Multinucleate Cell Angiohistiocytoma: 
-A Case Report-
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Multinucleate cell angiohistiocytoma (MCAH) is a rare skin lesion characterized by multiple papules, usually found on the extremities of middle-aged women. We report such a case in a 42-year-old woman who had noticed a gradually enlarging purpuric plaque and several brown-to-violet papules on her forehead for one year. A biopsy specimen of the plaque showed dermal vascular proliferation embedded in connective tissue containing a number of bizarre, multinucleated giant cells. Immunohistochemical study showed that the endothelial cells were positive for CD34, the multinucleate cells were positive only for vimentin, and the mononuclear interstitial cells were positive for CD68. A diagnosis of multinucleate cell angiohistiocytoma was made. We report this case and review the literature. (Dermatol Sinica 23: 154-157, 2005)

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INTRODUCTION

Multinucleate cell angiohistiocytoma (MCAH) usually occurs in middle-aged women, in whom asymptomatic, grouped, reddish-brown papular lesions develop over a period of a few weeks, mostly on the extremities. Histopathologically, MCAH is characterized by a proliferation of small blood vessels in the mid-dermis, a scattered lymphohistiocytic infiltrate, and large, bizarre cells, many of which are multinucleate and have an irregular outline. We present a 42 year-old woman who had MCAH on her face.

CASE REPORT

A 42-year-old woman presented with several pruritic skin lesions on her left forehead that had gradually increased in size over one year (Fig. 1). She sometimes scratched the area because of the itching, but there were no other symptoms. There was no tenderness, local heat, history of insect bite, or history of trauma. The skin lesions had been treated with topical steroid ointment for several months in our dermatology clinic, but it was ineffective. Her past medical history was significant for non-alcoholic steatohepatitis, essential hypertension, and iron deficiency anemia.

Physical examination revealed a 2 X 1.5 cm, firm, purpuric plaque and four brown-to-violaceous papules on her left forehead. The lesions were thought to be lichen planus. A biopsy specimen from the plaque showed psoriasiform acanthosis and hyperkeratosis of the epidermis. In the upper and mid-dermis there were an increased number of irregularly shaped small blood vessels typical of capillaries and small venules. In many vessels, the endothelial cells had a prominent ovoid nucleus protruding into the lumen (Fig. 2). There were no hemosiderin-containing macrophages seen. The surrounding connective tissue was composed of thickened collagen bundles and contained a variable number of bizarre, multinucleated giant cells. Many epithelioid histiocytes were scattered randomly between the collagen bundles. (Fig. 3)

The endothelial cells stained positively for CD34 and vimentin. The multinucleate cells were positive for vimentin and negative for CD34, CD68, and S-100, and the mononuclear interstitial cells were positive for CD68 (Fig. 4) and vimentin. Only a few dermal dendritic cells were labeled with S-100 antibody. A toluidine stain showed an increased number of mast cells in the biopsy specimen. These findings were consistent with a diagnosis of multinucleate cell angiohistiocytoma.

DISCUSSION

MCAH, a rare benign disorder of unknown etiology thought to be of vascular or stromal cell origin, was first described in 1985 by Smith & Wilson-Jones. Since then, 46 cases have been
reported in the literature. While uncommon, the disorder is probably underdiagnosed because clinicians and pathologists fail to recognize it.

MCAH most commonly affects middle-aged women. Clinically, the lesions appear as multiple red-brown to violet, dome-shaped or flat-topped grouped papules, sometimes in an annular distribution. A case of a solitary lesion has also been reported. MCAH occurs most frequently on the legs and arms and less commonly on the face, upper lips, orbit, and chest. Plaque-like MCAH and generalized MCAH have also been reported. Asymptomatic lesions generally persist indefinitely, although spontaneous regression has been observed. So far, no association with any other systemic disease has been reported.

The histo- and immunopathologic features in our case are similar to those previously reported. The diagnosis is based on histological examination, which demonstrates a proliferation of capillaries and venules involving the full thickness of the dermis. The vessels exhibit round lumina and prominent endothelial cells, and the surrounding tissue has a sparse inflammatory infiltrate composed mainly of lymphocytes. Occasional multinucleated giant cells with scalloped or angulated cytoplasm are scattered throughout the lesions. Epidermal hyperplasia and thickened collagen were also present in our case.

Fig. 3
There are bizarre, multinucleated giant cells surrounded by connective tissue composed of thickened collagen bundles. Many epithelioid histiocytes are scattered randomly between the collagen bundles. (H & E, 200X)

Fig. 4
The interstitial mononuclear cells are CD68 positive, and the multinucleated cells are CD68 negative. (CD 68, 400X)

The pathogenesis of MCAH is not clear. The scattered interstitial mononuclear cells are positive for CD68, lysozyme, alpha 1-antitrypsin and negative for S-100 and CD1a, supporting a monocyte-macrophage lineage. However, the multinucleate cells are only positive for vimentin, suggesting that these giant cells originate from fibroblasts. This hypothesis is supported by electronmicroscopic findings reported by Smolle et al. Ultrastructurally, they found a zonula nucleus limitans and a prominent rough endoplasmic reticulum in the multinucleate cells, which suggests fibroblastic differentiation. Jones et al. proposed that the multinucleate cells of MCAH represent degenerate or effete connective tissue cells that, under conditions of prolonged chronic stimulation, have failed to divide after mitotic division. Clinically, MCAH lesions tend to be multiple and eruptive, occurring preferentially on areas subject to trauma or arthropod bites, and in some cases undergo spontaneous regression. Based on all the evidence, some investigators have suggested that MCAH is an inflammatory disorder rather than a truly neoplastic process.

The differential diagnosis includes lichen planus, lupus erythematosus, granuloma annulare, histiocytoma, lymphocytoma, Kaposi’s sarcoma, and sarcoidosis. Most of these entities have distinct histopathologic appearances that can be differentiated from MCAH. Two of the most important histopathologic diagnoses that may be confused with MCAH are Kaposi’s sarcoma and angiofibroma.
Kaposi’s sarcoma has no angulated multinucleate cells, and there are bizarrely shaped, thin-walled, anastomosing vascular spaces that partially surround adnexal structures and venules of the superficial and periadnexal vascular plexus. HHV-8, a virus associated with Kaposi’s sarcoma, was not present in the skin lesions of two patients with MCAH when looked for by PCR. In that study, cells cultured from the MCAH lesions were short-lived and could not transverse the basement membrane as do cells from Kaposi’s sarcoma. This further supports the view that MCAH has an inflammatory origin.

Angiofibroma, particularly fibrous papules of the face (FP), resembles MCAH histopathologically. However, MCAH does not show the typical onion-skin arrangement of collagen fibers around follicles and blood vessels seen in FP. MCAH has proliferation of small, mostly narrow vessels with plump endothelial cells protruding into the lumen, whereas FP has larger vessels with irregular lumina without prominent endothelial cells. Furthermore, in MCAH, collagen fibers have a normal or horizontal orientation in contrast to the vertical orientation in the upper dermis in FP. Clinically, MCAH tends to occur as multiple lesions on the extremities, while angiofibromas are usually solitary lesions on or around the nose.

An increased number of mast cells in MCAH has been reported, which we also found in our case when the specimen was stained with toluidine blue. Mast cells may deserve increased attention in future studies of MCAH, exploring in particular their relationship with multinucleate cells in what is probably a reactive fibrohistiocytic proliferation.

If necessary, the lesions can be excised. Kopera et al. reported two cases of MCAH successfully treated with argon laser. In our patient, the lesions persisted despite topical steroids. Total excision by a plastic surgeon is planned.

In conclusion, MCAH is a rare disorder but one with distinct clinical and histopathologic characteristics. The etiology of MCAH remains uncertain, but the diagnosis is not difficult if the disorder is kept in mind.

REFERENCES