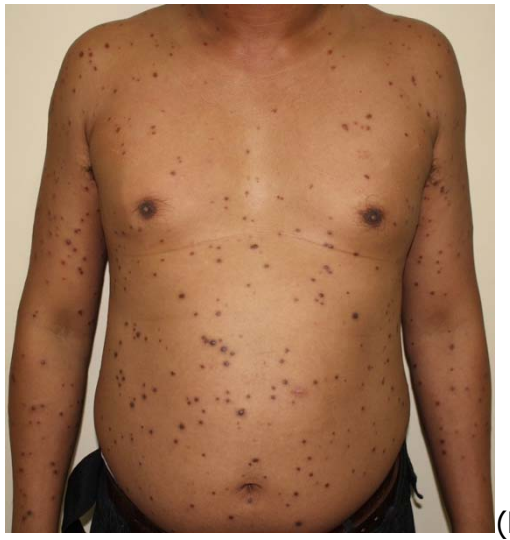
Case 5
A 42 year-old Thai man from Chumphon

Chief complaint: Multiple discrete asymptomatic papules on trunk and extremities for 8 years


(Fig. 5.1)

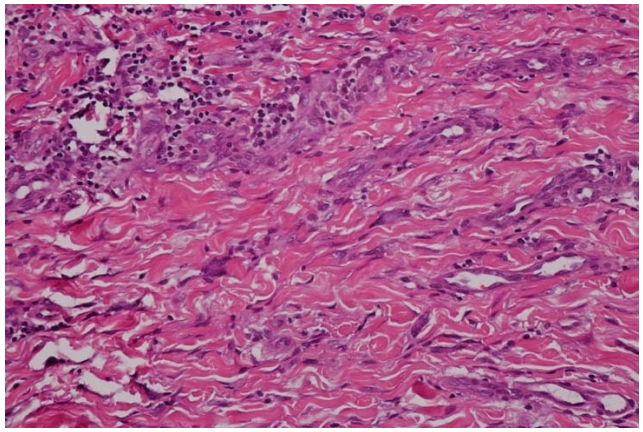
Present illness: He has developed multiple discrete asymptomatic lesions for 8 years. The lesions began on trunk, which subsequently spread to all extremities and progressed slowly over years. He also noticed partial regression of some lesions. He had no prior history of trauma, insect bites, and no history of similar lesions in any family member

Past history: No underlying disease

Physical examination:
A healthy man
Vital signs: Normal
HEENT: No pale conjunctivae, anicteric sclerae
LN: Non-palpable
Lungs: Clear
Other system: Unremarkable

Dermatological examination: (Fig**.** 5.1**)**
Multiple dark red to violaceous, dome-shaped papules of varying size, with a smooth surface scattered on the trunk, both arms and legs

Histopathology: (S16-035790, Back) (Fig. 5.2)


(Fig. 5.2)

- Hyperplasia and hyperpigmentation of overlying epidermis

- Proliferation of thick-wall small blood vessels in associated with scattered spindle and stellate cells and lymphoplasmacytic cell infiltration
- Bizarre shaped multinucleate cells with angulated cytoplasm are noted

Immunohistochemistry:

- Positive vimentin of multinucleate cells, vascular, spindle and stellate cells
- Positive CD34 of vascular channels
- Positive factor XIIIa of spindle and stellate cells
- Negative estrogen receptor, CD68, and HHV-8 staining

Investigations: CBC, liver function & renal function test: WNL

Diagnosis: Generalized multinucleate cell angiohistiocytoma

Treatment: Reassurance

Presenter: Kulsupa Nimmannitya, M.D.

Consultant: Suthinee Rutnin, M.D.

Discussion

Multinucleate cell angiohistiocytoma (MCAH) was first described by Smith and Wilson-Jones in 1985. Since then, less than 150 cases have been reported in the literature, with a female predominance.[1] It is a benign vascular proliferation of unknown pathogenesis, characterized by multiple firm circumscribed red to violaceous papules often grouped on an anatomic area, particularly the limbs, in middle-aged to elderly woman. The lesions develop more frequently on the dorsal part of the hands or wrists. Less commonly, it occurs on face including eyelids and lip, mucosa, and trunk.[2] Usually asymptomatic, some papules may be pruriginous. Linear, bilateral and generalized distribution have also been described.[3,4] To our knowledge, only 13 cases of generalized MCAH have been documented counting our patient.[5] It may be underdiagnosed owing to under-recognition by clinicians and pathologists. In generalized MCAH, the patients had from tens to hundreds of lesions. None of the patients had any prior history of trauma, insect bites, or scabies. There was no history of any family member with similar lesions. No associations with other cutaneous or systemic disease have been reported.

On histological examination, there was an increase of the dermal vessels, which show prominent endothelial cells and enlarged lumina. The dermal collagen bundle can be thickened. Numerous spindle-shaped cells and multinucleate cells of bizarre shape and angulated cytoplasm are located within the dermis. A perivascular infiltration consists of lymphocytes, with occasional plasma cells and neutrophils. Increased mast cell number can be seen inapposition to multinucleate cells, and epidermal hyperplasia may be present.[6] Immunohistochemical finding are variable depending on the cases reviewed. Multinucleate cells tend to be positive for vimentin, variably positive for CD68, and occasionally positive for factor XIIIa. Mononucleated spindle cells are positive for factor XIIIA and CD68, and are occasionally positive for vimentin and MAC387. The endothelial cells stain positively for vimentin, CD34, and factorVIII. Recent study also reported estrogen receptor alpha expression in MCAH, particularly in interstitial and perivascular spindle cells, and occasionally in multinucleate cells.[7] We found that the multinucleate cells do not stain with antibodies against factor XIIIa and CD68, which has been consistently reported in previous studies and might be related to their functional alteration or degeneration.[6]

MCAH may be mistaken for other vascular proliferation or reactive conditions. The differential diagnosis of MCAH includes dermatofibroma, microvenular hemangioma (MVH), angiofibroma, early Kaposi's sarcoma (KS), and pseudo-Kaposi

(acroangiodermatitis). Some can mimic granuloma annulare, lichen planus and even lymphocytoma.[8] In contrast to MCAH, dermatofibroma is usually solitary and histologically shows a more well-defined, nodular appearance at low-power magnification and, peripheral trapping of collagen bundles with more pronounced overlying epidermal hyperplasia. Microvenular hemangioma is an MCAH-like vascular tumor with a similar proliferation of dermal vessels. However, the present of multinucleate cells are typical of MCAH. Angiofibroma are quite distinct in clinical, which usually solitary and located on nose although multiple lesions on face can be observed in tuberous sclerosis, Histologically, the MCAH and the angiofibroma share a vascular prominence, multinucleate cells, and a fibroblastic proliferation. In contrast to MCAH, the overlying epidermis, if involved, are often atrophic, and there is a characteristic concentric orientation of collagen around follicles. Kaposi's sarcoma clinically are usually larger nodules or plaques. Histologically, KS consists of an increased number of anastomosing, jagged, bizarre shaped vascular channels, and the promontory sign is occasionally observed. There are more spindle cells and hemosiderin deposition and lack of multinucleate cell. Pseudo-Kaposi lesions typically have superficial and deep thick-walled vessels with abundant hemosiderin deposition. For generalized MCAH, the differential diagnosis includes eruptive MVH, generalized eruptive histiocytoma, eruptive leiomyomas, eruptive dermatofibroma, lymphomatoid papulosis, papulonecrotic tuberculid, leukemia and lymphoma with cutaneous involvement.[5]

MCAH has a benign course. The lesions show slow increase in size and number over the years. It generally persist indefinitely, although spontaneous regression was occasionally observed.[1] The pathogenesis of MCAH is unknown. Most investigators have suggested an inflammatory or reactive process rather than a neoplasm. The ultrastructural morphology of multinucleate cells in combination with the positive immunohistochemical stain for vimentin and negative for monocyte-macrophage markers provide evidence for a fibroblastic origin[5], in consistent with our finding which reveal immunohistochemical expression of only vimentin in multinucleate cells. The treatments are not generally recommended except for aesthetic reasons or for disseminated cases. Besides surgical excision, successful treatment options are argon laser, carbondioxide laser, cryosurgery, intense pulse light, and pulsed dye laser.[9]

References:

1. Frew JW. Multinucleate cell angiohistiocytoma: clinicopathological correlation of 142 cases with insights into etiology and pathogenesis. Am J Dermatopathol 2015;37:222-8.
2. Rawal YB, Anderson KM, Rawal SY. Multinucleate cell angiohistiocytoma: an uncommon mucosal tumour. Clin Exp Dermatol 2009;34:333-6.
3. Coco V, Guerriero C, Di Stefani A, Pennacchia I, Peris K. Linear and Bilateral Multinucleated Cell Angiohistiocytoma (MCAH). J Dermatol Case Rep 2016;10:58-61.
4. Pérez LP, Zulaica A, Rodríguez L, et al. Multinucleate cell angiohistiocytoma. Report of five cases. J Cutan Pathol 2006;33:349-52.
5. Wang M, Abdul-Fattah B, Wang C, et al. Generalized multinucleate cell angiohistiocytoma: case report and literature review. J Cutan Pathol 2017;44:125-34.
6. 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.
7. Cesinaro AM, Roncati L, Maiorana A. Estrogen receptor alpha overexpression in multinucleate cell angiohistiocytoma: new

insights into the pathogenesis of a reactive process. Am J Dermatopathol 2010;32:655-9.
8. Cribier B, Gambini C, Rainero M, Grosshans E. Multinucleate cell angiohistiocytoma. A review and report of four cases. Acta Derm Venereol 1995;75:337-9.
9. Richer V, Lui H. Facial multinucleate cell angiohistiocytoma: long-term remission with 585 nm pulsed dye laser. Clin Exp Dermatol 2016;41:312-3.