

Angiolymphoid hyperplasia with eosinophilia: A case report

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Abstract Angiolymphoid hyperplasia with eosinophilia (AHE) has an unknown pathogenesis but is considered a reactive phenomenon, possibly in response to or in association with an underlying vascular malformation. There is history of trauma in some cases, and hyperestrogenemia (e.g. pregnancy, oral contraceptive use) may foster lesion growth. T-cell monoclonality has been reported in few cases. We report such a case in a 39-year-old male who visited our hospital with multiple nodules on the occipital of his head.

Key words

Angiolymphoid, hyperplasia, eosinophilia, Kimura's disease.

Introduction

Angiolymphoid hyperplasia with eosinophilia (AHE) was first described in 1969 by Wells and Whimster. They considered AHE a late stage of Kimura's disease described in the Japanese literature in 1948. It is now generally accepted that these are two separate entities. AHE occurs in young to middle-aged adults without gender predilection. A history of trauma can be elicited in some patients.¹

The pathogenesis of AHE is unknown but is considered a reactive phenomenon, possibly in response to or in association with an underlying vascular malformation. There is history of trauma in some cases, and hyperestrogenemia (e.g. pregnancy, oral contraceptive use) may foster lesion growth. T cell monoclonality has been reported in few cases.²

AHE typically presents as papules or nodules that are tan, brown, pink or dull red in color and are located predominantly in the head and neck region, especially around the ears and on the forehead and scalp. Less commonly, lesions have been observed in the mouth and on the trunk, distal extremities, vulva, and penis. Most papulonodules are dermal in location, but some are subcutaneous; occasionally, AHE involves deeper soft tissues or arises from vessels. Approximately, half of patients have multiple lesions, generally in clustered pattern. AHE can be either asymptomatic or painful, pruritic or pulsatile. Some patients have regional lymph node enlargement and peripheral eosinophilia.¹

Although rare instances of spontaneous regression have been reported, surgical excision is generally required. About one-third of lesions recur after excision. Several treatment modalities have been used, including intralesional corticosteroid injections, interferon $\alpha 2b$, cytotoxic agents, cryotherapy, electrodesiccation, pulse-dye laser and carbon dioxide laser.³

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Figure 1 Erythematous papules and nodules on the scalp.

Case Report

A 39-year-old man visited our hospital with multiple nodules on the occipital of his head. That history did not reveal any previous trauma or bleeding, fever, headache, or jaw or tongue claudication; the nodules were not painful, and were casually noted by the patient nearly 1 year earlier. On examination, non-pulsatile space-occupying lesions were palpable in the occipital region, without changes in the overlying skin. (**Figure 1** and **2**).

Laboratory tests, including complete blood count and erythrocyte sedimentation rate were normal except eosinophilia. Skin biopsy revealed acanthosis of epidermis, a lymphocytic infiltrate with occasional eosinophils, and the presence of thick-walled vessels in the upper and middle portion of the dermis. The vascular channels were lined by enlarged plump endothelial cells with an 'epithelioid' appearance and cytoplasmic vacuolation. Immunohistochemical staining revealed that the enlarged endothelial cells were positive for CD31, CD34, and factor VIII. AHE was diagnosed on the basis of histological findings.

Discussion

Angiolymphoid hyperplasia with eosinophilia (AHE) has been known by a variety of different names, such as epithelioid hemangioma, pseudopyogenic granuloma, inflammatory angiomatous nodule, papular angioplasia, subcutaneous angioblastic lymphoid hyperplasia with eosinophilia and lymphofolliculosis, intravenous atypical vascular proliferation and histiocytoid hemangioma. This extensive list of nomenclature reflects the spectral variation in microscopic presentations of ALHE encountered by past investigators and, not least, the divided opinion as to whether the pathogenesis of the lesion is truly neoplastic or a reactive phenomenon.⁴

AHE occurs in young to middle-aged adults without gender predilection. Previous reports of a female predominance have not been supported by more recent series. A history of trauma can be elicited in some patients. The frequent presence of mural damage or rupture in intralesional large vessels of AHE has suggested a role for trauma or arteriovenous shunting in its pathogenesis. Cases have been described in association with arteriovenous fistulas and malformations. These findings suggest that, in some patients, AHE may be reactive, rather than neoplastic, especially in those with this latter type of lesion. AHE typically presents as papules or nodules that are tan, brown, pink, or dull red in color and are located predominantly in the head and neck region, especially around the ears and on the forehead and scalp.

Less commonly, lesions have been observed in the mouth and on the trunk, distal extremities, vulva, penis⁵ and submental area.⁶ Most papulonodules are dermal in location, but some are subcutaneous; occasionally, AHE involves deeper soft tissues or arises from vessels. Approximately half of patients have multiple

lesions, generally in clustered pattern. AHE can be either asymptomatic or painful, pruritic or pulsatile. Some patients have regional lymph node enlargement and peripheral eosinophilia.¹

Different diagnostic imaging modalities have been proposed for AHE, such as angiography, PET, CT, and MRI which confirm the vascular origin of the disease and the presence of perivascular masses of an inflammatory nature. Although being useful, these techniques cannot be effectively recommended in everyday practices because of their low cost-benefit ratio; in fact, none of them was performed in the present case. Ultrasound, on the other hand, is able to provide all the necessary information, and is cheap and widely available.^{7,8}

Only two reports exist of two cases of AHE involving the temporal artery evaluated with ultrasound, which demonstrated typical signs of arteritis not dissimilar from those normally seen in giant cell arteritis, such as an irregular thickening of the vascular wall detected as the ‘‘halo sign’’.^{9,10}

Although AHE might mimic superficial form of Kimura disease and the coexistence of the two entities has been reported,¹¹ they are presently considered to be separate entities: AHE lesions are localized in the superficial tissues, while Kimura disease involves deeper tissues such as lymph nodes and salivary glands.^{12,13}

There has been controversy over the exact relationship between Kimura’s disease (KD) and AHE; these two terms have been used interchangeably in many articles. KD was first described by Chinese authors Kimm and Szeto in 1937 and later made widely recognized by Kimura in 1947. KD is a chronic inflammatory disease of unknown etiology usually presents as solitary or multiple subcutaneous nodules in the head and neck region, often involving the

parotid or submandibular salivary glands. KD is associated with regional lymphadenopathy; this may become generalized in long-standing disease and systemic eosinophilia with raised IgE levels. It is most prevalent in Asians, with 85% of cases occurring in males.

Although KD has been thought to be integral to the spectrum of ALHE in the past, histological features show that these conditions represent two separate disease entities. KD is characterized by lymphoid nodules with germinal centers which may extend from the dermis to the underlying fascia and muscles.

Lesions show a distinct eosinophilic infiltrate with microabscesses. Vascular proliferation is not always present; however, when seen, there are many canalized capillaries lined by flat endothelial cells. Systemic eosinophilia is almost always present, seen in approximately 98% of cases in comparison to 20% in AHE.

In contrast to KD, AHE lesions are superficial containing blood vessels of varying luminal sizes, some of which may not be canalized, lined by distinctive endothelium of an epithelioid appearance. Eosinophilic abscesses are not seen and peripheral eosinophilia is not always present. KD is thought to be an allergic response, owing to the presence of eosinophilia and elevated IgE levels, whereas ALHE is believed to be a true neoplasm of the endothelium.³

Other differential diagnoses of AHE includes vascular tumors and tumor-like conditions of blood vessels, such as angiosarcoma, cutaneous epithelioid angiomatous nodule, bacillary angiomatosis, and epithelioid hemangioendothelioma.¹⁴

The histology of AHE shows a distinct proliferation of blood vessels with thickened

walls. These are lined with prominent epithelioid endothelial cells said to have a cobblestone appearance; some of them contain cytoplasmic vacuoles. Additionally, a characteristic chronic inflammatory infiltrate is seen in the perivascular and interstitial tissue, comprised of lymphocytes, plasma cells and eosinophils. Eosinophils usually account for 5-15% of the infiltrate, though in rare cases eosinophils may account for up to 50%.¹⁵

In our case, angiosarcoma was ruled out by the absence of conspicuous cytologic atypia, frequent mitotic figures, or piling up of cells.¹⁰ Unlike cutaneous epithelioid angiomatous nodule, the lesions were not composed of solid sheets of epithelioid endothelial cells.¹⁶ The absence of bacilli, acute neutrophilic inflammation, and capillary proliferation typical of pyogenic granuloma ruled out bacillary angiomatosis.¹⁶ Distinction from epithelioid hemangioendothelioma was made by the lesion's architecture and the presence of prominent inflammation and numerous well-formed blood vessels, with a lack of extravascular proliferation of epithelioid neoplastic cells.¹⁶

Although rare instances of spontaneous regression have been reported, surgical excision is generally required. About one-third of lesions recur after excision, sometimes due to incomplete excision of an underlying nidus of arteriovenous (AV) shunting (e.g. an AV malformation, an acquired AV fistula). Intraoperative bleeding can be problematic. Various lasers (e.g. CO₂, pulsed dye, copper vapor) have been used with variable success. Several treatment modalities have been used, including intralesional corticosteroid injections, interferon α 2b, cytotoxic agents, cryotherapy and electrodesiccation. We did not perform any active treatment (i.e., either systemic corticosteroid administration or excision)

because the patient lacked any disabling symptoms and did not prefer such treatment.

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