

Case Report

Multinucleate cell angiohistiocytoma: a case report and review of the literature.

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Abstract

Multinucleate cell angiohistiocytoma (MCAH) is a rare, benign vascular proliferation. Fewer than 80 cases have been reported to date, which may relate to under-recognition of this entity. Lesions are commonly asymptomatic and appear as erythematous to violaceous papules on the lower extremities and dorsal hands of middle-aged to elderly women. The characteristic histopathologic and immunohistochemical features of MCAH are essential for definitive diagnosis of MCAH. Multinucleate cell angiohistiocytoma follows a slowly progressive course, although spontaneous regression has been reported in rare cases. We present a case of MCAH to increase awareness and elucidate the characteristic clinical and histopathologic features of this disorder.

Introduction

Multinucleate cell angiohistiocytoma (MCAH) is a rare, benign, distinct, soft tissue tumor first described in 1985 by Smith and Wilson Jones [1]. Clinically, MCAH is characterized by erythematous to violaceous papules and plaques most commonly on the lower extremities and dorsal hands of middle-aged to elderly women [2,3,4]. Histologically, there is a vascular and fibrohistiocytic proliferation within the dermis [2,5]. Although spontaneous resolution has been described in a few cases, lesions tend to progress slowly without remission [3,5,6].

Case synopsis

A 70-year-old woman presented with a 5-year history of multiple erythematous to violaceous, smooth papules on bilateral medial thighs and calves. The lesions were asymptomatic but cosmetically displeasing to the patient and persisted with only mild improvement despite treatment with pulsed-dye laser and both topical and intralesional corticosteroids.

At initial presentation 5 years earlier, she had multiple soft, red, compressible papules of varying size. The clinical differential diagnosis included Kaposi sarcoma (KS), acroangiokeratosis, and angioma. Histologic examination revealed epidermal hyperplasia, mild dermal fibrosis and vascular proliferation, and a slightly increased number of stromal cells surrounding collagen fibers in the deep reticular dermis. The initial pathology diagnosis was early dermatofibroma, which was changed to acroangiokeratosis after clinical correlation. Repeat biopsy 1 month later revealed minimally increased vessels in the dermis and the presence of a small amount of hemosiderin. Histologically, the lesions were compatible with early acroangiokeratosis.

When the patient returned to clinic 1.5 years ago, the lesions clinically resembled papular granuloma annulare. Histopathologic examination revealed slight vascular proliferation and dermal fibrosis with occasional interstitial histiocytes and mucin, compatible with interstitial granuloma annulare.

At the most recent visit, 2 new papules, one on each medial shin, were biopsied. Histologic examination of each at low power demonstrated an increased dermal vasculature, sparse perivascular lymphocytes, and thickened collagen. High power magnification revealed a proliferation of bizarre multinucleated giant cells and surrounding fibrohistiocytic proliferation. A diagnosis of multinucleate cell angiohistiocytoma was made.



Figure 1. Multiple soft, red, compressible papules of varying size on the right thigh

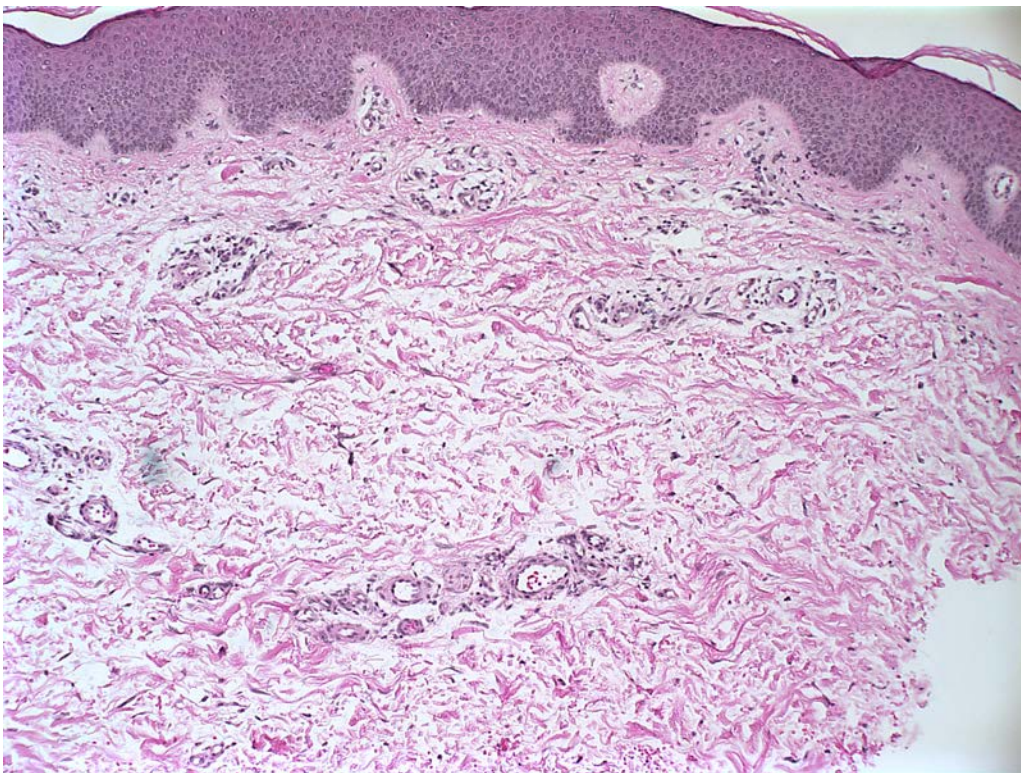


Figure 2. (H&E 10x) Increased dermal vasculature with surrounding sparse perivascular lymphocytic infiltrate and thickened collagen

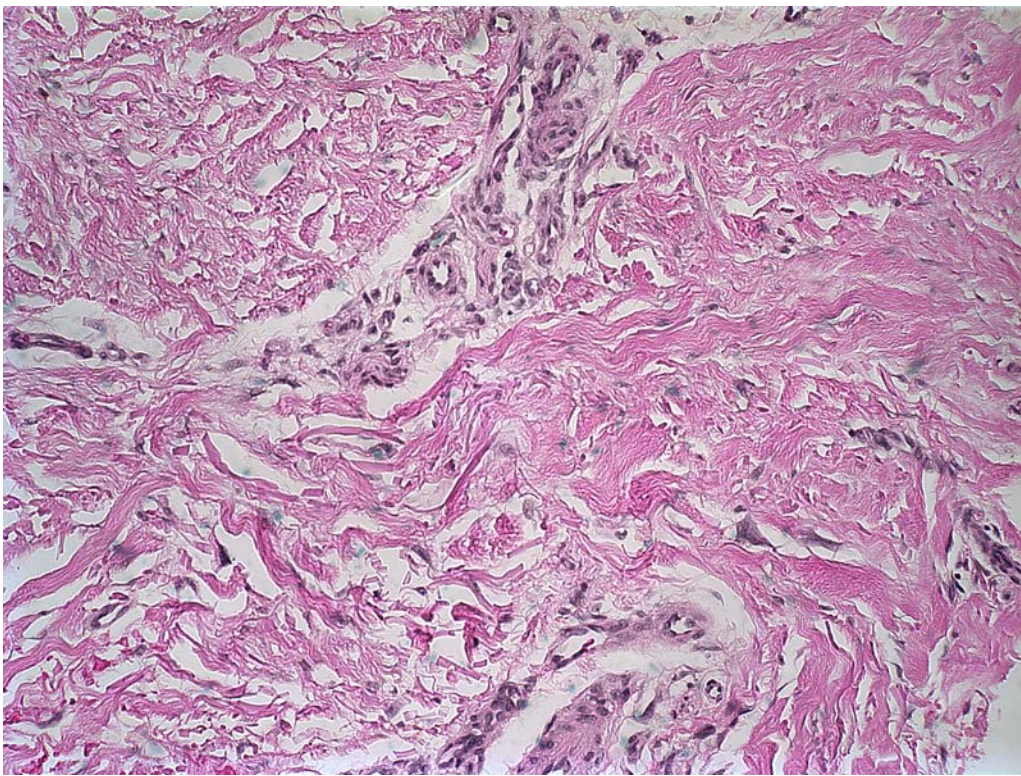


Figure 3. (H&E 20x) Bizarre multinucleated cells and a fibrohistiocytic proliferation surround the increased dermal vasculature

Discussion

Multinucleate cell angiohistiocytoma (MCAH) is a rare disorder. Fewer than 80 cases [8] have been described since Smith and Wilson Jones described it in 1985 [1]. Although it is an infrequent clinicopathologic diagnosis, MCAH is probably underreported owing to lack of clinician and pathologist knowledge of this entity [2,3,7]. Multinucleate cell angiohistiocytoma shows a predilection for middle-aged to elderly women (female to male ratio 3:1) [7], with the majority of cases diagnosed in the 5th to 8th decade [2,4,8]. Clinically, MCAH manifests as single or multiple, firm, reddish-brown to violaceous dome-shaped papules with a smooth surface [2,7,9]. Lesions are usually sharply demarcated and distributed in a random, linear, or annular pattern [2,3,7]. They appear most often over the extremities, including the distal thighs, calves, and dorsal aspect of the hands [4,7,9]. Although rare, there have been 4 reported cases of generalized MCAH [5,8]. In most cases, the lesions are asymptomatic, but pruritus may be present [6,9]. Spontaneous regression has been observed in a few cases, but lesions tend to persist with slow progression [2,6,7]. Clinical differential diagnosis includes Kaposi's sarcoma, acroangiokeratosis (pseudo-Kaposi sarcoma), granuloma annulare, lichen planus, and sarcoidosis [3,7,9]. Biopsy and histopathologic examination are essential to diagnosing MCAH.

Characteristic histopathologic features of MCAH include proliferation of poorly grouped capillaries and small venules in the upper to mid dermis with unique multinucleate giant cells against a collagenous stroma [2,4]. The endothelial cells are plump and oftentimes protrude into the lumen of the vessel, which may cause dilation or narrowing of the lumen [2,3,7]. The characteristic multinucleate cells exhibit scalloped or angulated cytoplasm with 3 to 10 hyperchromatic nuclei arranged around the periphery of the cells [2,3,8]. The surrounding dermis consists of haphazardly arranged collagen bundles and mononuclear cells with a fibrohistiocytic appearance [3,7]. A sparse perivascular and perifollicular infiltrate of lymphocytes, histiocytes, and occasional neutrophils and plasma cells may also be seen [7,8,9]. Few extravasated red blood cells may be present, but hemosiderin deposition is rarely observed [3,8]. The overlying epidermis may be normal or hyperplastic [2,3,7,8].

Electron microscopy demonstrates multinucleate cells with abundant rough endoplasmic reticulum, nuclear membrane reinforcement ('zonula nucleus limitans'), and numerous endocytotic/pinocytic vesicles and lysosomes. These findings, along with the lack of monocyte/macrophage markers on immunohistochemistry, reinforce the belief that the multinucleate cells are of fibrohistiocytic origin [2,4,7].

Immunohistochemistry reveals vascular endothelial cells positive for antibodies to Factor VIII, vimentin, CD31, and CD34, [2,4,7,8] and negative for Bcl-2 and HHV-8 antigen [4,8]. Mononuclear cells express vimentin, Factor XIIIa, CD68, alpha-1-antitrypsin, and lysozyme [2,4,7,8], but not S100 or CD1a [7]. The expression of MAC387 is variable [4,7]. Multinucleate cells are strongly positive for vimentin, but negative for other markers of the monocyte/macrophage lineage [2,4,5,7]. Expression of CD68 is variably positive [2,7] or negative [4,7]. Estrogen receptor α is strongly expressed in interstitial and perivascular spindle cells and occasionally in multinucleate cells [10].

Histopathologic differential diagnosis includes angiofibroma/fibrous papule, dermatofibroma, microvenular hemangioma, Kaposi's sarcoma, and acroangiokeratosis [6,7,8]. Like MCAH, angiofibroma and fibrous papule contain dilated capillaries in the dermis. However, collagen bundles are vertically oriented or perifollicular and there are only occasional multinucleate cells [3,7,8]. Compared to MCAH, dermatofibroma has a denser proliferation of cells and a coarser deposition of collagen, most prominent along the periphery of the lesion [3]. The vascular atrophic variant of dermatofibroma, like MCAH, has occasional multinucleate cells and prominent vessels [7,8]. Microvenular hemangiomas, which are also commonly located on the legs, consist of branching venules lined by prominent endothelial cells, but lack the characteristic giant cells [3,7]. Kaposi sarcoma lacks the multinucleate cells and is positive for human herpesvirus 8 [3,7,8]. Acroangiokeratosis has tortuous, thick-walled capillaries with abundant hemosiderin deposition, in contrast to MCAH [7,8].

Although the pathogenesis of multinucleate cell angiohistiocytoma remains unclear, stromal mast cells present in areas of neovascularization and edema have been implicated in the upregulation of Factor XIIIa-positive fibrohistiocytic cells [4,8]. Additionally, IL-4 from mast cell degranulation has been postulated to play a role in the morphogenesis of the multinucleate cells [2,4,8]. The female predominance along with the presence of estrogen receptor expression indicates a possible hormonal influence in the pathogenesis of MCAH [9,10] and the predilection for the dorsal hands and lower extremities suggests a traumatic etiology [3,8].

Multinucleate cell angiohistiocytoma is a benign entity that follows an indolent, yet progressive course [6,7]. Spontaneous resolution has rarely been reported, which suggests an inflammatory rather than a neoplastic process [2,3,7]. Given the benign course, treatment is not necessary, but may be recommended for pruritic or cosmetically displeasing lesions [2,6,7]. Treatment options that have been reported in the literature include surgical excision, cryosurgery, carbon dioxide and argon lasers, and intense pulsed light [2,6,9].

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