Table 1 Immunohistochemical phenotypic profile of the patients.

Positive markers	Negative markers
CD4	CD3
CD56	CD5
CD123	CD7
CD43	CD15
TdT	CD20
TCL-1 (Case 3)	Lysozyme
CD43	Myeloperoxidase
CD45RA	

Abbreviations: TdT, terminal deoxynucleotidyl transferase semicolon TCL-1, type 1 T-cell lymphoma.

With regard to treatment, different chemotherapy options—from CHOP to leukemia regimens—have been tested, but bone marrow transplantation is considered to be the best treatment. In a study of 57 patients, Dale et al[8] observed better survival in patients who had received transplants compared to other therapies (31.3 months vs 12.8 months). Preventive intrathecal chemotherapy has also been recommended.[9] Advanced age and the combination of negative TdT and positive BDCA-2 are negative prognostic factors.[10]

Of our 3 cases, only the patient who received a bone marrow transplant achieved remission lasting longer than 6 months. Thus, even though ours is a very small series, it supports the evidence for bone marrow transplantation as the best therapeutic option. Although TdT was positive in all our patients, this marker had no apparent bearing on survival. As has been reported in the literature, bone marrow involvement at the time of diagnosing the patients did not influence prognosis.[2]

Our 3 cases reflect the typical presentation of plasmacytoid dendritic cell tumor, and suggest the importance of early treatment in order to improve what is normally a poor prognosis.

References

1. Lim MS, Leval L, Quintanilla-Martínez L. Commentary on the 2008 WHO classification of mature T- and NK-cell neoplasms. J Hematopathol. 2009;2:65-73.
2. Jegalian AG, Facchetti F, Jaffe ES. Plasmacytoid dendritic cells: physiologic roles and pathologic states. Adv Anat Pathol. 2009;16:392-404.
3. Cerroni L,Wiesner T. Cutaneous lymphomas: from morphology to chip technology. Actas Dermosifiliogr. 2009;100:3-17.
4. López V, Martí N, Ferrández A, Martin JM, Jordá E. An atypical presentation of a blastic plasmacytoid dendritic cell tumors. J Cutan Pathol. 2010;37:e50-2.
5. Cota C, Vale E, Viana I, Requena L, Ferrara G, Anemona L, et al. Cutaneous manifestations of blastic plasmacytoid dendritic cell neoplasm-morphologic and phenotypic variability in a series of 33 patients. Am J Surg Pathol. 2010;34:75-87.
6. Marafioti T, Paterson JC, Ballabio E, Reichard KK, Tedoldi S, Hollowood K, et al. Novel markers of normal and neoplastic human plasmacytoid dendritic cell. Blood. 2008;111: 3778-92.
7. Kaune KM, Baumgart M, Bertsch HP, Mitteldorf C, Müller-Hermelink HK, Haase D, et al. Solitary cutaneous nodule of blastic plasmacytoid dendritic cell neoplasm progressing to overt leukemia cutis after chemotherapy: immunohistology and FISH analysis confirmed the diagnosis. Am J Dermatopathol. 2009;31:695-701.
8. Dalle S, Beylot-Barry M, Bagot M, Lipsker D, Machet L, Joly P. Blastic plasmacytoid dendritic cell neoplasm: is transplantation the treatment of choice? Br J Dermatol. 2010;162:74-99.
9. Kedward AL, McGalie C, Venkatraman L, Hamilton J, El-Agnaf M, McKenna K. Plasmacytoid dendritic cell neoplasm treated successfully with rituximab. J Eur Acad Dermatol Venereol. 2010;24:742-3.
10. Jaye DL, Geigerman CM, Herling M, Eastburn K, Waller EK, Jones D. Expression of the plasmacytoid dendritic cell marker BDCA-2 supports a spectrum of maturation among CD4+ CD56+ hematodermic neoplasms. Mod Pathol. 2006;19: 1555-62.

M. Pérez-Crespo,[a,*] M. Moragón,[a] J. Onrubia,[b] A. Sevila,[a] R. Alfonso,[a] J. Miralles,[a] L. Requena[c]

[a]*Servicio Dermatología, Hospital Universitario de San Juan, Alicante, Spain*
[b]*Servicio de Anatomía Patológica, Hospital Universitario de San Juan, Alicante, Spain*
[c]*Servicio de Dermatología, Fundación Jiménez Díaz, Madrid, Spain*

*Corresponding author.
E-mail address: mariaperezcrespo@hotmail.com (M. Pérez-Crespo).

Generalized Multinucleated Cell Angiohistiocytoma

Angiohistiocitoma de células multinucleadas generalizado

To the Editor:

Multinucleate cell angiohistiocytoma (MCA) is a benign fibrohistiocytic and vascular proliferation. This rare disorder was first described by Smith and Wilson Jones[1] in 1985, and since then about 80 cases have been reported in the literature. The disorder occurs most frequently in women. Lesions are in the form of clusters of erythematous, violaceous, or brownish-colored papules located in a single anatomical area, usually the lower extremities,[2] or the dorsal aspect of the hands, wrists, or fingers; however, it has also been described on the trunk, forehead, cheeks, oral mucosa, lips, and orbit. Generalized cases are exceptional.[3-5] Although lesions are usually asymptomatic, some are pruritic.

A 56-year-old man, with no past history of relevance, presented with a slightly pruritic rash that had slowly developed over the previous 6 years. Examination revealed numerous sharply circumscribed erythematous, violaceous papules, some slightly brown in color, firm in consistency, and measuring 4 mm to 10 mm. The lesions were distributed on the trunk and the extremities, but particularly affected the flanks and lower part of the back (Figure 1). The patient reported no previous injuries, bites, or stings. Skin biopsy demonstrated the presence of a proliferation of capillaries in the dermis, with increased numbers of fibrohistiocytic cells and bizarre multinucleated cells with angulated cytoplasm (Figure 2). Immunohistochemistry was negative for CD34, S-100, CD68, cytokeratin, and epithelial membrane antigen, but showed increased numbers of capillaries positive for CD31.

The clinical manifestations and biopsy findings indicated a diagnosis of generalized MCA. The benign nature of the condition was explained to the patient who decided against treatment.

MCA is a dermal dendrocytic proliferation, similar to dermatofibroma, and, as with that condition, it is still not known if it is a genuine neoplasm or a reactive condition.[6] Its benign course, its tendency to present as multiple lesions in the form of a rash in areas exposed to trauma and arthropod bites or stings, the absence of clonality, and cases of spontaneous regression would all support a reactive process.

From a histopathological point of view, MCA is characterized by a proliferation of capillaries and venules in the dermis, accompanied by an infiltrate of lymphohistiocytic cells and multinucleated cells with angulated or scalloped cytoplasm. The presence of mast cells in the dermal infiltrate has been described,[7] but they were absent in the biopsy from our patient. Immunohistochemistry shows endothelial cells positive for the CD31 and CD34 antigens, and mononuclear interstitial cells expressing vimentin and factor XIIIa, but not S-100 or CD1a. The characteristic multinucleated cells express vimentin, but positivity for CD68 is variable, and, in our case, was negative.

The pathogenesis of MCA is unknown. As for the histogenetic origin of the characteristic giant multinucleated cells, Wilson Jones et al[8] suggested that they are derived from fibroblasts or macrophages, which, in conditions of prolonged chronic stimulation, lose their ability to divide after mitosis and so become inactive. Puig et al[7] considered that the dermal angiogenesis and multinucleated cell formation processes were secondary to the release of cytokines by mononucleated fibrohistiocytic cells or mast cells present in the lesions.

The differential diagnosis of MCA (Table) primarily includes dermatofibroma. Requena et al[9,10] consider MCA to be a variant of dermatofibroma with a prominent vascular component and bizarre multinucleated cells. The differential diagnosis should also include Kaposi sarcoma, which is distinguished from MCA both by microscopy findings and by negative immunohistochemistry findings for human herpesvirus type 8.

MCA presenting with a generalized distribution of lesions is rare, with only 3 cases reported in the literature. In 1996, Chang et al[3] reported the case of a 24-year-old man with brownish-red papules affecting the trunk and extremities. In 1994, Del Rio et al[4] reported the case of a 42-year-old man with skin lesions clinically and histologically compatible with generalized MCA, which developed in the context of POEMS syndrome. More recently, a case has been reported of a 40-year-old woman with lesions affecting the upper chest area, abdomen, back, and limbs. [5] Lesion morphology and distribution in all the reported cases were consistent with those in our patient. Of the 4 patients (including our patient) diagnosed with generalized MCA, 3 were male; this contrasts with localized MCA, which predominates in women. Furthermore, although 1 patient developed generalized MCA in the context of POEMS syndrome, the other 3 cases of generalized MCA were not asociated with other conditions; the finding was thus coincidental, although, admittedly, a larger series would be necessary to confirm this tentative conclusion.

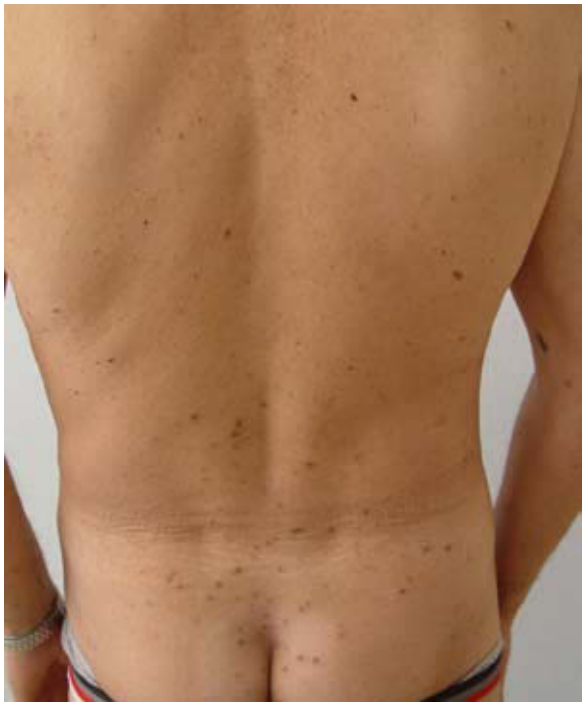

Figure 1 Papular rash affecting the trunk, back, and buttocks.

Table 1 Differential Diagnosis of Generalized Multinucleate Cell Angiohistiocytoma.

Clinical	Histological
Dermatofibroma	Atrophic dermatofibroma
Angiofibroma	Angiofibroma
Kaposi sarcoma	Microvenular hemangioma
Pseudo-Kaposi sarcoma	Kaposi sarcoma
Granuloma annulare	
Lichen planus	
Pyogenic granuloma	
Giant-cell fibroblastoma	

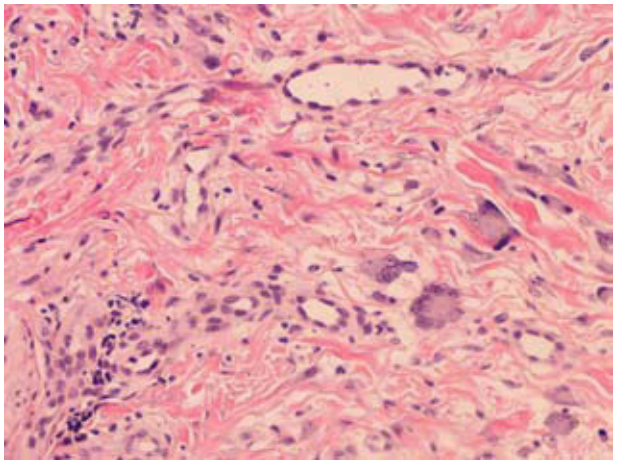

Figure 2 Image of the dermis showing vascular proliferation and an infiltrate formed of mixed cells and multinucleated giant cells with angulated cytoplasm (hematoxylin-eosin, original magnification ×100).

The generalized variant of MCA is extremely rare, with only 3 cases recorded in the literature, to which we add a new case that is not associated with any other disease.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgments

The authors thank Dr. Luis Requena for his assistance in confirming the diagnosis.

References

1. Smith NP, Wilson Jones E. Multinucleate cell angiohistiocytoma: a new entity. Br J Dermatol. 1985;113:15.
2. Monteagudo B, Labandeira J, Ginarte M, Álvarez JC, De las Heras C, Cacharrón JM, et al. Multinucleate cell angiohistiocytoma. Actas Dermosifiliogr. 2005;96:272-3.
3. Chang SN, Kim HS, Kim SC, Yang WI. Generalized multinucleate cell angiohistiocytoma. J Am Acad Dermatol. 1996;35:320-2.
4. Del Río R, Alsina M, Monteagudo J, Torremorell D, González U, Luelmo J, et al. POEMS sydrome and multiple angioproliferative lesions mimicking generalized histiocytomas. Acta Derm Venereol. 1994;74:388-90.
5. Leclerc S, Clerici T, Rybojad M, Girszyn N, Morel P, Janin A, et al. Angiohistiocytome à cellules multinucléées. Ann Dermatol Venereol. 2005;132:546-9.
6. Cabanillas M, Peteiro C, Toribio J. Angiohistiocitoma de células multinucleadas. Piel. 2006;21:453-6.
7. Puig L, Fernández-Figueras MT, Bielsa I, Lloveras B, Alomar A. Multinucleate cell angiohistiocytoma: a fibrohistiocytic proliferation with increased mast cell numbers and vascular hyperplasia. J Cutan Pathol. 2002;29:232-7.
8. Jones WE, Cerio R, Smith NP. Multinucleate cell angiohistiocytoma: an acquired vascular anomaly to be distinguished from Kaposi's sarcoma. Dr J Dermatol. 1990;122:651-63.
9. Requena L, Sangueza OP. Cutaneous vascular proliferations. Part III. Malignant neoplasm, other cutaneous neoplasms with significant vascular component, and disorders erroneously considered as vascular neoplasm. J Am Acad Dermatol. 1998; 38:143-75.
10. Requena L, Requena C, Pichardo RO, Sanguenza OP. Angiohistiocitoma de células multinucleadas. Monogr Dermatol. 2004;17:82-5.

C. López-Obregón,[a,*] M.A. Arregui-Murua,[a] P. Eguino,[b] C. Lobo[c]

[a]*Servicio de Dermatología, Hospital Donostia, San Sebastián, Spain*
[b]*Servicio de Dermatología, Hospital Bidasoa, San Sebastián, Spain*
[c]*Servicio de Anatomía Patológica, Hospital Donostia, San Sebastián, Spain*

*Corresponding author.
E-mail address: cris_lopez_obregon@hotmail.com (C. López-Obregón).

Simultaneous Presentation of Localized Basaloid Follicular Hamartoma and Epithelioid Blue Nevus in a 44-Year-Old Patient

Hamartoma folicular basalioide localizado y nevus azul epitelioide de presentación simultánea en una paciente de 44 años

To the Editor:

Basaloid follicular hamartoma is an uncommon benign neoplasm whose histological appearance is very similar to that of infundibulocystic basal cell carcinoma and trichoepithelioma. It may be familial or sporadic, generalized or localized, and is occasionally associated with autoimmune disease and cystic fibrosis. Some patients have a mutation in the *PTCH* gene that is similar to that observed in Gorlin syndrome and in up to 50% of isolated basal cell carcinomas.

Epithelioid blue nevus is a benign neoplasm whose histological diagnosis is complex due to its similarity with melanocytoma. It is closely associated with Carney complex.

We present the case of a 44-year-old woman with no relevant past history who consulted for a lesion on her back. The woman was unable to say how long she