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Clinical, dermoscopic and histopathologic findings of retiform hemangioendothelioma

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ABSTRACT Retiform hemangioendothelioma (RH) is an uncommon vascular neoplasm of borderline malignancy that clinically develops as a solitary, gradually enlarging exophytic mass, nodule or plaque, most often on the lower limbs, upper limbs and trunk. Clinical recognition of RH is troublesome because of its non-specific appearance, with differential diagnosis comprising a variety of benign and malignant tumors clinically presenting as reddish nodules. In this article we describe the clinical, dermoscopic and histopathologic findings in a case of RH developing on the flank of a 26-year-old woman, and discuss the possible role of dermoscopy in facilitating the clinical recognition of this rare tumor.

Introduction

Hemangioendothelioma is a term encompassing neoplasms with an intermediate biological behavior between benign hemangiomas and angiosarcomas. It affects the skin and the soft tissues and includes retiform hemangioendothelioma (RH), papillary intralymphatic angioendothelioma (PILA, Dabska's tumor), epithelioid, kaposiform, pseudomyogenic, and composite hemangioendotheliomas [1].

RH is an infrequently encountered vascular neoplasm of borderline malignancy that was originally classified as a distinct type of low-grade cutaneous angiosarcoma (CA) in 1994 by Calonje et al [2]. Histopathologically, the vascular channels of RH resemble the rete testis (retiform), while the term "hemangioendothelioma" reflects its putative borderline malignancy, as opposed to the benign angioma and the malignant angiosarcoma.

Morphologically, RH typically develops as a solitary, gradually enlarging exophytic mass, nodule or plaque, most often on the lower limbs, upper limbs and trunk. The tumor shows a predilection for young to middle-aged adults (mean age 36 years) and females (2:1) [2]. Duration of the disease and tumor size at the time of diagnosis have been reported to range from 2 months to several years and from 1 to 30 cm, respectively [2]. A case of RH presenting with multiple lesions on the limbs and trunk has also been described [3].

Surgical excision is the treatment of choice for RH [1-4]. However, accurately defining the excision margins in a vascu-

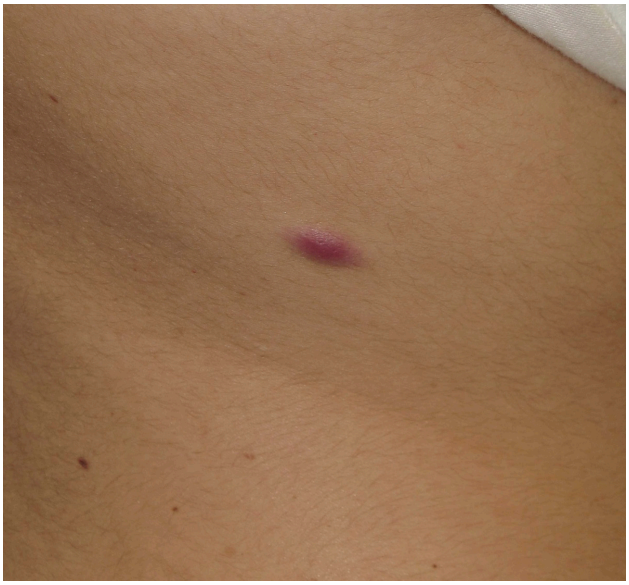

Figure 1. An asymptomatic, rapidly enlarging, infiltrated, red nodule. [Copyright: ©2013 Mota et al.]

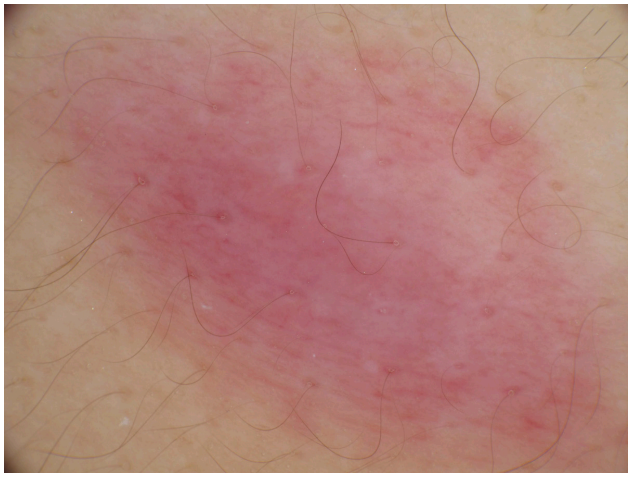

Figure 2. Dermoscopically, the tumor exhibited a pinkish background colour and few dotted and linear vessels. [Copyright: ©2013 Mota et al.]

lar neoplasm with a dissecting growth pattern is particularly troublesome. Indeed, the tumor is associated with a high rate of local recurrence (50%), which may occur from months to several years after surgery [2,3]. Regional lymph node metastasis was reported in a single patient, while no distant metastases have been reported to date [4].

Case report

A 26-year-old woman presented with a 2-month history of an asymptomatic, enlarging tumor of the right flank. The patient's previous medical history was unremarkable. Clinical examination revealed a well-defined, infiltrated red nodule, measuring a diameter of 3 cm (Figure 1). No regional lymphadenopathy was detected. Dermoscopic examination revealed a pinkish background color and few dotted and linear vessels (Figure 2).

Histopathologic examination (Figures 3 and 4) following punch biopsy revealed that the tumor was dermal based and ill defined. It was characterized by an infiltrative growth pattern, involving the entire dermis but sparing the subcutis, and consisted of long and thin arborizing vessels dissecting the dermal collagen. The vessels were lined by plump endothelial cells with frequent hobnail features and papillary projections. Rare solid endothelial areas were present in the superficial part of the lesion. No cytological atypia nor mitotic activity were noted. Extravasation of erythrocytes, hemosiderin deposition and inflammatory infiltrate were absent. On immunohistochemistry, the lesion reacted diffusely with CD31 and focally with D2-40. The monoclonal antibody against the latent nuclear antigen-1 of HHV8 was negative.

Based on the aforementioned histopathologic findings, the diagnosis of RH was established and the tumor was subsequently excised. On histopathology, some residual dissecting vessels were present besides the dermal scar.

Discussion

Clinical recognition of RH is troublesome because of its nonspecific appearance, with differential diagnosis comprising a variety of benign and malignant tumors clinically presenting as reddish nodules. RH has to be differentiated from other hemangioendotheliomas, CA, hemangioma, targetoid hemosiderotic hemangioma, blue-rubber bleb nevus syndrome, Kaposi's sarcoma (KS), lymphoma, dermatofibrosarcoma protuberans, amelanotic melanoma (AM) and cutaneous metastases [2,3].

Although the diagnosis of RH is based on histopathologic examination, discrimination from other vascular tumors might be challenging even histopathologically. The presence of infiltrative vascular spaces allows ruling out benign proliferations as hobnail hemangioma, which typically is more superficial and well defined. Differentiation from Kaposi's sarcoma (KS) is based mainly on the different clinical setting, the typical cellular spindling and the HHV8 immunoreactivity of the neoplastic cells that characterize KS. CA is characterized by cellular pleomorphism and prominent mitotic activity, features that allow discrimination from RH. Distinguishing between RH and PILA is highly challenging, since they both affect young patients, are characterized by a predilection for the limbs, and share similar histopathologic characteristics [5-7]. The architecture of the vessels, which are thin and arborizing in RH and often dilated in PILA, and the immunohistochemical reactivity of the latter to markers of lymphatic differentiation like D2-40 and VEGFR-3 represent clues for differentiating between the two entities [7].

In our case, D2-40 antibody reacted only in normal vascular endothelium, representing the internal control, and

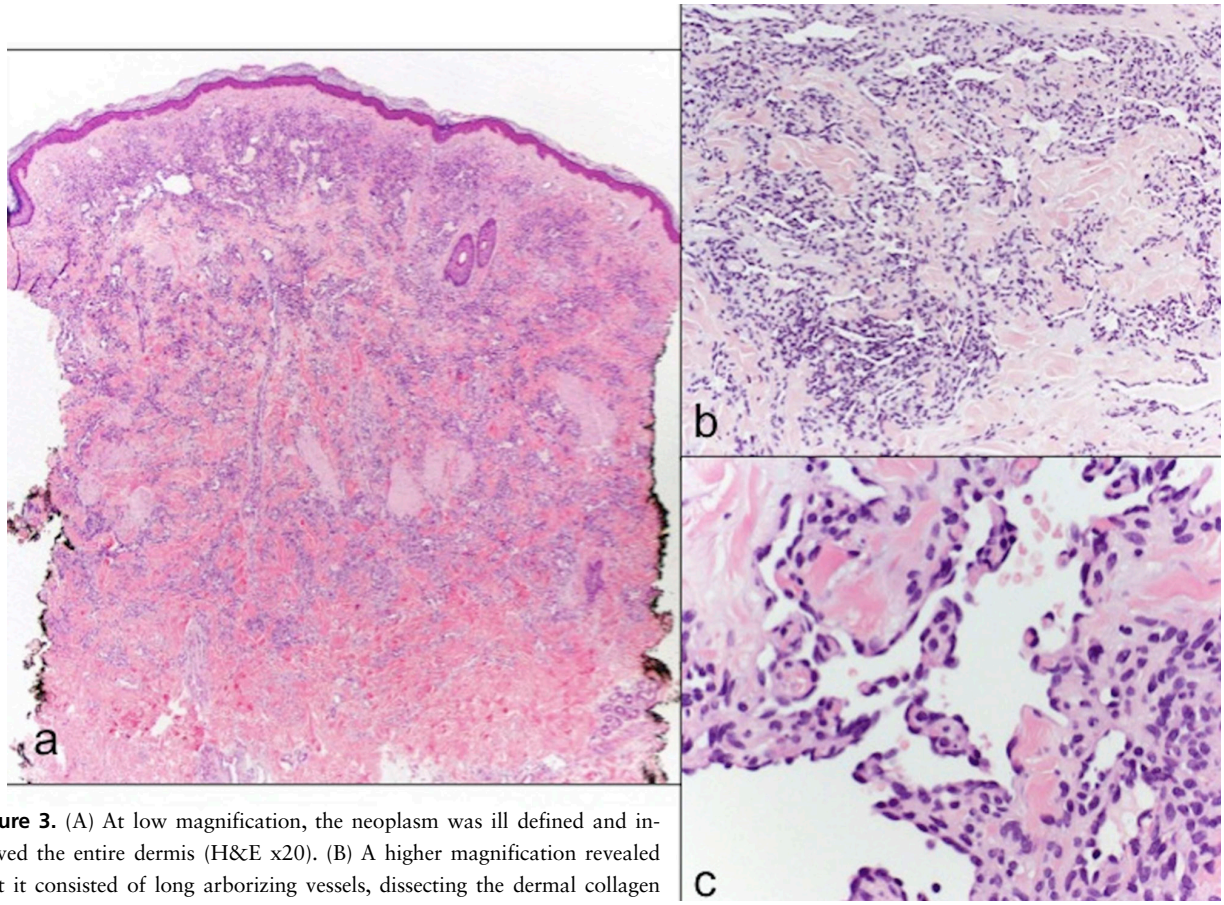

Figure 3. (A) At low magnification, the neoplasm was ill defined and involved the entire dermis (H&E x20). (B) A higher magnification revealed that it consisted of long arborizing vessels, dissecting the dermal collagen (H&E x100). (C) The vessels were lined by plump endothelial cells with frequent papillary projections (H&E x200). [Copyright: ©2013 Mota et al.]

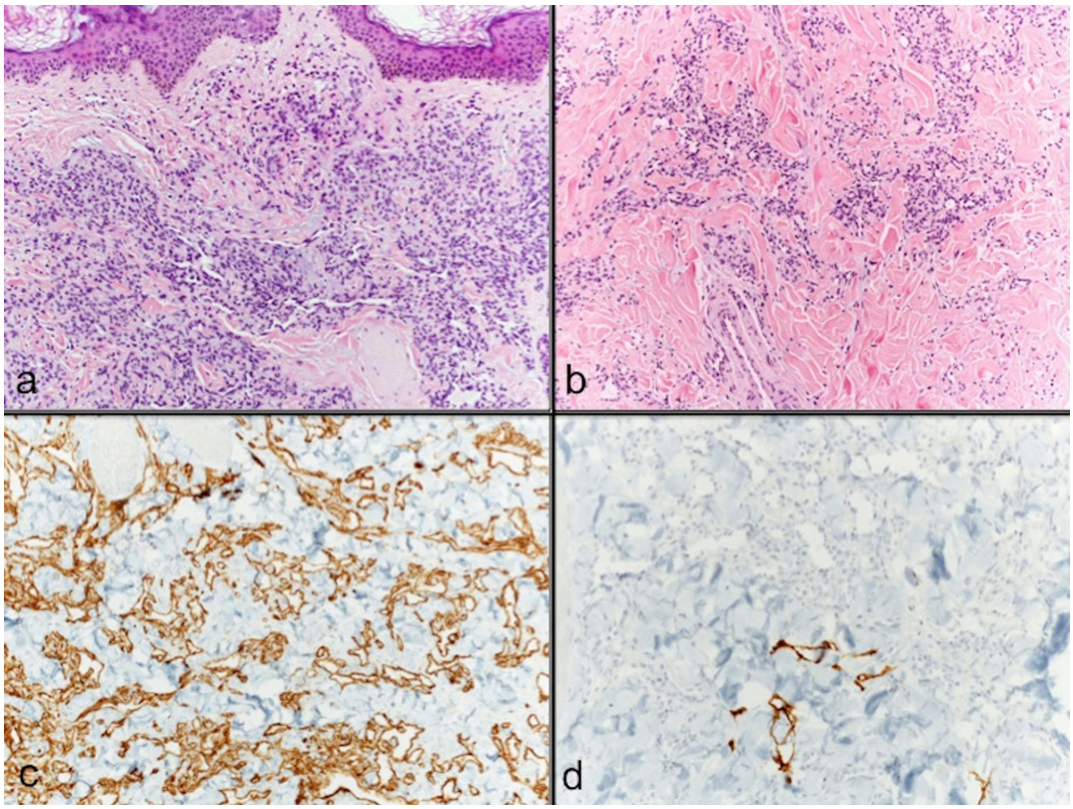

Figure 4. (A) Few solid areas were present in the upper dermis (H&E x100). (B) In the lower dermis, the neoplastic proliferation showed an infiltrative growth pattern among the collagen bundles (H&E x100). (C) The diffuse immunohistochemical positivity with CD31 confirmed the endothelial origin of the neoplastic proliferation, (D) while antibody D2-40 stained only rare lymphatic vessels. [Copyright: ©2013 Mota et al.]

failed to demonstrate a convincing lymphatic differentiation, findings suggestive of the diagnosis of RH [8,9].

Given that the choice treatment of RH is surgical excision to tumor-free margins, the most relevant differential diagnostic problem in clinical terms, is to discriminate RH from benign vascular tumors, whose management is essentially conservative.

Dermoscopy has been shown to improve the clinical evaluation of pigmented and non-pigmented skin tumors, enabling the visualization of morphologic structures that might be critical for the differential diagnosis [10].

In our case, dermoscopy revealed a pinkish color, which is also known to characterize AM, KS and CA and, effectively, cannot be considered as predictive of a specific diagnosis [10,11]. However, since it has been only described in the context of malignant tumors, the detection of pinkish (milky red) color enhanced us to avoid misinterpretation of the tumor as benign and prompted us to perform a biopsy.

In conclusion, although the dermoscopic criteria of RH and other endotheliomas require further investigation, our case highlights that dermoscopy should always be performed when clinically evaluating skin tumors, since the additional morphologic information provided might facilitate the appropriate clinical decision. Undoubtedly, dermoscopic findings should always be integrated with clinical information, such as patient's age and history. Furthermore, the current case further supports the previously reported observation that detection of pinkish color on dermoscopy of nodular lesions is suggestive of malignancy and should warrant excision. Finally, RH should be added in the differential diagnostic spectrum when evaluating a red nodule exhibiting a pinkish color under dermoscopy.

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