Sonographic Characteristics of Apocrine Nodular Hidradenoma of the Skin

Ximena Wortsman, MD, Carlos Reyes, MD, Camila Ferreira-Wortsman, MS, Alberto Uribe, MD, Carlos Misad, MD, Sergio Gonzalez, MD

Videos online at wileyonlinelibrary.com/journal/jum

Nodular hidradenomas are benign sweat gland–derived tumors that can produce clinical and dermatoscopic misdiagnoses. Histologically, these tumors can be classified into eccrine and apocrine subtypes. We present the sonographic characteristics of 6 cases of apocrine nodular hidradenomas, which, to our knowledge, is so far the largest series reported. A detailed sonographic analysis included layers, body location, shape, diameters, echostructure patterns, and vascularity. Two sonographic signs not previously reported in these or other common dermatologic lesions were detected: "snow falling" and "fluid-fluid level." The sonographic characteristics of apocrine nodular hidradenomas can support their earlier and more precise diagnosis.

Key Words—dermatologic ultrasound; dermatology; hidradenoma; hidradenoma ultrasound; nodular hidradenoma ultrasound; skin ultrasound; sweat gland tumor ultrasound

Received May 18, 2017, from the Department of Imaging, Institute for Diagnostic Imaging and Research of the Skin and Soft Tissues, Clinica Servet, Santiago, Chile (X.W.); Departments of Dermatology (X.W., C.R.) and Pathology (S.G.), Faculty of Medicine, Pontifical Catholic University of Chile, Santiago, Chile; Departments of Dermatology (X.W.) and Pathology (C.M.), Faculty of Medicine, University of Chile, Santiago, Chile; Faculty of Medicine, University Finis Terrae, Santiago, Chile (C.F.-W.); and Dermatology Division, Integramedica Health Center, Santiago, Chile (A.U.). Manuscript accepted for publication June 6, 2017.

Address correspondence to Ximena Wortsman, MD, Department of Imaging, Institute for Diagnostic Imaging and Research of the Skin and Soft Tissues, Clinica Servet, Lo Fontecilla 201, of 734, Las Condes, Santiago, Chile.

E-mail: xworts@yahoo.com

Abbreviations
BCC, basal cell carcinoma

doi:10.1002/jum.14379

Nodular hidradenoma, also called acrospiroma, is a benign tumor derived from the sweat glands.[1,2] Clinically, these tumors present as painless solitary erythematous or violaceous nodules on the head, trunk, limbs, or oral cavity, which rarely show malignant transformation.[2,3] Their differential clinical diagnosis is wide and includes some variants of dermatofibromas, angiomatous tumors, ganglion cysts, and malignant tumors such as basal cell carcinomas (BCCs), squamous cell carcinomas, and melanomas, among others.[4,5] Importantly, this benign tumor has been described as a dermatoscopic pitfall because it is a great simulator of other entities.[4–7]

Histologically, nodular hidradenomas can show eccrine or apocrine differentiation.[1] Due to the complex and variable histologic presentations of sweat gland–derived tumors, there has been some controversy on their categorization.[6] Recently, nodular hidradenomas have been reclassified on histologic examinations[1]; thus, tumors that arise from eccrine cells are named poroid hidradenomas, and if they come from apocrine cells, they are named clear cell hidradenomas.[1] Apocrine nodular hidradenomas are now reported to be more frequent than the eccrine variants[1]; however, both subtypes may be present in the same lesion, and it has been described that, irrespective of the subtype, nodular hidradenomas may show a predominantly solid-cystic morphologic pattern.[6]

The use of sonography has been reported in hidradenoma as case reports with 1 or 2 cases.[8–15] Mostly, these showed hidradenomas with the eccrine differentiation, and in most cases, the examinations were performed without following the guidelines and technical considerations for studying dermatologic lesions.[16] In these case reports, hidradenomas were described on sonography as a well-defined solid-cystic mass with mural hypervascular or hypovascular nodules, a cyst with a solid papillary lesion protruding from the wall, or a well-defined hypoechoic solid tumor with hypervascularity. The aim of this series was to analyze the sonographic appearance of apocrine nodular hidradenomas and look for sonographic patterns that may help in their diagnosis.

Materials and Methods

A review was made of the sonograms of apocrine nodular hidradenoma cases confirmed by histologic examinations performed between January 2016 and April 2017. The following sonographic parameters were analyzed:

1. Age and sex of patients;
2. Layers involved (dermis and hypodermis);
3. Body location;
4. Size (transverse diameter, thickness, and longitudinal diameter; centimeters);
5. Shape, margin definition, and contour;
6. Nature (solid, cystic, or mixed);
7. Echogenicity (anechoic, hypoechoic, or hyperechoic);
8. Internal echoes and septa;
9. Artifacts and calcifications;
10. Vascularity presence and distribution (internal at the solid part and peripheral at the rim or vicinity);
11. Type and maximum thickness of the vessels (millimeters); and
12. Peak systolic velocity of the arterial vessels (centimeters per second).

The ultrasound equipment and transducers were similar for all patients (LOGIQ E9 XD Clear; GE Healthcare, Milwaukee, WI; variable-frequency transducers: compact linear 8–18 MHz and linear 5–16 MHz). All the sonographic examinations were performed by following the recommendations of the already-published guidelines for studying dermatologic lesions that include grayscale and color Doppler imaging.[16] The same settings previously reported for sonography in dermatology were used in all the examinations.[17,18] The same radiologist trained in dermatologic sonography performed all the examinations. All cases were extracted from the database of the Institute of Diagnostic Imaging and Research of the Skin and Soft Tissues. The study was approved by the Institutional Review Board of Clinica Servet. The patients signed an informed consent form for publishing their images, and all the examinations followed the Helsinki principles of medical ethics.

Results

A total of 6 cases of apocrine nodular hidradenoma were reviewed. Of these, 67% were female and 33% male (mean age, 53 years; range, 43–84 years; SD, 14 years). All cases were single lesions, and their body locations were 83% lower extremities and 17% abdominal wall (Table 1).

All the cases involved the dermis and hypodermis and presented as a well-defined oval structure with a solid-cystic appearance that showed a hypoechoic rim and an inner mixed structure with hypoechoic solid and anechoic lacunar fluid-filled components as well as a posterior acoustic enhancement artifact. Vascularity was detected in all hidradenomas, with vessels at the periphery of the lesion (rim or vicinity) and within the hypoechoic inner solid component.

Sixty-seven percent of cases showed smoothly lobulated borders, inner septa, and moving echoes that resembled the falling of snow; therefore, we called this appearance the "snow falling" sign. Fifty percent of the lesions showed a "fluid-fluid level" sign with anechoic-hypoechoic fluid levels within the structure. Fifty percent of the cases showed both arterial and venous blood flow,

Table 1. Grayscale Sonographic Data on Apocrine Nodular Hidradenoma

Case	Age, y	Sex	Body Location	Transverse cm	Thickness, cm	Longitudinal cm	Snow Falling Sign	Fluid-Fluid Level Sign
1	43	Male	Left leg	2.2	1.7	1.8	Present	Present
2	59	Female	Abdominal wall	2.0	1.4	1.6	Present	Present
3	52	Female	Right thigh	1.0	0.8	1.2	Present	Absent
4	52	Male	Left foot	1.5	1.0	1.7	Absent	Present
5	84	Female	Left leg	1.6	0.5	1.0	Absent	Absent
6	54	Female	Right leg	1.8	1.2	2.4	Present	Absent

and 50% showed only arterial vessels. The mean maximum thickness of these vessels was 1.1 mm (range, 0.7–1.2 mm; SD, 0.2 mm). The mean maximum peak systolic velocity of the arterial vessels was 10.9 cm/s (range, 6.5–23.0 cm/s; SD, 5.8 cm/s; Table 2). Perilesional hypodermal edema was absent in 83% of cases. In 17% (n = 1), hypodermal edema was detected; however, in this case, there was a history of recent regional trauma. No signs of calcification were detected within or at the periphery of these lesions.

A correlation of the clinical, sonographic, and histologic presentations of these cases is shown in Figures 1–7. Videos 1–5 illustrate the sonographic patterns and signs described in this section in real time.

Discussion

As far as we know, these cases compose the largest series of nodular hidradenomas studied with sonography and may provide tools for supporting their differential diagnosis with other dermatologic entities. The main sonographic characteristics of apocrine nodular hidradenomas are a well-defined, solid-cystic dermal and hypodermal structure that tends to show smoothly lobulated borders, an inner solid component, lacunar fluid-filled spaces, septa, moving echoes with a snow falling sign, as well as a fluid-fluid level sign. Thin low-velocity arterial or venous vessels are commonly detected within or at the periphery of the lesion or in both locations.

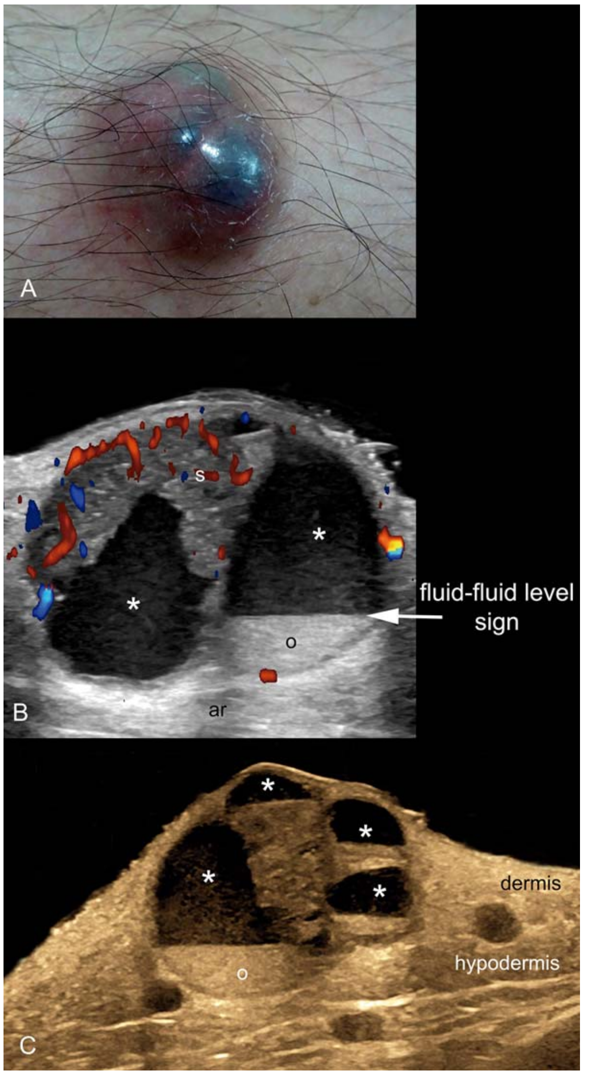
Interestingly, the snow falling and fluid-fluid level signs have not been previously reported in nodular hidradenomas, and to our knowledge, they have not been described in the sonographic appearances of other dermatologic conditions. These particular sonographic signs might be produced by the presence of mucoid viscous material and hemorrhage within the tumor.

Table 2. Color Doppler Data on Apocrine Nodular Hidradenoma

Case	Type of Vessels	Thickness, mm	Maximum Peak Systolic Velocity, cm/s
1	Arterial	1.2	8.7
2	Arterial and venous	1.2	12.3
3	Arterial and venous	1.0	13.3
4	Arterial	1.2	23.0
5	Arterial	0.7	6.5
6	Arterial and venous	1.0	9.5

The correlation of the clinical and sonographic appearances of apocrine nodular hidradenomas showed that all cases were clinically different. Thus, some of them appeared as mainly erythematous lumps, and others showed hyperpigmented or dark pseudonodular areas within the lesions, which may explain the clinical and dermatoscopic difficulties for diagnosing these

Figure 1. Apocrine nodular hidradenoma in a 43-year-old man **A**, Clinical photograph of the lesion at the anterior aspect of the left leg. Notice the dark oval areas. **B** and **C**, Sonograms (**B**, color Doppler, longitudinal view; and **C**, grayscale, panoramic transverse view, color filter) show a well-defined oval dermal and hypodermal solid-cystic structure. Notice the fluid-fluid level sign and the vascularity of the lesion; ar indicates posterior acoustic reinforcement artifact; asterisks, lacunar areas with fluid; o, thick fluid at the bottom; and s, solid part.



entities. The variable clinical presentation of these tumors may be related to their growth rate, degree of vascularity, as well as the size and proportion of the fluid-filled cavities with viscous mucous material and the presence of internal hemorrhage.

Considering the usual clinical and dermatoscopic differential diagnoses, the sonographic pattern of apocrine nodular hidradenoma differs from the sonographic features of other dermatologic lesions that have been reported to be clinically or dermatoscopically confused with hidradenoma. For example, the most common forms of presentation of dermatofibromas tend to be a poorly defined hypoechoic structure and distortion of the regional hair follicles with variable degrees of vascularity.[19] A recent case report with 2 cases of aneurysmal dermatofibroma, an uncommon subtype of dermatofibroma, showed a well-defined oval structure with a solid-cystic appearance, lacunar areas, septa, and internal vascularity in one of the cases.[19] This case could have represented a challenge for performing a sonographic differential diagnosis with apocrine nodular hidradenoma; nevertheless, no snow falling or fluid-fluid level signs were described within the lesion in this case. Angiomatous tumors are mostly hypoechoic hypervascular solid lesions without septa or cystic areas.[17,18,20] Ganglion cysts usually appear as anechoic, avascular and sometimes lobulated cystic structures commonly attached or close to tendons, ligaments, or joints.[21]

Of paramount importance would be the differential diagnosis with skin cancer. Among the types of skin cancer, BCC, the most common form of cutaneous cancer, has some rare subtypes that show cystic areas on histologic examinations; these are the adenocystic and infundibulocystic variants.[22] However, in our experience, these subtypes also show the classic hyperechoic spots within the hypoechoic solid component of the tumor that have been reported for BCC.[23] These hyperechoic spots within BCCs seem to be good predictors of the BCC subtypes with a high or low risk of recurrence.[24]

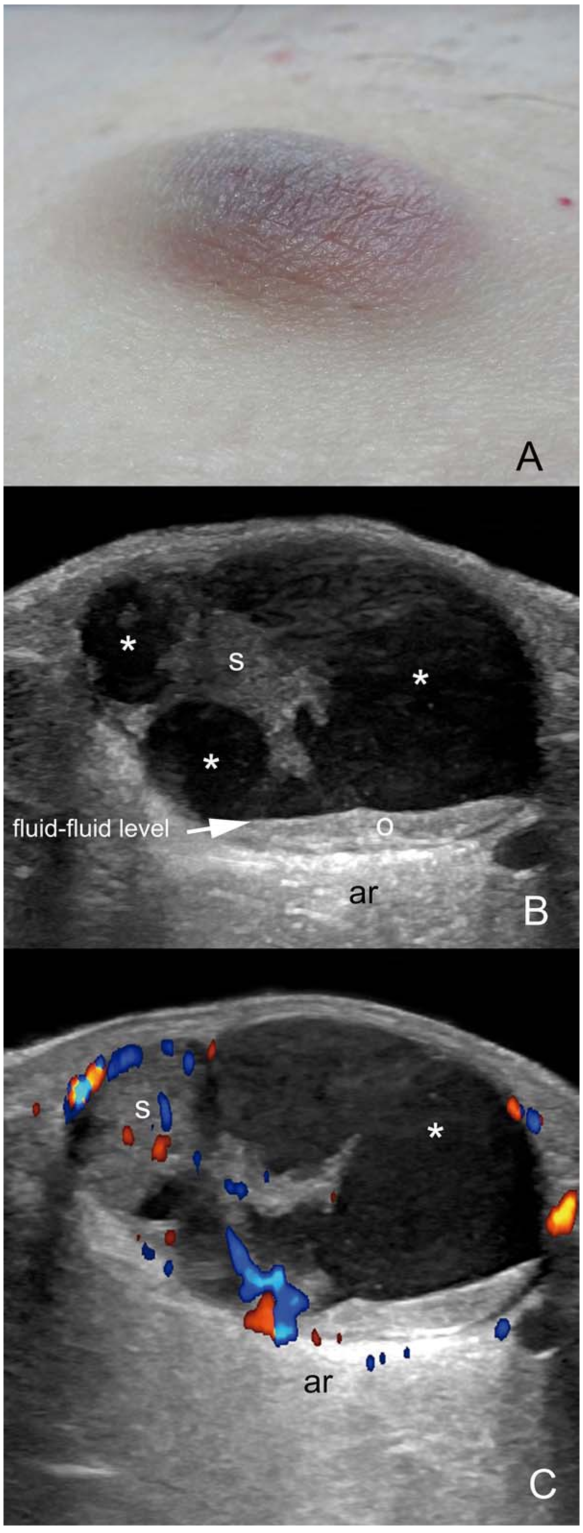


Figure 2. Apocrine nodular hidradenoma in a 59-year-old woman. **A**, Clinical photograph of the lesion at the left lower quadrant of the abdominal wall. Notice the hyperpigmented swelling. **B** and **C**, Sonograms (transverse views; **B**, grayscale; and **C**, color Doppler) show a well-defined oval dermal and hypodermal solid-cystic lesion. There is a fluid-fluid level sign (arrow, single asterisk, and o) and several lacunar fluid-filled areas (asterisks). Vascularity is detected within the solid part (s) and at the periphery of the tumor; ar indicates posterior acoustic reinforcement artifact.

Figure 3. Apocrine nodular hidradenoma in a 52-year-old woman. **A**, Clinical photograph of the lesion at the posterior aspect of the proximal part of the right thigh. **B** and **C**, Sonograms (**B**, color Doppler transverse view; and **C**, 3-dimensional reconstruction, grayscale, color filter) show a well-defined oval dermal and hypodermal solid-cystic lesion. Notice the prominent echoes within the fluid component (asterisks) that resemble the falling of snow. There is increased vascularity at the most superficially located solid part and at the periphery of the tumor; ar indicates posterior acoustic reinforcement artifact; and s, solid part.

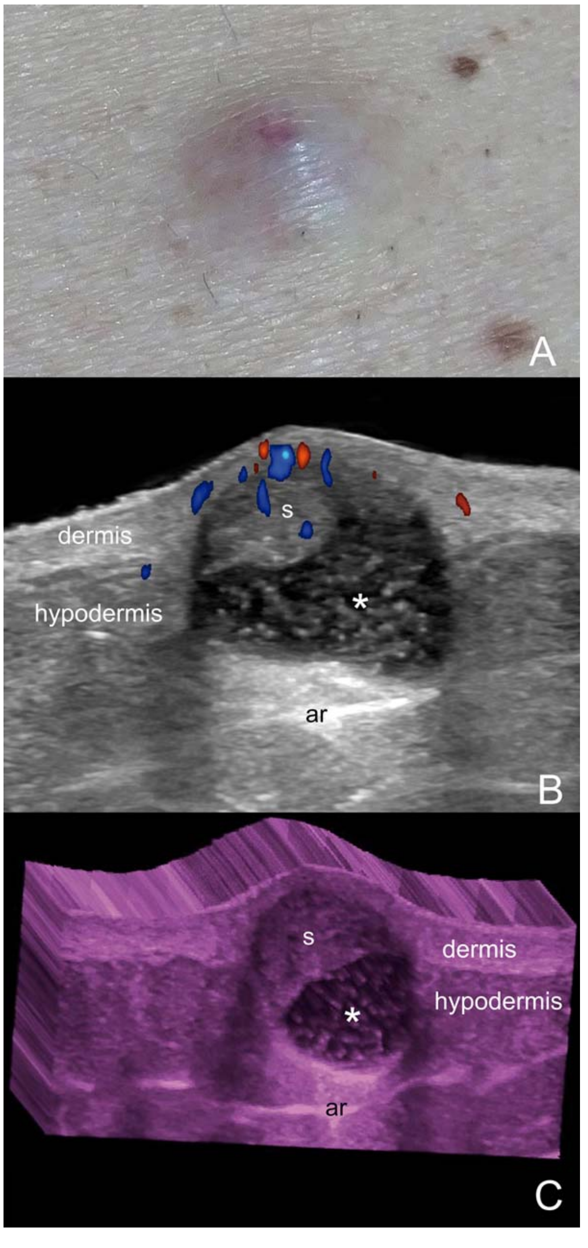


Figure 4. Apocrine nodular hidradenoma in a 52-year-old man. **A**, Clinical photograph of the lesion at the lateral aspect of the left foot. **B** and **C**, Sonograms (**B**, grayscale, transverse view; and **C**, color Doppler, longitudinal view) show a well-defined oval dermal and hypodermal solid-cystic lesion. Notice the anechoic lacunar areas (asterisks) and the presence of vascularity at the periphery and within the lesion; ar indicates posterior acoustic reinforcement artifact; and s, solid part.

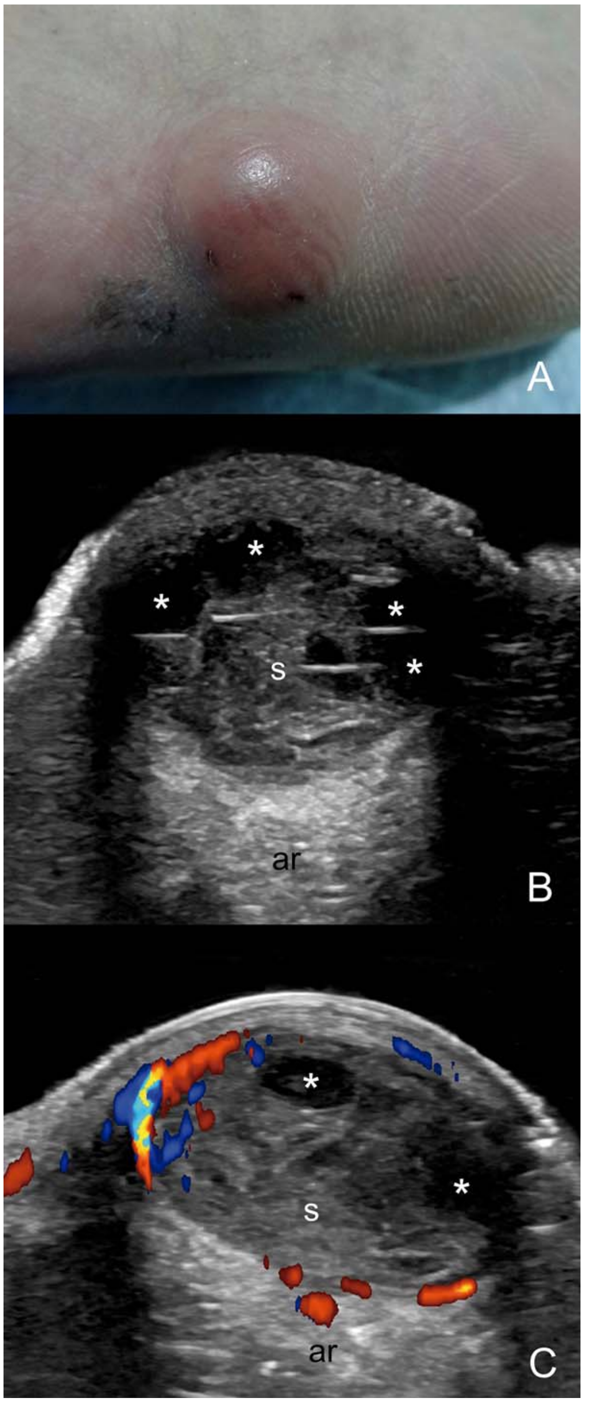


Figure 5. Apocrine nodular hidradenoma in an 84-year-old woman. **A**, Clinical photograph of the lesion at the anterior aspect of the left leg. **B** and **C**, Sonograms (transverse views; **B**, grayscale; and **C**, color Doppler) show a well-defined oval dermal and hypodermal solid-cystic lesion. The tumor contains solid (s) and fluid-filled (asterisks) parts. Increased blood flow is detected in the periphery and within the lesion (**C**). Additionally, there is increased echogenicity of the hypodermis due to edema, presumably after trauma; ar indicates posterior acoustic reinforcement artifact; and s, solid part.

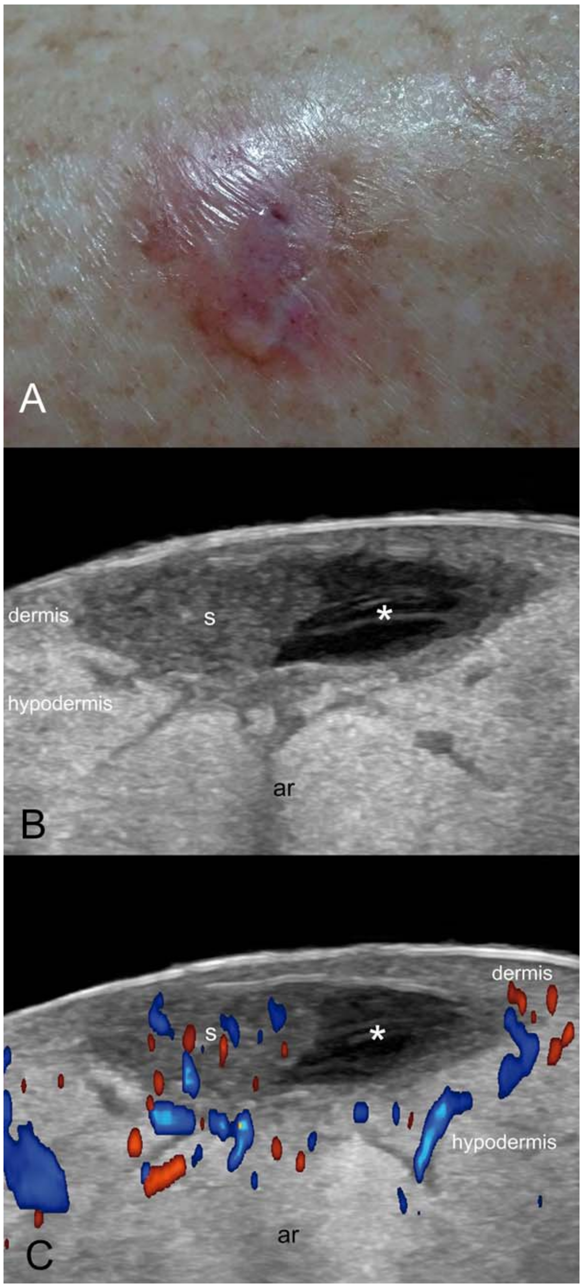
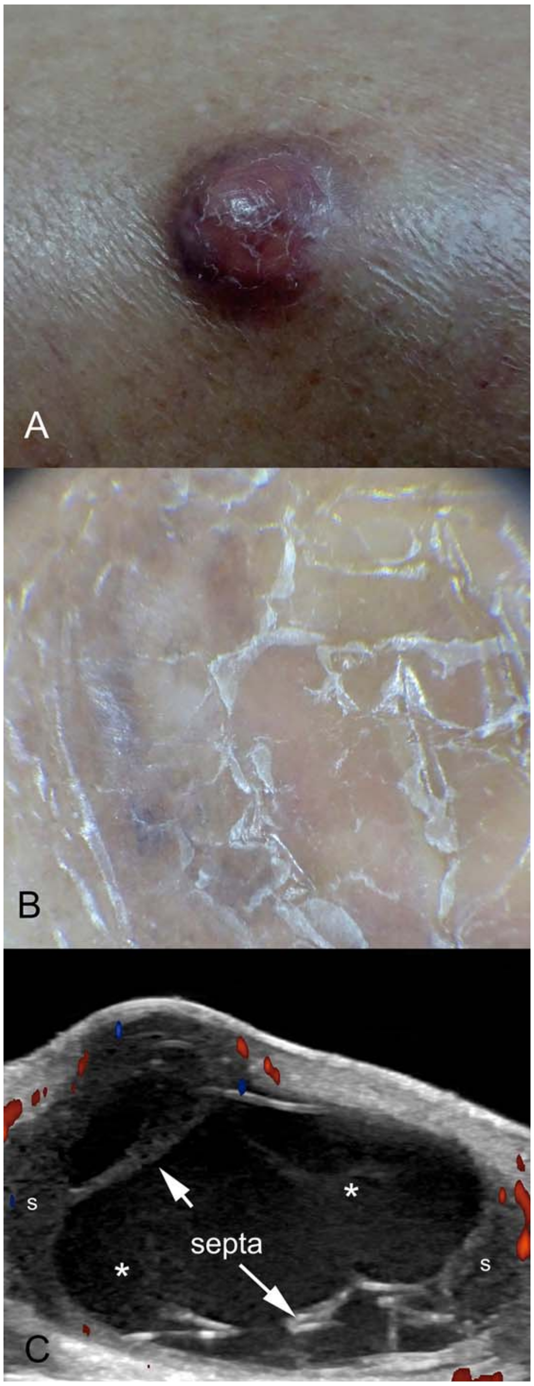


Figure 6. Apocrine nodular hidradenoma in a 54-year-old woman. **A** and **B**, Clinical images (**A**, clinical photograph; and **B**, dermoscopy) of the lesion at the anterior aspect of the right leg. **C**, Sonogram (color Doppler, longitudinal view) shows a well-defined oval dermal and hypodermal solid-cystic lesion. Notice the smoothly lobulated borders, the inner septa (arrows) and the blood flow in the periphery of the lesion; asterisks indicate fluid-filled lacunar area; and s, solid part.

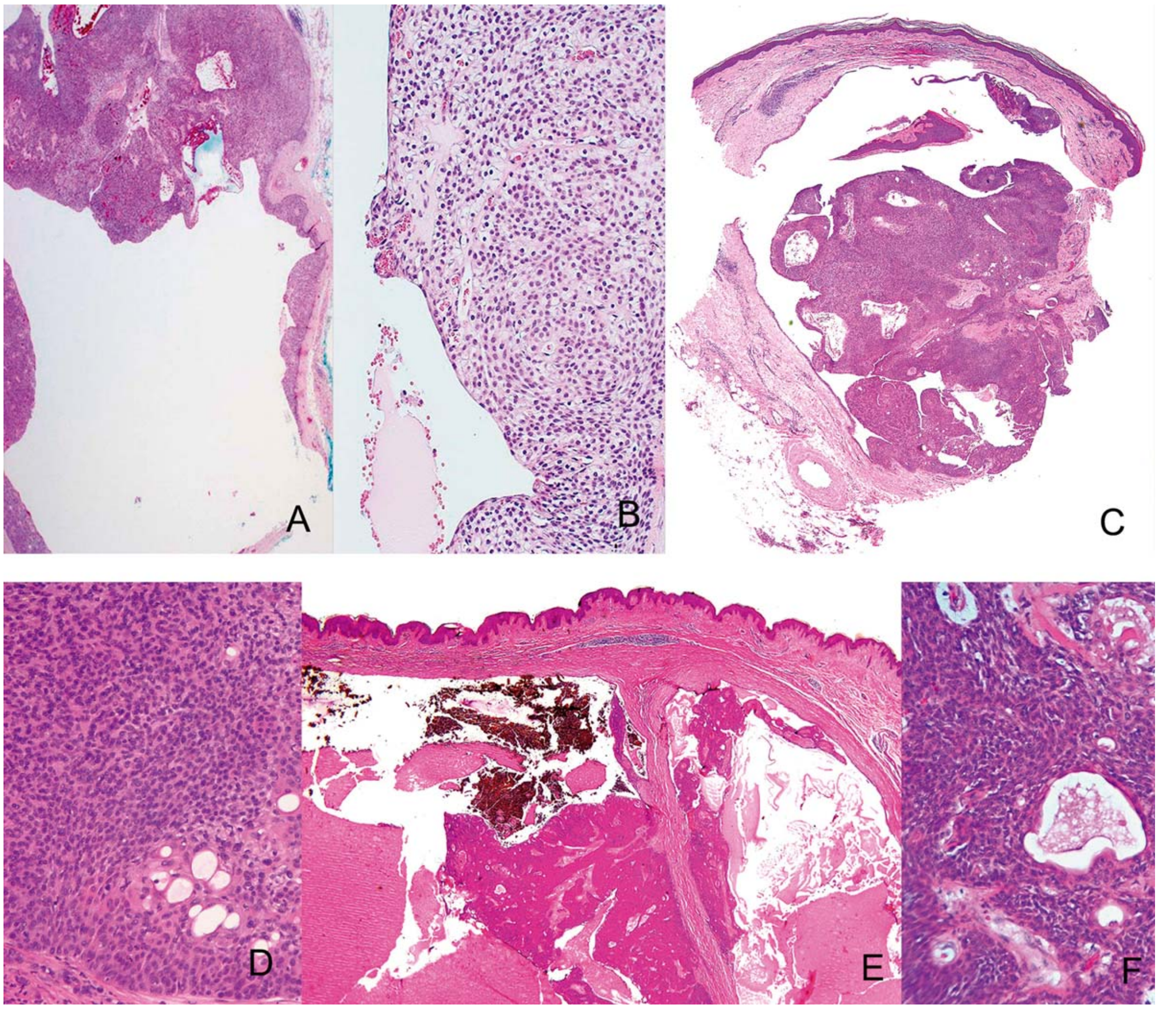


The rest of the BCC subtypes, squamous cell carcinomas and melanomas, mostly present as hypoechoic solid structures with variable degrees of vascularity and no cystic areas or septa.[16,17,25]

From the sonographic perspective, the latter signs plus the previously mentioned sonographic features of apocrine nodular hidradenoma can support the differential diagnosis with common cystic cutaneous lesions that show hypoechoic keratinous content such as epidermal cysts.[16,17,26] On the other hand, schwannomas with cystic degeneration can appear as solid-cystic tumors with hypoechoic areas and septa.[27,28] However, most of these tend to be located deeper in the hypodermis, rarely involve the dermis, and are usually closer to vascular or neural bundles and tendons. Furthermore, these neurogenic benign tumors commonly appear as hypovascular (with mostly peripheral blood flow) or avascular structures.[29] So far, no snow falling or fluid-fluid level signs have been reported in superficial schwannomas.

The detection of a wider range of sonographic characteristics in the apocrine nodular hidradenomas in this series relied on the permanent use of protocol established by dermatologic ultrasound guidelines.[16–18] In addition, reports on the use of sonography for studying

Figure 7. Apocrine nodular hidradenoma histologic specimens (hematoxylin- eosin stain). **A** and **B**, Case 1. **A**, Panoramic view of a cavity within the tumor (original magnification × 20). **B**, Multilayer of epithelial cells (original magnification × 200). **C** and **D**, Case 2. **C**, Panoramic view of the dermal part of a solid-cystic benign epithelial neoplasm (original magnification × 80). **D**, Polyhedric epithelial cells, with squamoid and ductal differentiation and focal decapitation secretion (original magnification × 200). **E** and **F**, Case 5. **E**, Dermal nodular solid-cystic tumor with focal hemorrhage (original magnification × 100). **F**, Epithelioid nests with apocrine ductal differentiation (original magnification × 200).



dermatologic lesions have increased in recent times; therefore, there are more data on the sonographic patterns of lesions available in literature, which can support a more accurate diagnosis.

A limitation to this series could be the small number of cases; however, in comparison with other dermatologic lesions, these sweat gland–derived tumors are not so common. Nevertheless, their sonographic detection may be relevant for avoiding clinical or dermatoscopic misdiagnoses, which might even confuse these lesions with malignant cutaneous tumors.

Further research may be needed to compare these sonographic morphologic characteristics with larger samples of eccrine or apocrine nodular hidradenomas. Additionally, this information can support an improvement of the cosmetic prognosis of these cases by providing detailed anatomic data, which may contribute to better presurgical planning.

In conclusion, apocrine nodular hidradenomas present different sonographic characteristics in comparison with other common cutaneous lesions, which may support their earlier and more precise sonographic diagnosis and also avoid clinical and dermatoscopic misdiagnosis.

References

1. Nandeesh BN, Rajalakshmi T. A study of histopathologic spectrum of nodular hidradenoma. *Am J Dermatopathol* 2012; 34:461–470.
2. Demirci GT, Atis G, Altunay IK, Sakiz D. A giant benign clear cell hidradenoma on the anterior trunk. *Dermatol Rep* 2011; 3:e45.
3. Paranjyothi M, Mukunda A. Clear cell hidradenoma: an unusual tumor of the oral cavity. *J Oral Maxillofac Pathol* 2013; 17: 136138.
4. Serrano P, Lallas A, Del Pozo LJ, et al. Dermoscopy of nodular hidradenoma, a great masquerader: a morphological study of 28 cases. *Dermatology* 2016; 232:78–82.
5. Makaram N, Chaudhry IH, Srinivasan MS. Hidradenoma masquerading digital ganglion cyst: a rare phenomenon. *Ann Med Surg (Lond)* 2016; 10:22–26.
6. Lallas A, Chellini PR, Guimarães MG, et al. Eccrine poroma: the great dermoscopic imitator. *J Eur Acad Dermatol Venereol* 2016; 30: e61–e63.
7. Robles-Mendez JC, Martínez-Cabriales SA, Villarreal-Martínez A, et al. Nodular hidradenoma: dermoscopic presentation. *J Am Acad Dermatol* 2017; 76:S46–S48.
8. Obaidat NA, Alsaad KO, Ghazarian D. Skin adnexal neoplasms—part 2: an approach to tumours of cutaneous sweat glands. *J Clin Pathol* 2007; 60:145–159.
9. Takasaka M, Saeki H, Ito K, Matsuo K, Ishiji T, Nakagawa H. Skin ultrasound examination proves useful in diagnosing two cases of solid cystic hidradenoma. *Int J Dermatol* 2014; 53:e146–e147.
10. Mullaney PJ, Becker E, Graham B, Ghazarian D, Riddell RH, Salonen DC. Benign hidradenoma: magnetic resonance and ultrasound features of two cases. *Skeletal Radiol* 2007; 36:1185–1190.
11. Ghai S, Bukhanov K. Eccrine acrospiroma of breast: mammographic and ultrasound findings. *Clin Radiol* 2004; 59:1142–1144.
12. Horie K, Ito K. Ultrasonographic diagnosis of nodular hidradenoma. *J Dermatol* 2016; 43:449–450.
13. Balaban M, Idilman IS, Unal O, Dumlu EG, Yazgan A, Ipek A. Sonographic and sonoelastographic findings of a rarely seen soft tissue tumor: eccrine spiradenoma. *J Med Ultrason (2001)* 2015; 42:587–590.
14. Jin W, Kim GY, Lew BL, et al. Sonographic findings of an eccrine spiradenoma: case report and literature review. *J Ultrasound Med* 2008; 27:813–818.
15. Lee HH, Park SH, Choi HY, Park HK. Eccrine spiradenoma arising in the breast misdiagnosed as an epidermal inclusion cyst. *Korean J Radiol* 2011; 12:256–260.
16. Wortsman X, Alfageme F, Roustan G, et al. Guidelines for performing dermatologic ultrasound examinations by the DERMUS Group. *J Ultrasound Med* 2016; 35:577–580.
17. Wortsman X. Ultrasound in dermatology: why, how and when? *Semin Ultrasound CT MR* 2013; 34:177–195.
18. Wortsman X. Common applications of dermatologic sonography. *J Ultrasound Med* 2012; 31:97–111.
19. Echeverría-García B, García-Donoso C, Tardío JC, Borbujo J. Doppler ultrasound of aneurysmal dermatofibroma. *Actas Dermosifiliogr* 2017; 108:159–161.
20. Wortsman X, Carreño L, Morales C. Cutaneous vascular tumors. In: Wortsman X, Jemec GBE (eds). *Dermatologic Ultrasound With Clinical and Histologic Correlations.* 1st ed. New York, NY: Springer; 2013: 235–248.
21. Giard MC, Pineda C. Ganglion cyst versus synovial cyst? Ultrasound characteristics through a review of the literature. *Rheumatol Int* 2015; 35:597–605.
22. Saxena K, Manohar V, Bhakhar V, Bahl S. Adenoid basal cell carcinoma: a rare facet of basal cell carcinoma. *BMJ Case Rep* 2016; 2016: 10.1136/bcr-2015-214166.
23. Wortsman X. Sonography of facial cutaneous basal cell carcinoma: a first-line imaging technique. *J Ultrasound Med* 2013; 32:567–572.
24. Wortsman X, Vergara P, Castro A, et al. Ultrasound as predictor of histologic subtypes linked to recurrence in basal cell carcinoma of the skin. *J Eur Acad Dermatol Venereol* 2015; 29:702–707.
25. Wortsman X, Carreño L, Morales C. Skin cancer: the primary tumors. In: Wortsman X, Jemec GBE (eds). *Dermatologic Ultrasound With Clinical and Histologic Correlations.* 1st ed. New York, NY: Springer; 2013:249–282.

26. Huang CC, Ko SF, Huang HY, et al. Epidermal cysts in the superficial soft tissue: sonographic features with an emphasis on the pseudotestis pattern. *J Ultrasound Med* 2011; 30:11–17.
27. Tatar IG, Yilmaz KB, Arikok A, et al. Cystic schwannoma of the axillary region: imaging findings of a rare disease. Case report. *Med Ultrason* 2015; 17:126–128.
28. Lee SJ, Yoon ST. Ultrasonographic and clinical characteristics of schwannoma of the hand. *Clin Orthop Surg* 2017; 9:91–95.
29. Wortsman X, Bouer M. Common benign non-vascular skin tumors. In: Wortsman X, Jemec GBE (eds). *Dermatologic Ultrasound With Clinical and Histologic Correlations*. 1st ed. New York, NY: Springer; 2013:119–175.