

## Merkel Cell Carcinoma: Is There a Distinctive Ultrasound Pattern?☆



### Carcinoma de células de Merkel: ¿existe un patrón ecográfico distintivo?

To the Editor:

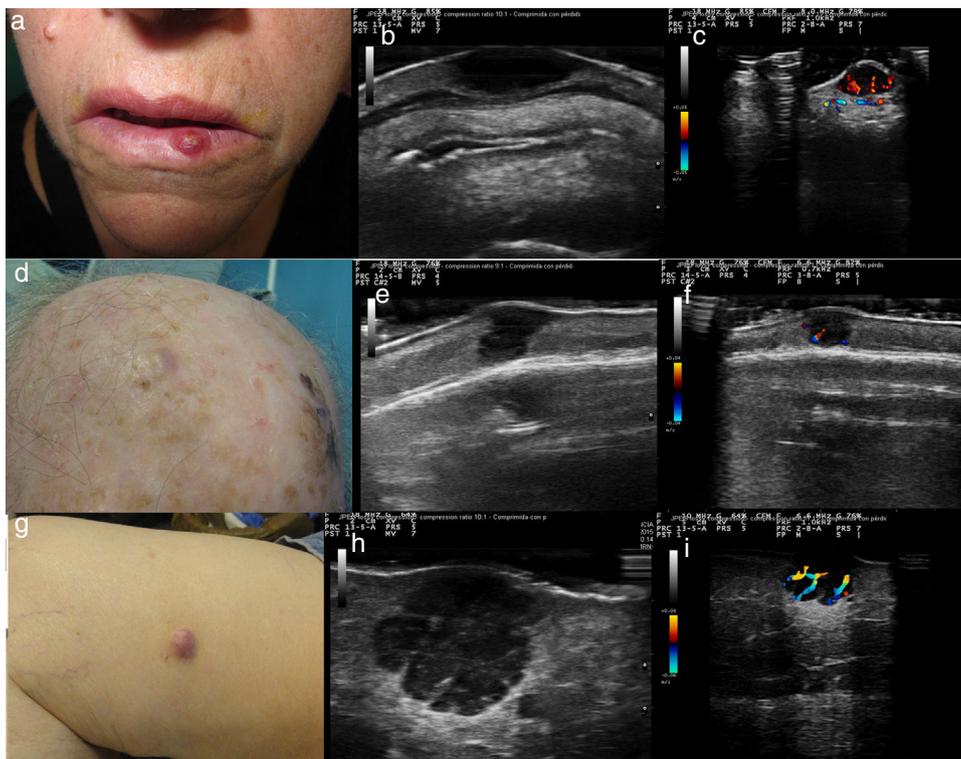
Merkel cell carcinoma (MCC) is a rare, fast-growing, aggressive neuroendocrine tumor that frequently causes locoregional recurrence and distant metastasis. It tends to affect sun-exposed areas (mainly the head, neck, and upper extremities) and associated risk factors include immune suppression, elderly age, fair skin, and a history of prior malignancy.<sup>1</sup> Imaging modalities used to stage disease and plan surgery include computed tomography and magnetic resonance imaging,<sup>2,3</sup> but very few studies have described the ultrasound features of MCC.

We present the ultrasound findings of 5 cases of primary MCC analyzed using an 18-MHz linear transducer. In all cases, diagnosis was confirmed by preoperative skin biopsy.

B-mode imaging showed well-defined, hypoechoic dermal and hypodermal lesions. Two of the tumors had homogeneous content. The other 3 were heterogeneous and contained hyperechoic septae in 1 case and hypoechoic lines running perpendicular to the skin surface in the other 2. The B-mode images also showed posterior acoustic enhancement in 3 of the tumors and thinning of the overlying epidermis in 2.

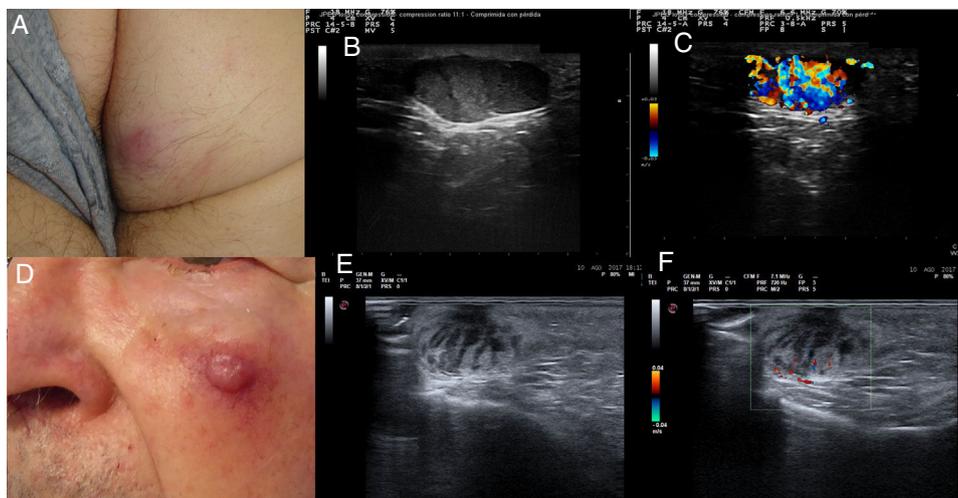
Most of the tumors had intense intralesional hypervascularity on color Doppler ultrasound. The vascular structures were predominant in the basal area of all tumors except the one in which hyperechoic lines had been observed by B-mode ultrasound. In this case, a strong Doppler signal was detected among the septae (Figs. 1 and 2).

A full histologic examination was possible in 3 of the tumors; the other 2 (cases 2 and 5) regressed spontaneously after the skin biopsy (diagnosis was confirmed by histologic



**Figure 1** A (case 1), Firm, indurated, erythematous lesion with a diameter of 1 cm on the left side of the lower lip; B, B-mode image showing a homogeneous hypoechoic dermal lesion with well-defined margins; C, Color Doppler image showing predominant hypervascularity in the basal area; D (case 2), Subcutaneous nodule with a diameter of 8 mm located in the right parietal region and covered by pink skin; E, B-mode image showing a hypoechoic dermal/epidermal lesion; F, Color Doppler image showing a weak signal around the lesion; G (case 3), Pink nodule with a diameter of 18 mm on the internal aspect of the right thigh; H, B-mode image showing a hypoechoic polylobular dermal/hypodermal lesion with well-defined margins, posterior acoustic reinforcement, and predominant intralesional vascularity in the septae.

☆ Please cite this article as: García-Harana C, Fernandez-Canedo I, Rodríguez-Lobalzo S, de Troya-Martín M. Carcinoma de células de Merkel: ¿existe un patrón ecográfico distintivo? . 2019;110:503–506.



**Figure 2** A (case 4), Subcutaneous lesion with a diameter of 20 mm, an elastic consistency, and a violaceous surface on the right buttock; B, B-mode image showing a hypoechoic hypodermal lesion with heterogeneous content and hypoechoic plume-of-smoke lines running perpendicular to the epidermis, well-defined margins, and posterior acoustic reinforcement; C, Color Doppler image showing intralesional vascularity; D (case 5), Erythematous nodule over a subcutaneous lesion with a diameter of a 22 mm on the left cheek; E, B-mode image showing a hypoechoic dermal lesion with heterogeneous content and hypoechoic plume-of-smoke lines running perpendicular to the epidermis; F, Color Doppler image showing predominant intralesional vascularity in the basal area.

examination of the surgical specimen). Three of the tumors showed a solid growth pattern. One had spiculated margins and the other 2 had better defined margins and a lobular structure. All 3 tumors had fibrous trabeculae separating the cells; the first tumor had fine bands with scant vascular structures, while the other 2 had thick fibrous bands containing numerous vascular structures (Fig. 3). All 5 tumors were studied by immunohistochemistry and were positive for chromogranin, synaptophysin, and CD56. Paranuclear staining was observed for cytokeratin 20 and negative results were detected for CD45, S-100 protein, and thyroid transcription factor 1.

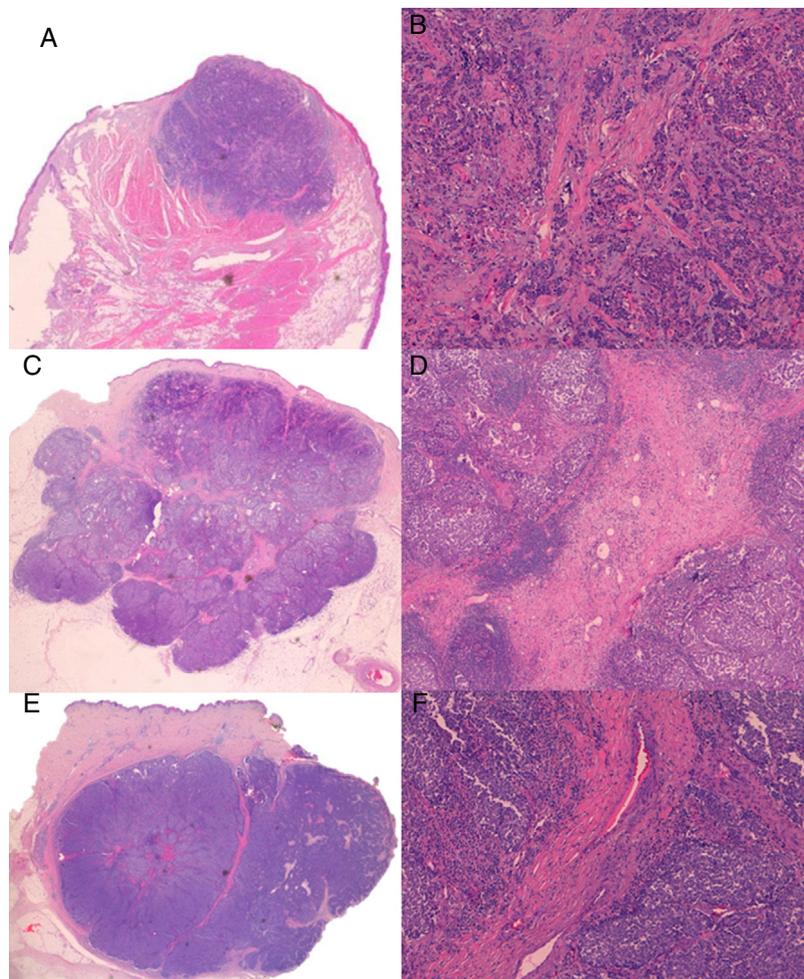
There are very few descriptions of the ultrasound features of MCC in the literature, as ultrasound is mainly used to study locoregional lymph nodes in this setting.<sup>4,5</sup> Wortsman et al.<sup>6</sup> described hypoechoic dermal and hypodermal lesions with ill-defined margins and intense hypervascularity. Although the ultrasound findings for the 5 tumors in our series were quite diverse, they all had similar characteristics to those described in the literature, except for the tumor margins, which were well-defined in all cases.

Other common ultrasound findings reported for MCC, and also observed in our series, are posterior acoustic reinforcement and thinning of the overlying epidermis.<sup>7-9</sup> In a recent article, Hernández-Aragüés et al.<sup>7</sup> described hypoechoic linear bands with a plume-of-smoke appearance perpendicular

to the skin surface in 2 cases of primary MCC; Doppler imaging showed vascularity in these areas. Two of the tumors in our series had hypoechoic bands, but the vascular structures were located elsewhere.

Histologically, 2 of the tumors in our series (the one with the plume-of-smoke appearance on ultrasound and the one containing hyperechoic septae) had thick fibrous bands separating the cells. Although these fibrous trabeculae featuring abundant vascular structures appeared to correspond to the perpendicular hypoechoic lines and the hyperechoic septae detected by ultrasound, we found no histologic differences to explain the different echogenicity of these structures.

In conclusion, our analysis of the 5 cases in our series and those reported in the literature did not reveal a distinctive ultrasound pattern for MCC and we were also unable to determine the diagnostic and prognostic significance of some of the features observed. Notwithstanding, skin ultrasound is undoubtedly a useful imaging tool for determining tumor location, extension, vascularity, and relationship to adjacent structures. As such, it can aid in the planning of surgery. In addition, it provides an objective measure of tumor size and extent of deep invasion and can also identify subcutaneous or in-transit metastases, enabling better staging and providing preliminary prognostic information.<sup>10</sup>



**Figure 3** A, Case 1: Lesion with solid growth pattern and slightly spiculated margins (hematoxylin-eosin [H-E]); B, Detail of fibrous trabeculae in the form of fine bands with scant vascular structures (H-E, original magnification  $\times 100$ ); C (case 3), Tumor with clearer margins and a lobular structure with fibrous bands that appear to correspond to the hyperechogenic intralesional lines observed by B-mode ultrasound (H-E); D, Detail of thick fibrous bands containing numerous vascular structures (H-E, original magnification  $\times 40$ ); E (case 4), Lobular lesion with a thick fibrous band perpendicular to the epidermis that appears to correspond to the hypoechoic line detected by B mode ultrasound; F, Detail of thick central fibrous band with wider vascular structures than in case 3 (H-E, original magnification  $\times 100$ ).

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## References

- Saini AT, Miles BA. Merkel cell carcinoma of the head and neck: Pathogenesis, current and emerging treatment options. *Onco Targets Ther.* 2015;8:2157–67.
- Müller-Richter UDA, Gesierich A, Kubler AC, Hartmann S, Brands RC. Merkel Cell Carcinoma of the head and neck: Recommendations for diagnostics and treatment. *Ann Surg Oncol.* 2017;24:3430–7.
- Humphreys TR, Shah K, Wysong A, Lexa F, MacFarlane D. The role of imaging in the management of patients with nonmelanoma skin cancer: When is imaging necessary? *J Am Acad Dermatol.* 2017;76:591–607.
- Lebbe C, Becker JC, Grob JJ, Malvehy J, del Marmol V, Pheamberger H, et al. Diagnosis and treatment of Merkel Cell Carcinoma European consensus-based interdisciplinary guideline. *Eur J Cancer.* 2015;51:2396–403.
- Zager JS, Brodsky S, Berman CG. Imaging of Merkel cell carcinoma. *Curr Probl Cancer.* 2010;34:65–76.
- Wortsman X, Carreño L, Morales C. Skin cancer: The primary tumors. In: *Dermatologic ultrasound with clinical and histological correlations.* 1st edition Berlin: Springer Verlag; 2013. p. 249–82.
- Hernández-Aragüés I, Vázquez-Osorio I, Alfageme F, Ciudad-Blanco C, Casas-Fernández L, Rodríguez-Blanco MI, et al. Skin ultrasound features of Merkel cell carcinoma. *J Eur Acad Dermatol Venereol.* 2017;31:e315–8.
- Enzenhofer E, Ubl P, Czerny C, Erovic BM. Imaging in patients with Merkel cell carcinoma. *J Skin Cancer.* 2013;2013:973123.
- Catalano O, Alfageme Roldán F, Scotto di Santolo M, Solivetti FM, Wortsman X. Color Doppler sonography of Merkel cell carcinoma. *J Ultrasound Med.* 2018;37:285–92.
- Llombart B, Requena C, Cruz J. Actualización en el carcinoma de células de Merkel: epidemiología, etiopatogenia, clínica, diagnóstico y Estadificación. *Actas Dermosifiliogr.* 2017;108:108–19.

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1578-2190/

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## Ultrasound in the Evaluation of Cutaneous Metastases of Internal Tumors<sup>☆</sup>



### Estudio ecográfico de metástasis cutáneas de origen visceral

To the Editor:

Cutaneous metastasis is the clinical manifestation of neoplastic cells that have spread to the skin from a visceral tumor. Its prevalence, which is rising due to higher rates of histologic diagnosis and/or evaluation, is estimated at between 0.7% and 9% depending on the series.<sup>1</sup> Cutaneous metastases are a common reason for consultation between dermatologists and are often suspected as an initial diagnosis because the lesions are easily identifiable during physical examination. They are important to recognize as they can lead to the diagnosis of an unknown primary tumor, indicate the spread of a known tumor, or be an early sign of recurrence of a tumor thought to be in remission.<sup>2</sup> The most common visceral tumors that cause cutaneous metastasis are lung cancer in men, breast cancer in women, and gastric adenocarcinomas in both men and women.<sup>3</sup> Cutaneous metastases can present as any number of elementary lesions, which can be solitary or multiple or asymptomatic or painful.

Diagnosis must be confirmed histologically and in some cases an immunohistochemical panel may be necessary. Few studies and case series have analyzed the value of imaging studies prior to biopsy in cutaneous metastasis. High-frequency skin ultrasound is a fast, safe technique that can provide diagnostic information and, on occasions, pre-operative information following a clinical diagnosis. Findings often lead to a change in disease stage.

We present 6 cases of cutaneous metastasis from visceral tumors evaluated in our department between January and July 2017. We describe clinical and epidemiological characteristics and B-mode and Doppler ultrasound features. All the metastases were studied using the Esaote Mylab ultrasound system equipped a transducer that operates between 18 and 20 MHz. The Doppler pulse repetition frequency was

750 MHz for a 20-MHz frequency, and the gain was adjusted to the level immediately before the flash artifact.

There were 4 men and 2 women aged between 45 and 75 years. All the patients were referred to the medical oncology department for evaluation of skin lesions suspected to be cutaneous metastases. Just 1 patient was receiving adjuvant therapy. The other 5 were under treatment for a previously diagnosed tumor. Three of the patients had just 1 lesion when evaluated by the dermatology department. All the lesions had a diameter of over 9 mm except for some smaller lesions (4-6 mm) in patient #6. The epidemiologic, clinical, and B-mode ultrasound characteristics are summarized in [Table 1](#).

Large series have reported on the ultrasound features of cutaneous metastases from melanoma,<sup>4</sup> but this has not been the case for metastases from visceral tumors.<sup>5,6</sup> Moreover, most of the series that do exist have been published by radiologists and deal mainly with subcutaneous lesions (both palpable and nonpalpable). The authors of these studies stress that while cutaneous metastases do not necessarily indicate terminal disease, they are always a sign of disease spread. From an ultrasound perspective, all the lesions studied were located in the subcutaneous tissue, whereas in our series, given their accessibility, they were also observed in the epidermis and dermis. The most characteristic B-mode ultrasound finding for metastatic cutaneous lesions is an irregular, polycyclic shape, which was observed in 5 of the 6 patients in our series ([Fig. 1](#)).

Giovagnario et al.<sup>7</sup> described 4 vascular patterns for cutaneous metastases evaluated by ultrasound: avascular, hypovascular with a single vascular pole, hypervascular with multiple peripheral poles, and hypervascular with internal vessels. All 4 patterns were observed in our series. Some authors have claimed that vascularization is highly suggestive and predictive of malignancy, with a sensitivity of 91% and a specificity of 93%.<sup>8</sup> Avascular and hypovascular patterns may be due to lesion size, necrosis, or the presence of vessels that are too small to detect with the equipment used. This was the case with patient #6 in our series ([Fig. 2](#)).

In conclusion, we have described the ultrasound features of a series of cutaneous metastases from visceral tumors with similar clinical features to those described in the literature. B-mode ultrasound does not reveal any specific patterns and must be complemented by Doppler imaging, which offers greater diagnostic sensitivity and specificity. High-frequency skin ultrasound is a useful diagnostic method for planning treatment and monitoring cutaneous metastases from visceral tumors.

<sup>☆</sup> Please cite this article as: Cuenca-Barrales C, Aguayo-Carreras P, Bueno-Rodríguez A, Ruiz-Villaverde R. Estudio ecográfico de metástasis cutáneas de origen visceral. 2019;110:506–509.