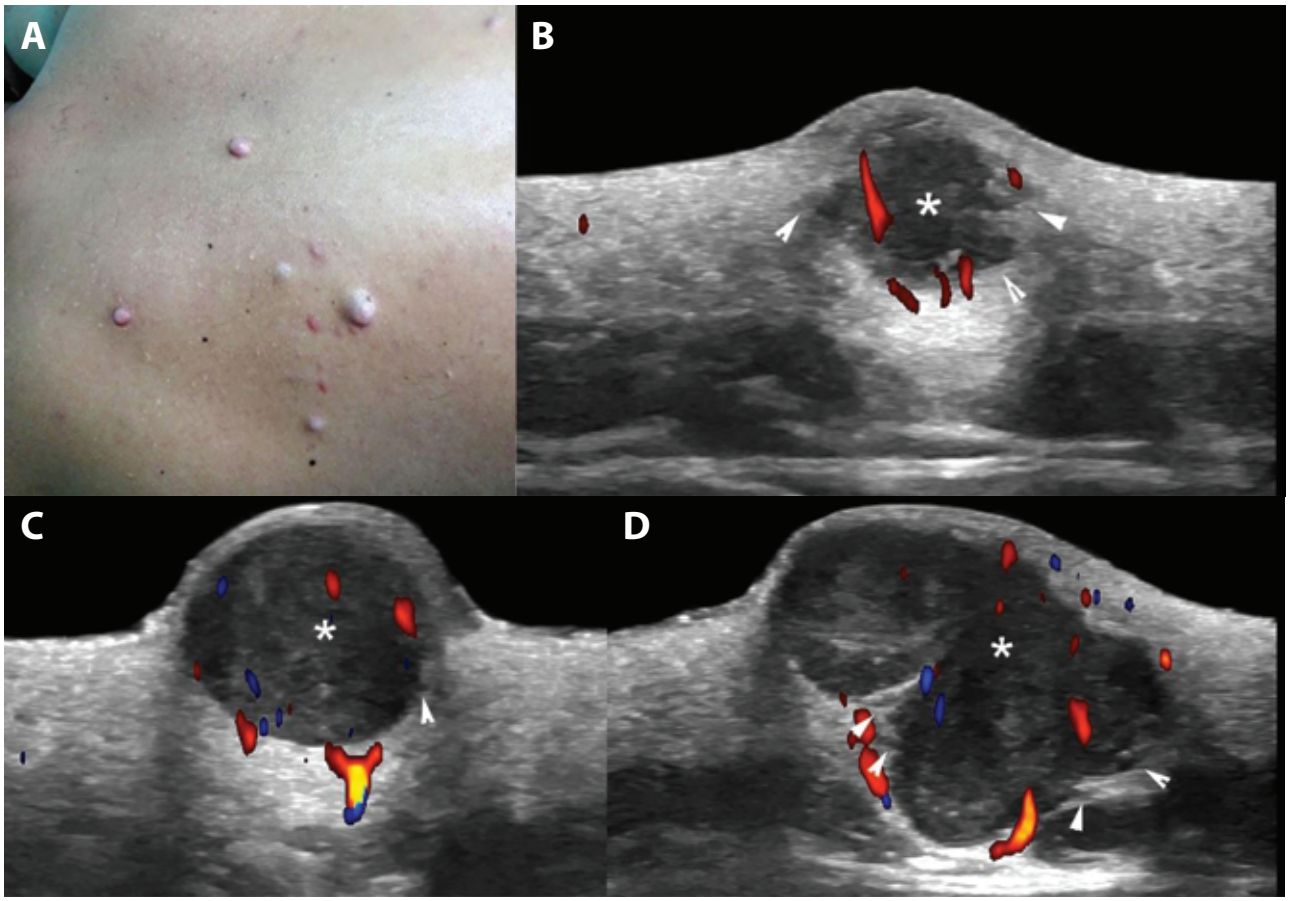

Figure 2. 36-year-old man with multiple leiomyomas in case 2. (B-D, color Doppler). (A) Clinical image. (B) Dermal pseudo-nodular structure (*) with peripheral bundles (arrowheads) that may resemble a distorted "pine tree". (C) Dermal nodule (*) with small and isolates peripheral bundle (arrowhead). (D) dermal and hypodermal lobulated and hypoechoic structure (*) with peripheral bundles (arrowheads). In B-D there are internal Band peripheral vessels.

the nail bed were seen. The nail plate was displaced upward and maintained its bilaminar structure. Some irregularities and a lack of the distal part of the bony margin of the distal phalanx were demonstrated. On color Doppler, the lesion showed low flow arterial vessels (Figure 3, B-D). The histologic diagnosis was compatible with a subungual leiomyosarcoma with a high mitotic rate and increased cellularity. The patient went through 2 surgeries due to the recurrence of the tumor and later an amputation of the toe. A thorough imaging evaluation didn't reveal any systemic metastases.

The ultrasonographic features of the cutaneous smooth muscle tumors (Table 1) include multiple dermal and predominantly hypodermal deeply hypoechoic solid structures with posterior acoustic reinforcement artifact and internal low flow vascularity. The hypodermal central part tends to be well-defined and contains hyperechoic spots within it. No evidence of edema or gross calcifications were noted in any of the 3 cases. In the periphery of the nodules, there are hypoechoic pseudo-tubules that can protrude into the dermis, creating a "pine tree" sign on sonography.

Conclusions

Our results clearly demonstrate common and particular sonographic features of leiomyomatous tumors. Clinically, these tumors appear as a firm, pink to brown color papule or nodule, located mostly on the extremities or trunk, and may be painful in up to 75% of patients [1,3,4]. In some patients, multiple cutaneous leiomyomas may be the initial presentation. These leiomyoma multiplex may occur sporadically or may be part of Reed syndrome [5,6,16]. The latter is inherited in an autosomal dominant manner due to a mutation in the gene that encodes fumarate hydratase, an enzyme of the Krebs cycle, and is composed of cutaneous and uterine leiomyomas and renal cell carcinoma [6,15].

Regarding our ungual case, longitudinal band, yellow discoloration, and distal onycholysis are possible, nonspecific, clinical manifestations of this unique subungual mass[11-13]. Accordingly, the nonspecific clinical characteristics of cutaneous tumors may be potent simulators of other dermatologic entities such as cutaneous sweat glands tumors, sarcoidosis, and neurofibromatosis, among other

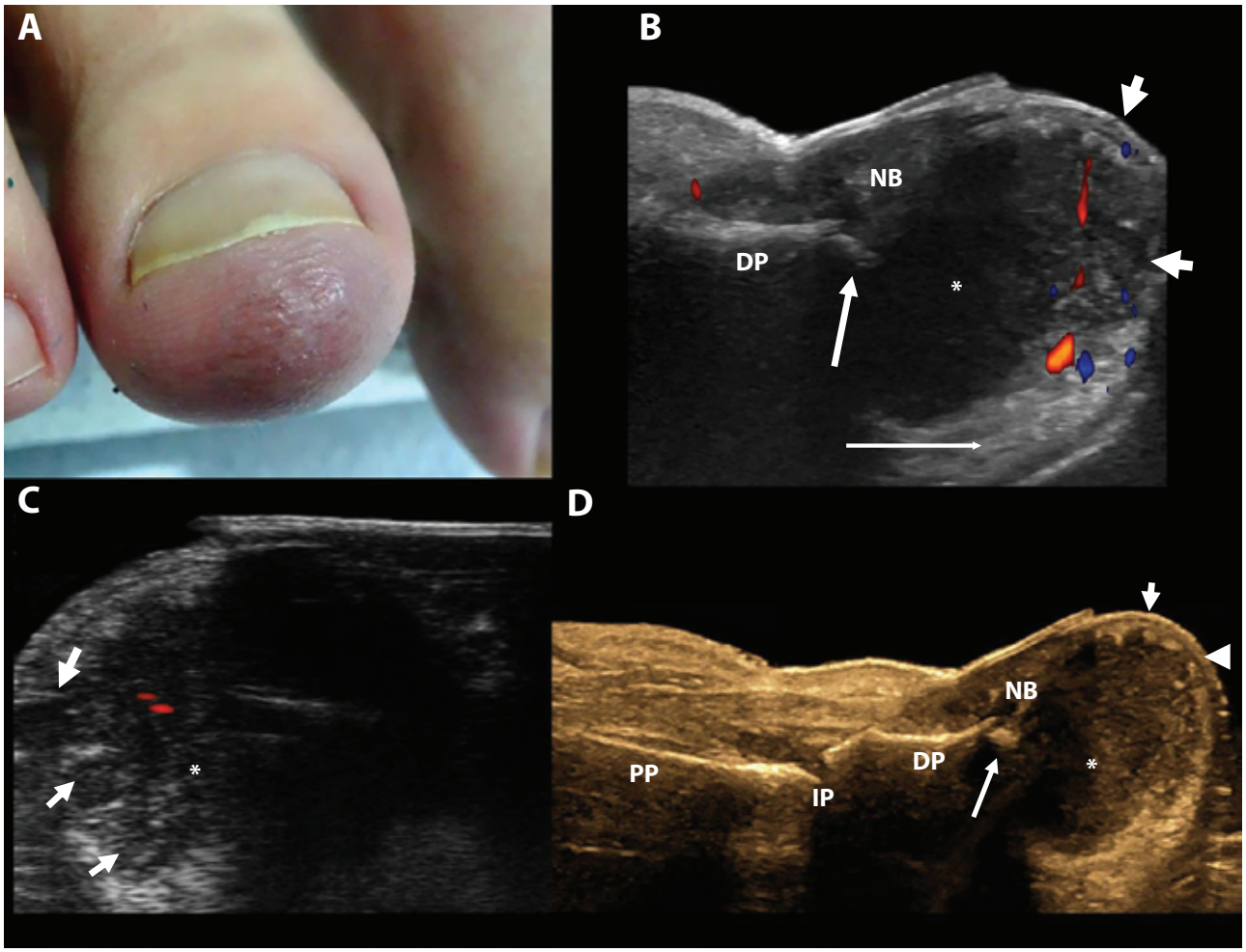

Figure 3. 32-year-old woman with periungual and subungual leiomyosarcoma in case 3. (A) Clinical photograph shows swelling and erythema of the hyponychium. (B-D). Ultrasound images (longitudinal views; B and C, color Doppler ultrasound, B at 18 MHz; C, zoom of the distal part at 22 MHz and D, greyscale with color filter) show hypoechoic structure at the hyponychium that involves the nail bed. (C) Notice the hypoechoic peripheral bundles (arrows) that protrude into the dermis of the hyponychium. (B and D). S small fracture (oblique large arrow pointing up) and a missing distal part of the distal phalanx. Additionally, in B and D, there are hypoechoic peripheral bundles (short arrows and arrowheads). (B and c) Low grade of vascularity. DP = distal phalanx; IP = interphalangeal joint; PP = proximal phalanx; NB=nail bed.

Table 1. Sonographic Characteristics of Leiomyomatous Tumors

Dermal and hypodermal hypoechoic well-defined solid structure
Psuedo-tubules at the lesion's periphery. May protrude to dermis, creating the "pine tree" sign
Hyperechoic spots within the lesion without acoustic shadow
Posterior acoustic reinforcement artifact
Internal mild-moderate low flow vascularity on color Doppler

conditions [1-3,9,10]. Therefore, the use of HFUS may assist in differentiating between these conditions (Table 2). For instance, in contrast to leiomyoma, an intact epidermal cyst also demonstrates posterior acoustic enhancement without internal vascularity. In case of a ruptured cyst, internal vascularity is present, but the cyst borders become ill-defined, and there are signs of edema in the surrounding tissue [17].

Cutaneous sarcoidosis, another possible mimicker of leiomyoma cutis, may also present clinically as solitary or multiple papules and nodules. Via ultrasound, hypoechoic dermal and hypodermal nodules can also be detected; however, in sarcoid nodules, usually, there are signs of edema in the nodules periphery which seems to be absent in smooth muscle tumors [18].

Neurogenic tumors, such as neurofibromas and schwannomas may also present as multiple and painful cutaneous nodules. Their sonographic appearance portrays a dermal or hypodermal ill-defined hypoechoic or heterogeneous mass but may also have a round, oval, or fusiform shape [19]. Hypoechoic neural tracts may be found at their periphery,

Table 2. Sonographic Characteristics of Selected Lesions Mimicking Leiomyomatous Tumors

Diagnosis	Sonographic characteristics
Epidermal cyst [9,17]	Round shape anechoic or hypoechoic structure located in the dermis or hypodermis with anechoic epidermal tract, and posterior enhancement. May also have "pseudo-testes" appearance. In case of rupture or inflammation, increased echogenicity of the periphery and increased vascularity is detected with color Doppler.
Pilomatrixoma [9]	Round or lobulated nodule with a hypoechoic rim and hyperechoic center in the dermis and hypodermis. Hyperechoic spots may be preset within the center of the lesion, creating a "target lesion" appearance. May have acoustic shadow artifact. Vascularity may vary from hypovascular to hypervascular.
Neurofibroma [19]	Round, oval or fusiform shaped hypoechoic nodules. May be less well defined. Hypoechoic neural tracts can be found centrally. Vascularity may vary from hypovascular to hypervascular.
Schwannoma [19,20]	Well-defined round or oval shaped hypoechoic or heterogeneous nodule in the subcutaneous tissue with posterior enhancement. Hypoechoic neural tracts can be found eccentrally. Occasionally presenting anechoic areas and hyperechoic spots. mostly hypovascular on color Doppler.
Dermatofibroma [9,34]	Ill-defined hypoechoic dermal lesions, usually heterogeneous. Frequently hypovascular on color Doppler
Lipomatous tumors [9]	Well defined hyperechoic oval or round-shaped structures following the skin layers. Fibrous septa are detected within the lesions, and are usually hypovascular.
Hidradenoma [21]	Well defined, solid cystic dermal and hypodermal structures that tends to show smoothly lobulated borders, an inner solid component, lacunar fluid-filled spaces, septations and moving echoes creating the "snow falling" sign. Slow flow hyper-vascularity is commonly detected within and in the periphery of the lesion.
Sarcoidosis [18]	Well-demarcated areas with inhomogeneous hypo-echogenicity, surrounded by an edematous zone pressing down on the adjacent subcutaneous tissue ("a mass effect"). increased vascularity within the lesions and in the surrounding dermis is frequently detected.
Subungual fibroma [10,14]	Eccentric oval-, round-, fusiform- or polypoid shaped hypoechoic structure, mostly hypovascular on color Doppler.
Subungual glomus tumor [10,14]	Hypoechoic well defined nodule, centrally located within the nail bed with increased internal vascularity. Scalloping of the bony margin beneath the tumor is a frequent finding.

located centrally or eccentrically, respectively. Moreover, in schwannomas, hyperechoic spots resulting from real calcifications may be observed, and posterior enhancement may also be detected [2], but none of these neurogenic tumors demonstrate the "pine tree" sign seen in leiomyomas [20].

Other differential diagnoses may include sweat gland tumors such as nodular hidradenomas, which tend to show a mixed echogenicity with anechoic and hypoechoic areas due to their solid-cystic structure. It also frequently presents fluid-fluid levels, known as the "snow falling sign," and internal vascularity in its hypoechoic part [21].

For the ungual case, the differential ultrasonographic diagnosis includes ungual fibromas that may present as hypoechoic eccentric periungual hypoechoic masses that involve the nail bed. However, posterior acoustic reinforcement artifact, hyperechoic spots or well-defined borders are not commonly part of fibromas sonographic features [10,22].

Glomus tumors, usually located in the ungual region, tend to be well-defined round or oval-shaped hypoechoic subungual nodules with internal hypervascularity. Scalloping of the adjacent bony margin of the distal phalanx is a common trait. The proximal part of the nail bed is a relatively common location. So far, no signs of hypoechoic pseudo-tubules at their periphery or the presence of hyperechoic spots have been reported [10,22].

In comparison to the repeatedly reported sonographic features of uterine leiomyomas, cutaneous leiomyomas features are less well established [23,24]. The ultrasonographic features of cutaneous leiomyomatous tumors present some similarities to their uterine counterparts, such as their predominant hypo-echogenicity and mainly well-defined borders [24]. However, the intensity of the hypo-echogenicity seems to be higher in the cutaneous tumors. Moreover, although the cutaneous lesions were present for many years, there were no sonographic signs of gross calcifications, commonly found in uterine leiomyomas.

Interestingly, our cases present a different sonographic appearance than other cutaneous leiomyoma cases reported in the literature [25-27]. Stock et al described a lesion with a more heterogeneous echogenicity, hypoechoic capsule at the periphery, internal septations, and multiple hyperechoic calcifications [25]. However, cutaneous leiomyomas are usually

not encapsulated and rarely present calcifications on histology unless they involve deeper soft tissues or vascular structures [4]. Sardanelli et al also depicted cutaneous leiomyoma as a well-defined subcutaneous homogeneous nodule but with high flow internal vascularity [26]. In the latter case, the leiomyoma originated from a large vascular branch that may explain the hyper-vascular pattern.

Some case reports of cutaneous leiomyosarcoma used ultrasound for their initial evaluation, and similar to our ungual case described it as a well-circumscribed hypoechoic mass that may sometimes show ill-defined borders [28,29]. An important additional finding in our case is the missing part of the distal phalanx margin, a sign that should raise the suspicion of malignancy and must be differentiated from the scalloping that is commonly seen in the bony margin attached to some benign slow-growing ungual tumors [6,13,28].

The presence of the pseudo-tubules, generating the "pine tree "sign, correlates well with the thick bundles of smooth muscle seen on histology [4,33]. Of interest is the presence of a posterior acoustic reinforcement artifact, frequently seen in fluid-filled structures such as epidermal cyst [9]. We postulate that this artifact could be due to the presence of numerous slow-flow vessels within the lesions or increased transmission of the sound waves through the cells of the tumor [10]. Likewise, the origin of the hyperechoic spots within the lesions is not entirely clear. The hyperechoic spots in the leiomyomas and leiomyosarcoma may be due to molecular components because no signs of calcium deposits were detected on histology. As aforementioned above, only a few reports describe this histologic feature in cutaneous leiomyomas, making it less probable to be the cause [29].

Furthermore, this sonographic finding is repeatedly detected in other malignant skin tumors such as basal cell carcinoma (BCC), where they are usually more prominent [30]. Even in BCC, these hyperechoic spots are not thought to represent calcium deposits since calcification is also not a common histological finding in BCC [31]. Alternatively, they are thought to be produced by an increased transmission through the tumoral cells [31]. Worth mentioning that a high number of these hyperechoic spots within BCCs have been reported to be associated with the more aggressive subtypes that present a high- risk of recurrence rates [32].

In conclusion, leiomyoma cutis and nail leiomyosarcoma show ultrasonographic signs that differ from other cutaneous and nail tumors. The provision of these ultrasonographic characteristics can be relevant to improve the precision of their diagnosis and management.

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