Actas Dermosifiliogr. 2009;100:137-41

CASE REPORTS

Proliferative Cutaneous Epithelioid Angiomatous Nodule

C. Requena,[a] M.J. Nicolau,[b] R. Haro,[c] A. Martorell,[a] O. Sanmartín,[a] B. Llombart,a R. Botella,[a] C. Guillén,[a] and L. Requena[c]

[a]Servicio de Dermatología, [b]Servicio de Anatomía Patológica, Instituto Valenciano de Oncología, Valencia, Spain cServicio de Dermatología, Fundación Jiménez Díaz, Madrid, Spain

Abstract. The cutaneous epithelioid angiomatous nodule is an uncommon benign vascular proliferation that has only recently been described. Clinically, it usually presents as a solitary, fast-growing, small reddish papulous or nodular lesion on the trunk or limbs of adults. Histopathologic study reveals a proliferation of epithelioid cells and predominantly solid, well delimited, unilobular growth in the superficial dermis. Well defined vessels are often found permeating the lesion, which also shows a certain degree of inflammatory infiltration. The cells contain abundant pink cytoplasm, often with vacuoles, and vesicular nuclei with prominent nucleoli. The morphology of these cells is relatively uniform, without atypia or pleomorphism, although mitoses are not uncommon.
We report 2 new cases of cutaneous epithelioid angiomatous nodules, the first in a 28-year-old pregnant woman and the second in a 27-year-old man. In both cases, the usual characteristics of this entity were present, but with the peculiarity of a high mitotic index. We discuss the differential diagnosis of cutaneous epithelioid angiomatous nodules with other vascular proliferations that exhibit epithelioid cytology.

Key words: epithelioid, vascular neoplasm, cutaneous.

NÓDULO ANGIOMATOSO EPITELIOIDE CUTÁNEO PROLIFERATIVO

Resumen. El nódulo angiomatoso epitelioide cutáneo es una proliferación vascular poco frecuente de naturaleza benigna y de reciente descripción. Clínicamente es una lesión rojiza, pequeña, papulosa o nodular, habitualmente única, de crecimiento rápido en el tronco o las extremidades de una persona adulta. Histopatológicamente se trata de una proliferación de células de hábito epitelioide y crecimiento predominantemente sólido, bien delimitada, unilobular, localizada en la dermis superficial. Es común encontrar vasos bien conformados salpicando la lesión, así como cierto infiltrado inflamatorio acompañante. Las células muestran amplios citoplasmasrosados, muchas veces con vacuolas, y núcleos vesiculosos con nucléolos prominentes. La morfología de las células es relativamente uniforme y no se encuentran atipias ni pleomorfismo, aunque no son raras las mitosis. Describimos dos nuevos casos de nódulo angiomatoso epitelioide cutáneo, el primero en una mujer embarazada de 28 años y el segundo en un varón de 27 años, ambos con todos los rasgos descritos como propios de esta entidad, pero con la peculiaridad de que presentaban un elevado índice mitósico. Discutimos el diagnóstico diferencial entre el nódulo angiomatoso epitelioide cutáneo y otras proliferaciones vasculares con citología epitelioide.

Key words: epitelioide, neoplasia vascular, cutáneo.

Introduction

The cutaneous epithelioid angiomatous nodule (CEAN) is a benign, probably reactive, vascular proliferation that manifests as a small, fast-growing nodular lesion located in the trunk or limbs of adult patients.[1] The histopathology of the disease is characterized by a solid, clearly circumscribed proliferation located in the superficial dermis and composed of epithelioid cells, occasionally with vacuoles in the cytoplasm, without atypia or pleomorphism but with some degree of mitosis.

It is a rare entity and, to date, only 28 cases have been reported.[1-5] It is important because it can sometimes be used in differential diagnosis with malignant epithelioid vascular proliferations. We report 2 cases of CEAN that are unusual due to the high mitotic index.

Correspondence:
Celia Requena Caballero
Servicio de Dermatología
Instituto Valenciano de Oncología,
C/ Beltrán Báguena 8 y 19
46009 Valencia, Spain
E-mail: celiareq@hotmail.com

Manuscript accepted for publication April 10, 2008.

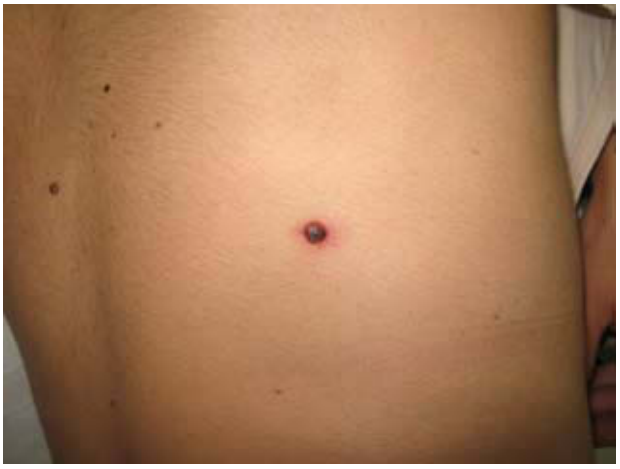

Figure 1. Reddish nodule with blackened areas and an erythematous halo, located on the back.

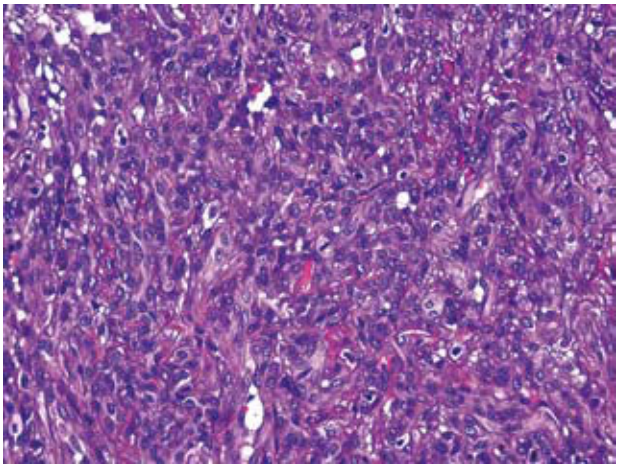

Figure 3. Detail of epithelioid cells, some with intracytoplasmic vacuoles and abundant mitoses (hematoxylin-eosin, ×200).

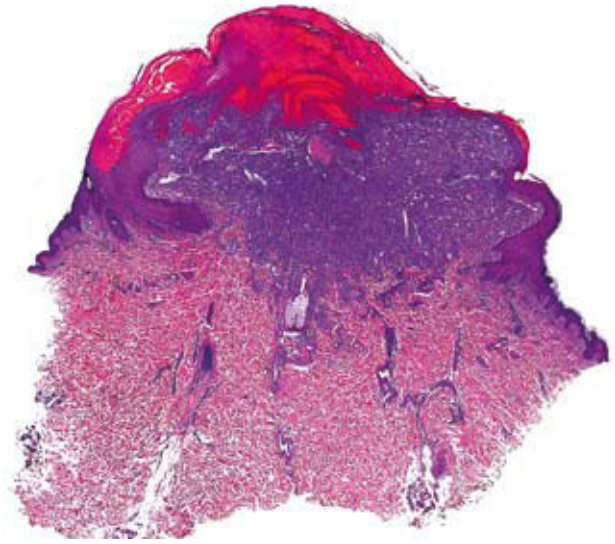

Figure 2. Figure 2. Solid proliferation in the superficial dermis circumscribed by an ulcerated surface adnexal collar of poorly demarcated depth (hematoxylin-eosin, ×10).

Case Descriptions

Case 1

A 28-year-old woman in the 7th month of pregnancy, with no relevant history of disease, visited our department with a nodular lesion measuring approximately 7 mm in diameter, in the right subscapular region. The lesion had grown suddenly in the previous month and physical examination revealed a small reddish nodule with blackened areas of necrotic appearance and surrounded by an erythematous halo (Figure 1). The lesion was resected with close margins and showed a solid proliferation in the superficial dermis, demarcated by an ulcerated surface epidermal collar, covered by a serous crust (Figure 2). The proliferation consisted of epithelioid cells with vesicular nuclei and prominent nucleoli; some of the cells had vacuoles in the cytoplasm. The proliferation contained scattered endothelium-lined lumens. The cells show no marked atypia but were notable due to abundant mitosis (Figure 3). Immunostaining was positive for Ki-67 in up to 40% of the cells and tests for CD31 and CD34 were also positive. However, the cells were not stained with caldesmon, cytokeratin, or epithelial membrane antigen.

Case 2

A 27-year-old man with no relevant history visited our department with a lesion that had recently appeared on the face. The physical examination revealed an angiomatous papule that was clinically diagnosed as pyogenic granuloma. The lesion was resected and histology revealed a lesion circumscribed to the superficial dermis, surrounded by an epidermal collar, and with ulcerated surface areas covered by a squamous crust (Figure 4). The lesion showed an infiltrate of epithelioid cells with vesicular nuclei and prominent nucleoli, with abundant intracytoplasmic vacuoles. Some vascular spaces were observed between these cells (Figure 5). Histology was positive for CD31 in the epithelioid cells. As in the previous case, abundant mitosis was notable.

Discussion

CEAN was described in 2004 by Brenn and Fletcher[1] in a study of 15 cases. Only 13 further cases have been

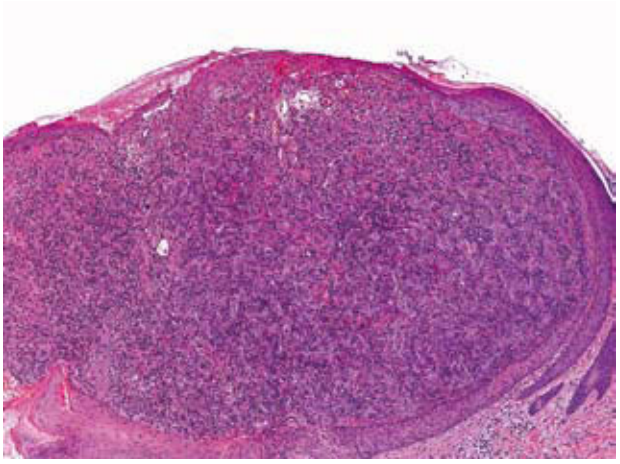

Figure 4. Clearly demarcated unilobular solid proliferation in the superficial dermis (hematoxylin-eosin, ×40).

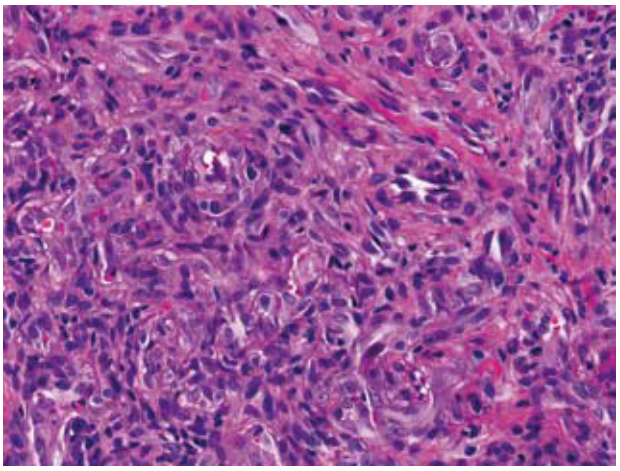

Figure 5. Detail of epithelioid cell proliferation (hematoxylin-eosin, ×200).

reported since the condition was first described.[2-5] CEAN is a benign, probably reactive, vascular proliferation that appears as single or, less frequently, multiple fast-growing (usually in months) papular or nodular lesions, usually located on the trunk of adults, though cases have been reported in patients aged between 14 and 79 years (Table). The histopathology study revealed a solid, clearly defined unilobular proliferation in the superficial dermis; the proliferation was composed of epithelioid cells. These are large cells with abundant pink cytoplasm, vesicular nuclei with prominent nucleoli, and frequently with intracytoplasmic vacuoles as a manifestation of primitive vascular differentiation. The cells show no atypia or pleomorphism, though mitosis is not uncommon. While this is a predominantly solid proliferation, it is usual to find vascular lumens scattered focally throughout the lesion. In many cases, an accompanying predominantly lymphocytic inflammatory infiltrate can be observed.

Misago et al[6] described a lesion that was histologically identical to CEAN but located in the subcutaneous tissue. This case also bore clinical similarities to other cases of CEAN—a fast-growing lesion located on the trunk of a young man.

The causes of CEAN are unknown but its rapid growth and benign course suggest that it is a reactive process, ie, it is hyperplastic rather than tumoral. It has been suggested that the entity is closely related to angiolymphoid hyperplasia with eosinophilia (ALHE), also known as epithelioid hemangioma.[1,2,5] In our opinion, however, there are sufficient clinical and, particularly, histopathologic criteria to justify the hypothesis that CEAN is a different entity than ALHE, as explained below. CEAN appears to us to be much closer to pyogenic granuloma but with a solid growth pattern and frequent mitosis.

Differential diagnosis of CEAN should be performed with other tumors and vascular proliferations composed of epithelioid cells. We can therefore use clinical and histopathologic criteria to differentiate it from ALHE. Clinically, ALHE typically appears on the head or neck and often presents in the form of a group of several lesions[7], whereas CEAN appears to predominate on the trunk and usually presents as a single lesion. Histopathology findings show that ALHE usually penetrates to the deep dermis and the hypodermis, whereas CEAN is confined to the superficial dermis. ALHE is typically multilobular, whereas CEAN is typically unilobular. Furthermore, ALHE is predominantly vasoformative, whereas CEAN is essentially a solid proliferation. Finally, in ALHE there is greater inflammation, a larger number of accompanying eosinophils, and the stroma are more abundant than in CEAN.

Bacillary angiomatosis affects predominantly, though not exclusively, immunocompromised patients, particularly patients who are seropositive for the human immunodeficiency virus. Until now, CEAN had not been linked to immunosuppression or other underlying diseases. Bacillary angiomatosis commonly occurs as multiple and even disseminated lesions, whereas most cases of CEAN present as single lesions, as has already been mentioned. Furthermore, in terms of histopathology, bacillary angiomatosis is multilobular and typically has a neutrophilic infiltrate and clumps of a purplish material (concentrations of *Bartonella* bacilli).[8] None of these 3 histologic features is typical of CEAN.

Differential diagnosis with epithelioid hemangioendothelioma and with epithelioid angiosarcoma was of particular importance in our cases as these 2 diseases have a clinical course that is much worse than that of CEAN. Epithelioid angiosarcoma shows clinical

Table. Summary of the Main Clinical Characteristics of Cutaneous Epithelioid Angiomatous Nodules

	Sex	*Age, y*	*Location*	*Clinical Manifestation*
Sagüenza et al[5] (2008)	M	57	Thorax	Multiple lesions
	F	14	Back	Nevus
	M	45	Behind right ear	Hemangioma
	M	35	Left eyebrow	Cyst
	M	42	Left shoulder	Angioleiomyoma
	M	55	Left hand	Reaction to foreign body
	M	72	Neck	Cancer
	F	20	Right breast	Single lesion
	F	74	Right side of forehead	Epidermal cyst
	M	39	Right upper eyelid	Inflamed vascular lesion
Brenn and Fletcher[1] (2004)	M	55	Thorax	Small nodule
	F	27	Back	Exophytic nodule
	F	28	Right buttock	Erythematous nodule
	M	48	Back	Unknown
	F	48	Finger	Nodule
	M	15	Sole of foot	Bluish lesion
	F	55	Right side of trunk	Pruriginous papule
	F	79	Right shoulder	Nodule
	M	17	Nasal cavity	Reddish polyp
	F	41	Lumbar region	Friable reddish polyp
	M	29	Right forearm	Nodule
	F	37	Nose	Reddish papule
	M	26	Thorax	Bluish nodule
	M	44	Left arm	Erythematous-violet papules
	F	20	Right leg	Painful nodule
Fernández-Flores et al[3] (2001)	F	30	Fold behind right ear	Bluish nodule
Zamecnik[2] (2004)	F	54	Unknown	Nodule
Kantrow et al[4] (2007)	F	43	Back	Pruriginous papule
Our cases	F	28	Scapular region	Reddish nodule
	M	27	Face	Angiomatous papule
Total	15 M 15 F	14-79	13 trunk 7 limbs 9 head and neck 1 unknown	

Abbreviations: F, female; M, male.

characteristics typical of a malignant tumor (larger and less clearly defined than CEAN). Histologically, epithelioid angiosarcoma is similar to a carcinoma as it infiltrates the dermis to considerable depth and often presents scattered or massive areas of necrosis. The epithelioid cells of which it is composed show high levels of atypia and pleomorphism not seen in CEAN.[9] Immunostaining can be of help in some cases as cytokeratin is positive in up to 50% of epithelioid angiosarcomas, whereas they are negative in the angiomatous nodule.

As with epithelioid angiosarcoma, epithelioid hemangioendothelioma[10] presents clinical signs of malignancy, ie, it is larger and less clearly demarcated than CEAN. The pathology of epithelioid hemangioendothelioma shows an entity that reaches a greater depth than CEAN, shows considerably more stroma (usually hyaline), and does not usually contain structured vessels, which are not uncommon as a focal feature in CEAN. Cytokeratin is positive in up to 25% of cases of epithelioid hemangioendothelioma.

In conclusion, we report these cases of CEAN not only because it is a rare process, with only 28 previously reported cases, but also because they represent an unusual variety of CEAN, which we have called proliferative due to its high mitotic index. We suggest that the fact that the patient was pregnant may have favored the proliferative and, to an extent, infiltrative nature of the first case. We also believe that it is important to be aware of this variety of CEAN because it is histologically very similar to angiosarcoma.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Brenn T, Fletcher CD. Cutaneous epithelioid angiomatous nodule: a distinct lesion in the morphologic spectrum of epithelioid vascular tumors. Am J Dermatopathol. 2004;26:14-21.
2. Zamecnik M. Relationship between cutaneous epithelioid angiomatous nodule and epithelioid hemangioma. Am J Dermatopathol. 2004;26:351-2.
3. Fernández-Flores A, Montero MG, Renedo G. Cutaneous epithelioid angiomatous nodule of the external ear. Am J Dermatopathol. 2005; 27:175-6.
4. Kantrow S, Martin JD, Vnencak-Jones CL, Boyd AS. Cutaneous epithelioid angiomatous nodule: report of a case and absence of microsatellite instability. J Cutan Pathol. 2007;34:515-6.
5. Sangüeza OP, Walsh SN, Sheehan DJ, Fernández Orland A, Llombart B, Requena L. Cutaneous epithelioid angiomatous nodule: A case series and proposed classification. Am J Dermatopathol. 2008;30:16-20.
6. Misago N, Inoue T, Narisawa Y. Subcutaneous epithelioid angiomatous nodule: a variant of epithelioid hemangioma. J Dermatol. 2006;33:73-4.
7. Olsen TG, Helwig EB. Angiolymphoid hyperplasia with eosinophilia: A clinicopathologic study of 116 patients. J Am Acad Dermatol. 1985;12:781-96.
8. Requena L, Sangüeza OP. Cutaneous vascular proliferation. Part II. Hyperplasias and benign neoplasms. J Am Acad Dermatol. 1997;37:887-919.
9. Requena L, Sangüeza OP. Cutaneous vascular proliferations. Part III. Malignant neoplasms, other cutaneous neoplasms with vascular component, and disorders erroneously considered as vascular neoplasms. J Am Acad Dermatol. 1998;38:143-75.
10. Quante M, Patel NK, Hill S, Merchant W, Courtauld E, Newman P, et al. Epithelioid hemangioendothelioma presenting in the skin: A clinicopathologic study of eight cases. Am J Dermatopathol. 1998;20:541-6.