Cutaneous Perivascular Epithelioid Cell Tumor of Gynecologic Origin Metastatic to Skin, Lung, Stomach, and Brain

To the Editor:

Regarding the first case report recently published by Navale et al[1] about a skin perivascular epithelioid cell tumor (PEComa) with focal melanin pigmentation, we wish to present another exceptional case of a malignant uterine PEComa metastatic to skin and lung, gastric lymph-vascular invasion, and brain dissemination, which was also initially misdiagnosed as skin melanoma because of the presence of epithelioid features and the expression of some melanocytic markers.

Our patient was a 62-year-old woman, who presented with abnormal uterine bleeding that prompted hysterectomy 3 years ago. An extrainstitutional pathology report on the surgical specimen revealed a lesion compatible with a uterine leiomyosarcoma that was managed with adjuvant radiotherapy. At the 2-year clinical follow-up, the patient presented with a mass on the posterior region of the neck, which required undergoing surgical excision. The pathology study features were compatible with a malignant melanoma. Other reassessment and follow-up studies evidenced a compromise of the lung, with histopathological diagnosis of metastatic melanoma. A year ago, the patient presented with a new pigmented lesion on the right cheek. Once again, the biopsy study revealed a melanoma.

This case was referred to our institution, and a reassessment of all lesions was conducted. The histopathological examination from the uterus, skin, and lung (Figs. 1A–C) revealed the same tumor which was characterized by nests and occasionally fascicles of epithelioid cells with characteristically

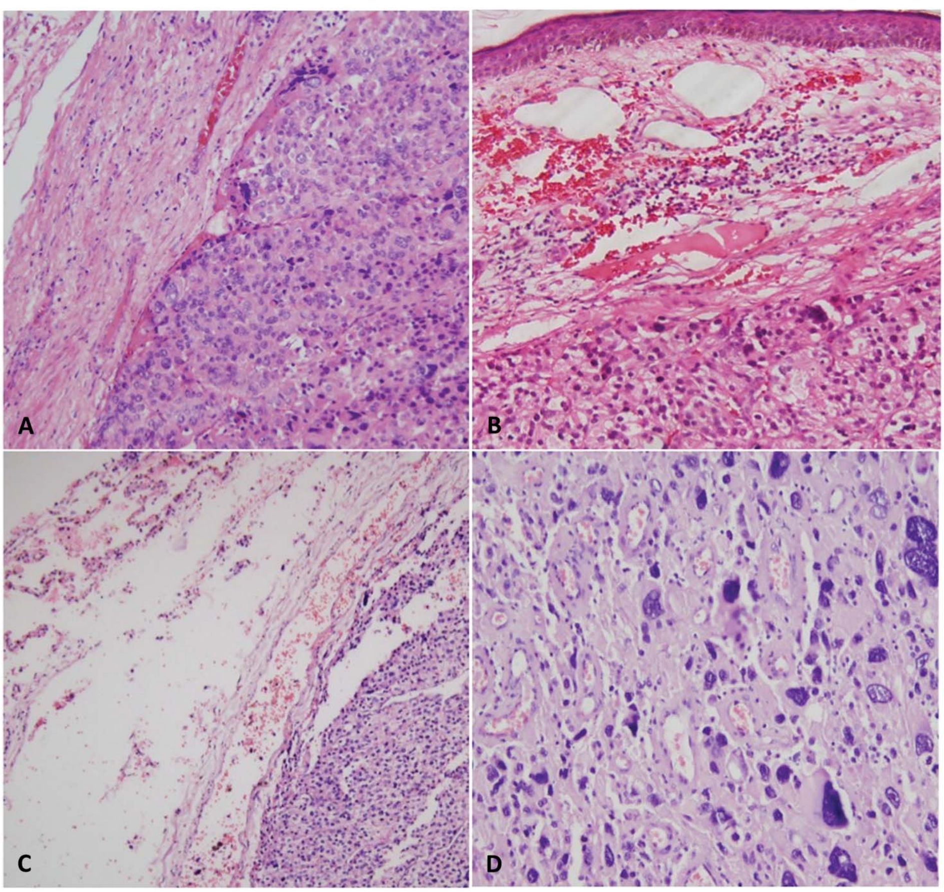

FIGURE 1. Presence of the same tumor in (A) uterus, (B) skin, (C) lung, and (D) brain. The tumor is characterized by a malignant epithelioid tumor with nests. High-magnification view of cells with uniform nuclei, higher grade nuclei, and nuclear pleomorphism. In skin (B), the nests of epithelioid cells have cleared-out cytoplasm.

The authors declare no conflicts of interest.

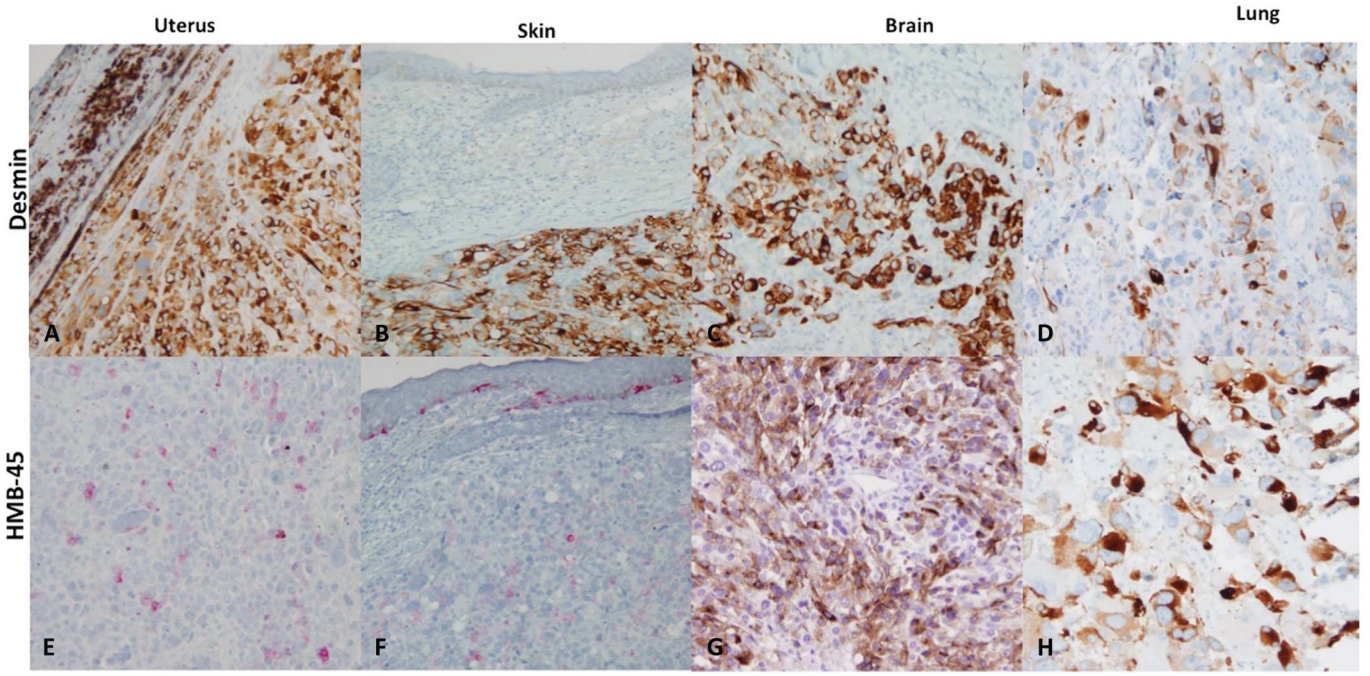

FIGURE 2. In all cases, the presence of positivity to desmin (A–D) and HMB-45 (E–H) is noted.

delicate collagen and vascular septa. The cells at higher magnification showed uniform round nuclei and acidophilic cytoplasms (Fig. 1), although in some areas, large hyperchromatic and vesicular chromatin or prominent nucleoli with severe pleomorphisms were also seen. On the skin (Fig. 1B), some nests of epithelioid cells have cleared-out cytoplasm. With those particular morphological characteristics presented by these different organs, we necessarily have to think about some differential mesenchymal and epithelial diagnosis. Additionally, a complete panel of immunohistochemistry is significantly important to exclude carcinomas (squamous cell, clear renal cell, etc), melanoma, leiomiosarcoma, vascular tumors and, as in this case, PEComa. In all cases, the immunohistochemistry study indicated positivity for desmin, HMB-45 (anti-Melanosome), and smooth muscle actin and negativity for S100, CK AE1/AE3, CK7, CK20, Synaptophysin, Melan-A, Chromogranin-A, and thyroid transcription factor-1 and a 40% Ki-67 immunostaining level (Fig. 2). In the uterus, estrogen and progesterone receptor expression was 80% and 70%, respectively. Recently, the patient presented with febrile neutropenia and upper gastrointestinal tract bleeding. Radiologic and endoscopic imaging and histologic examination confirmed a metastatic involvement by gastric lymphovascular invasion and brain compromise (Fig. 1D and Figs. 2D, H). The morphological characteristics of the brain lesions with vascular proliferation and significantly large pleomorphic cells mimicked a glioblastoma multiforme. However, the medical record, the previous pathologic material, and the immunohistochemistry study confirmed metastatic PEComa excluding glioblastoma.

As it was reported in the case study by Navale et al,[1] the skin and metastatic lesions of our case were first reported as melanoma because of melanocytic marker expression, even in the absence of pigment. Additionally, because of the precedent involvement of a similar lesion and the expression of melanocytic markers, new lesions in other organs were interpreted in the same way. PEComas typically show immunohistochemical evidence of both smooth muscle and melanocytic differentiation. HMB-45 was the most sensitive reagent (92%), followed by Melan-A (72%) and MiTF (50%). Smooth muscle actin expression was seen in 80% of the cases, and coexpression of HMB-45 and/or Melan-A with smooth muscle actin was seen in 83% of the cases.[2] It is worth noting that the coexpression of these 2 markers (smooth muscle and melanocytic markers) is useful for diagnosing these neoplasms; however, the absence of smooth muscle marker expression does not exclude a PEComa[3] diagnosis. S100 protein, mistakenly taken as positive, was consistently negative in all lesions, including the central nervous system lesions. Melanomas negative to this marker are rare. Identifying the metastatic lesions from a malignant metastatic PEComa played an important role in determining that the patient was not a candidate to receive radiotherapy but rather was a candidate for chemotherapy.

Cutaneous metastatic PEComa is exceptionally rare. Only one case has been reported in a series of 26 patients with PEComa of gynecologic and soft tissue origin. Pathology reports before reaching a diagnosis were reviewed finding one case similar to ours, a uterine leiomyosarcoma with a synchronous cutaneous melanoma, followed by a diagnosis of malignant PEComa after conducting lesion reassessment.[2]

Our case, similar to the case published by Navale et al,[1] demonstrates that a full diagnostic work-up is required to obtain an accurate diagnosis, for sometimes smooth muscle markers are not assessed initially in epithelioid neoplasms. Similarly, it is very important to count on detailed clinical information,

especially information about the clinical history of the patient, which in our case, was represented by an important history of hysterectomy for a uterine neoplasm.

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Unusual Presentation of Cutaneous Chromoblastomycosis

To the Editor:

Chromoblastomycosis (CBM) is a localized form of fungal infection. It is caused by 5 closely related species of pigmented fungi. Of those, *Fonsecaea pedrosoi* alone is responsible for 90%–96% lesions.[1] Direct traumatic inoculation into the skin from natural reservoirs like wood, soil, or rotting vegetables is the most common pathogenesis.[2] The cutaneous lesions generally present as slowly progressive scaly–warty plaque in the lower extremities. That is why CBM is often clinically confused with verrucous carcinoma, squamous cell carcinoma (SCC), and some other infectious processes. Such an enigma is settled on routine histopathological examination. Moreover, CBM carries a much more favorable prognosis than those of mimickers. Its treatment is based on surgery or other physical modalities like antifungal chemotherapy, etc.[3]

The authors declare no conflicts of interest.

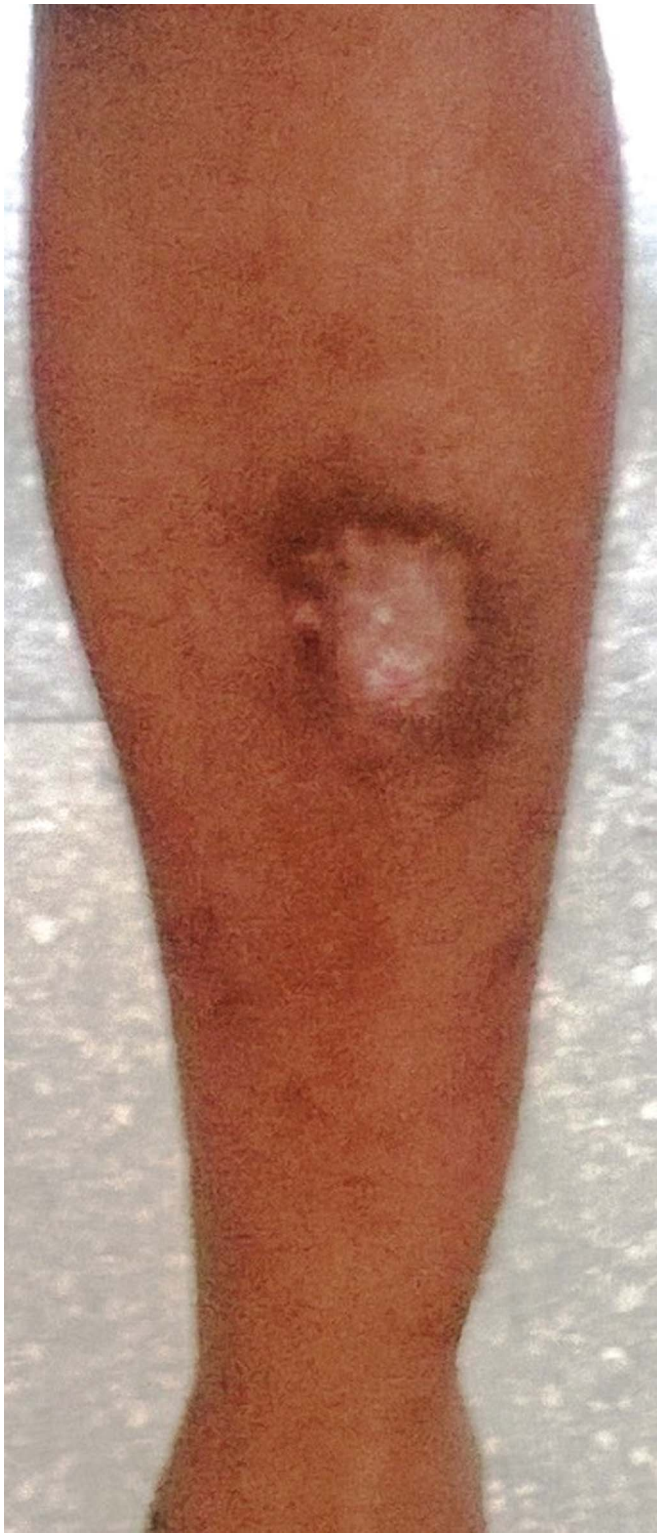

FIGURE 1. Cutaneous CBM: hypopigmented irregular ulcerated patch.

A 55-year-old tea-garden laborer attended the Dermatology outpatient clinic with an irregular hypopigmented, focally ulcerated cutaneous patch over his mid-shin part of left lower limb since 4 months (Fig. 1). The patient was neither