

Multinucleate Cell Angiohistiocytoma



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PRACTICE POINTS

- Multinucleate cell angiohistiocytoma (MCAH) is a rare underrecognized cutaneous tumor presenting as erythematous to violaceous papules.
- Although it clinically mimics Kaposi sarcoma, MCAH may be distinguished histopathologically by negative immunostaining for human herpesvirus 8.
- Surgical excision and laser therapies are definitive treatments for MCAH, which is a benign lesion.

Multinucleate cell angiohistiocytoma (MCAH) is a rare cutaneous entity described as grouped erythematous to violaceous papules. Histopathologic findings include vascular proliferations with multinucleate giant cells and dermal fibrosis. We report a case of MCAH in an 83-year-old white man affecting both the right anterior thigh and left posterior calf. Additionally, the pathogenesis of MCAH and different therapeutic modalities are reviewed.

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Multinucleate cell angiohistiocytoma (MCAH) is a rare benign, soft-tissue tumor first described in 1985 by Smith and Jones¹ that presents clinically as erythematous to violaceous papules most commonly affecting females on the dorsal aspect of the hands and face.² Multinucleate cell angiohistiocytoma is histologically characterized by vascular and histiocytic proliferations with dermal fibrosis. Few cases have been reported of lesions affecting the lower extremities. We report a case of MCAH affecting the legs.

Case Report

An 83-year-old white man with a history of basal cell carcinoma presented for evaluation of grouped, well-circumscribed, soft, red-violet, painless papules on the

right anterior thigh that had been present for 8 months (Figure 1A). A review of symptoms was negative for immunologic, respiratory, and hematologic changes. The patient's medical history also was remarkable for prostate cancer treated with radiation 18 years prior as well as right hip and left knee implants. The initial clinical impression was Kaposi sarcoma or a granulomatous disorder.

Histopathologic evaluation of a deep shave biopsy initially determined the lesion to be scar tissue without other pathologic findings. The patient returned to the clinic 12 months later for a complete skin examination given his history of skin cancer. Compared to clinical photographs taken a year prior, new violaceous papules were noted on the right thigh (Figure 1B) and left calf. Furthermore, there was no recurrence of the lesion at the prior biopsy site. Shave biopsies of the papules on the right thigh and left calf demonstrated similar histologic findings to each other. There was a mild increase in the number of small blood vessels in the superficial dermis (Figure 2A). A mild perivascular lymphocytic infiltrate surrounded some of these blood vessels. The endothelial cells had small nuclei with no evidence of nuclear pleomorphism. Careful examination of the interstitial dermis revealed scattered multinucleate cells with angulated cytoplasm (Figure 2B). Immunostaining for CD31 and human herpesvirus 8 were negative, excluding an infiltrative vascular tumor and Kaposi sarcoma, respectively. The diagnosis of MCAH was made based on the histopathologic findings.

At 1-year follow-up, the condition was stable with no gross changes in the lesions based on prior photographs. Once again, there was no recurrence of the excised lesions at both biopsy sites.

Comment

Presentation—A systematic review of published reports determined that 79% of MCAH cases occur in females, with an average age of onset of 50.1 years.² However, MCAH likely is underreported due to the overall lack of

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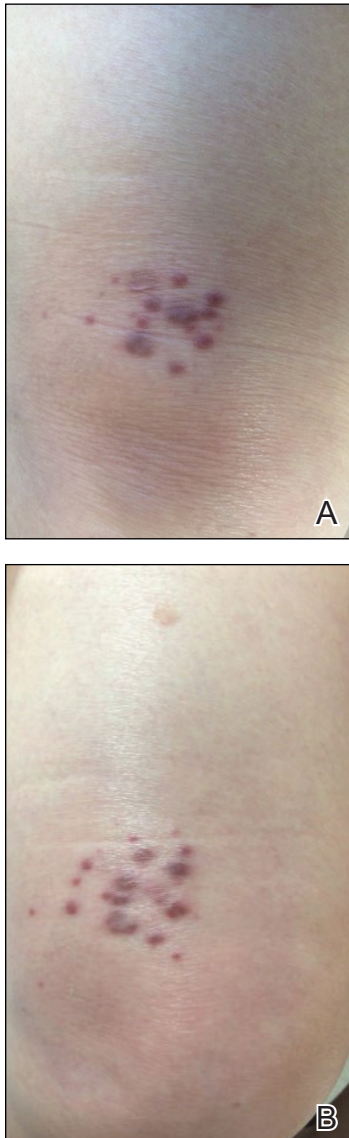


FIGURE 1. Multinucleate cell angiohistiocytoma at initial visit presenting as grouped, well-circumscribed, soft, red-violet, painless papules on the right anterior thigh (A), with new lesions noted on the right thigh at 1-year follow-up.

knowledge regarding this condition by physicians and pathologists. The hands and face are the most commonly affected areas, though other sites of involvement have been reported, including the lower extremities,^{3,4} oral mucosa and upper lip,^{5,6} and trunk,^{7,8} as well as generalized distribution.⁹⁻¹² Additionally, 1 case presented as a single plaque on the trunk rather than having papular or nodular morphology.⁸ Multinucleate cell angiohistiocytoma lesions generally are asymptomatic, though pruritus may be present.¹³ The condition is regarded as benign, though a minority of cases have exhibited spontaneous resolution.¹⁴⁻¹⁶

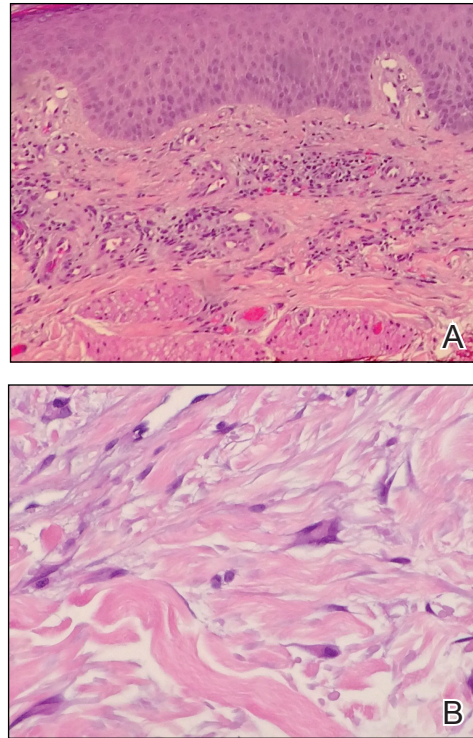


FIGURE 2. Histologic evaluation of multinucleate cell angiohistiocytoma demonstrated an increased number of small blood vessels in the superficial dermis (A) and large angulated multinucleate cells (B) (both H&E, original magnifications $\times 40$ and $\times 100$).

Histopathology—Multinucleate cell angiohistiocytoma histology demonstrates full-thickness dermal microvessel proliferation and fibrosis with characteristic multinucleate giant cells.^{2,3} Vascular endothelial cells stained positive for CD68 in 60% of cases² as well as the normal endothelial markers (ie, factor VIII, CD31, CD34). The multinucleate giant cells exhibit immunoreactivity for macrophage/histiocytic markers factor XIIIa and CD68.

Etiology—The pathogenesis of MCAH is not yet fully understood, but it is considered to be a benign vascular or fibrohistiocytic neoplasm.¹⁷ Calderaro et al¹⁸ described a series of 8 patients who developed MCAH either within a cutaneous neoplastic process or in conjunction with various cutaneous reactive conditions, including hidradenitis suppurativa and chronic radiation dermatitis, as well as overlying a bone prosthesis placed due to degenerative arthritis. These cases suggest that MCAH, or possibly a subset of the disease, is a reactive process. Suggested inciting events include cancer with stromal inflammatory reaction, chronic inflammation (as seen in hidradenitis suppurativa), chronic radiation dermatitis, scarring, and vascular injury.¹⁸ Retrospective immunohistochemical evaluation of a series of MCAH cases demonstrated intralésional spindle cells to strongly express estrogen receptor alpha and factor XIIIa. Additionally, these cells sparsely expressed progesterone receptor and demonstrated no

vascular endothelial growth factor immunoreactivity.¹⁹ This immunohistochemical profile supports MCAH as a distinct entity from dermatofibromas. These findings also suggest a role of hormone signaling, namely estrogen receptor alpha, in MCAH tumor biology and may offer an explanation for the predilection of MCAH in females. Furthermore, estrogen receptor positivity offers a possible mechanism for the highly vascular nature of the lesions, considering the angiogenic properties of estrogen signaling.²⁰ In a systematic review of 142 published cases of MCAH, CD68 positivity on multinucleate cells in MCAH lesions suggested a fibrohistiocytic origin.² However, a number of these cases exhibited CD34 positivity, thus a macrophage origin may not be excluded.

Differential Diagnosis—The differential diagnosis for MCAH includes Kaposi sarcoma clinically and dermatofibroma and fibrous papules histologically. Sass et al²¹ determined the in vitro behavior of cultured MCAH cells to contrast markedly with Kaposi sarcoma-derived cells. Although Kaposi sarcoma-derived cells exhibited invasive behavior, cells isolated from MCAH lesions were less elongated and were unable to traverse basement membranes.

Treatment—Surgical excision or cryotherapy appear to be definitive treatments of MCAH; however, a number of cases have reported light and laser modalities as successful alternatives to excision. One case of MCAH affecting the face was treated with pulsed dye laser monotherapy.²² This modality allowed selective coagulation of the vascular structures in MCAH. At 8-month follow-up, the initial lesion was noted to be completely cleared, though similar lesions had recently appeared elsewhere on the face.²² Another case of MCAH affecting the leg was treated with pulsed dye laser and both topical and intralesional corticosteroid combination therapy. In this case, the lesion failed to respond to treatment, which may suggest that facial localization could influence response in pulsed dye laser treatment.³

Intense pulsed light also has been reported as a definitive treatment in 2 cases.^{2,13} Slight erythema and transient pruritus have been reported immediately following treatment. In this case, complete resolution with only residual hyperpigmentation was reported at 2-month follow-up, with no recurrence during 12 months of follow-up.¹³

Argon laser therapy has been used in 2 cases. After a single session, lesions were no longer palpable, with no scarring noted at 8 weeks follow-up.²³ Lastly, 2 cases of MCAH have been successfully treated with the CO₂ laser, with no relapse noted at 2.5- or 5-month follow-up, respectively.²⁴

Conclusion

Multinucleate cell angiohistiocytoma is a rare and likely underdiagnosed dermatologic condition that is believed to be a reactive process. Characteristic histology of MCAH demonstrates microvascular proliferations of the dermis with multinucleate giant cells amidst a fibrous background.

Although surgical excision is curative, there are reports in which laser and light therapies were used to effectively treat MCAH.

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