

Case Report

Report of Two Cases of Angiolymphoid Hyperplasia with Eosinophilia and Review of Literature

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ABSTRACT

Angiolymphoid hyperplasia with eosinophilia, also known as epithelioid hemangioma, is a rare endothelioproliferative disorder which clinically presents with reddish to reddish brown, single or multiple, papules and nodules predominantly on head and neck region in middle aged women. Its aetiopathogenesis is still unclear. Histopathologically, it is characterized by proliferation of plump or epithelioid endothelial cells, prominent eosinophilic and monoclonal lymphocytic proliferation with or without elevated blood eosinophilia. Herein we are documenting two cases of angiolymphoid hyperplasia with eosinophilia in 15-year-old girl and 19-year-old young male. Both the clinically diagnosed cases were further confirmed on histopathological examination.

Key Words: Angiolymphoid, endothelioproliferative, eosinophilia, epithelioid.

INTRODUCTION

Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare benign reactive angioproliferative disorder characterized by proliferation of epithelioid endothelial cells and dense infiltrate chiefly consisting of lymphocytes, eosinophils and mast cells. [1] Clinically, it presents with multiple erythematous papulonodular lesions mostly appearing on head and neck. Herein we are documenting two cases of ALHE, one of which had atypical verrucous appearance of lesions in linear pattern that, to the best of my knowledge, is not reported in previous literature.

CASE REPORT

Case 1

A 15-year-old girl presented with asymptomatic multiple grouped erythematous papulonodular lesions on right ear for last 6 years. It started developing at

the age of 9 years, increased in number over the years and now stable for 3 years. Previous history of trauma or any pre-existing localized dermatomes was also absent but history of bleeding on manual manipulation was present. There was no regional lymphadenopathy. Local cutaneous examination demonstrated multiple erythematous to violaceous soft papulonodular lesions of size 2 mm to 1 cm over the cavum conchae and external meatus of right ear ([Figure 1a](#)). Systemic examinations were also not remarkable. Other routine laboratory parameters including total serum IgE level were within normal limits except 12% eosinophils.

Histopathologic examination (HPE) of erythematous nodule revealed clusters of proliferating plump epithelioid endothelial cells surrounded by lymphocytes and eosinophils ([Figure 1b](#)) Classical clinical picture and supportive HP findings

suggested the diagnosis of ALHE and patient was offered no treatment owing to their small size and no complications and kept under observation.

Case 2

A 19-year-old male came to our outpatient door presenting with multiple, mildly painful, erythematous to brownish, verrucous, haemorrhagic and crusted nodules and plaques over postauricular area of left side extending to the side of the neck in linear pattern for last 8 years. No previous history of trauma, pre-existing skin lesions or family history was noted. Local cutaneous examination revealed the presence of multiple grouped dull red to violaceous nodules forming plaques on lower half of retroauricular groove, with some atrophic and hyperpigmented surrounding skin (Figure 2a). Largest size of the nodule was 2 cm in diameter. Haemorrhagic crusting was noted on the surface due to bleeding on unavoidable repeated trivial trauma. Regional lymphadenopathy was absent and systemic examinations were not remarkable. Total serum IgE level and other routine laboratory parameters were within normal limits.

HPE of one of the verrucous nodular lesions was done which demonstrated endothelial cell proliferation associated with dense infiltration of mainly lymphocytes and eosinophils. Endothelial cells were seen to be plump and 'epithelioid' in appearance (Figure 2b).

On the basis of history, clinical presentation and HPE, diagnosis of ALHE was made and patient was advised intralesional injection of steroid but he did not turn up further.

DISCUSSION

"ALHE" term was coined by Wells and Whimster in 1969 and later on in 1982, it was also given another name 'Epithelioid hemangioma' by Weiss and Enzinger due to the peculiar morphology of the proliferating endothelial cells.^[1,2] Initially it was thought to be a late stage of Kimura's disease but then over the time, ALHE and Kimura's

disease were established as two different clinical entities. Although it is a disease of young women of age 20-40 years, few cases in male (as in one of our two cases) have also been reported in previous literature.^[3] Its aetiopathogenesis is yet to be fully explained. Causative role of some inciting factors such as trauma, insect bite, arteriovenous shunting, infections (Human herpes virus-8 and Human T cell leukemia virus) and sex hormones (estrogen and progesterone) has only been suggested which results in monoclonal proliferation of T cells, eosinophilia, elevated serum IgE levels and endothelial cell proliferation.^[4,5] In one case, mutation in TEK gene encoding endothelial cell tyrosine kinase receptor Tie-2, has been found.^[6] Monoclonal nature of lymphocytic infiltrates on TCR gene rearrangement further supports the 'reactive' nature of the disease rather than the true neoplasm.^[7]

Clinically, ALHE presents with solitary or multiple, usually erythematous or violaceous grouped papules and nodules on head (predominantly on and around ear) and neck but may also occur on extremities, trunk, genitalia or even oral mucosa.^[8] Location of the nodules may either be dermal or subcutaneous.

Histopathologic hallmark of ALHE consists of proliferation of blood vessels lined by plump, endothelial cells surrounded by diffuse or perivascular dermal infiltrate chiefly composed of lymphocytes and eosinophils with or without forming follicles with germinal centers.^[8] Endothelial cells are peculiarly seen with epithelioid or histiocytoid morphology or sometimes in cobblestone pattern, containing vesicular or lobulated ovoid nuclei and intracytoplasmic vacuoles.^[8] Tissue eosinophilia usually constitute 5-15% of cellular infiltrate which may be up to 50% while peripheral eosinophilia has been noted in less than 20% cases.^[8,9] Predominance of vascular and inflammatory component usually depends upon the duration of the lesion and its depth. Early and deeper subcutaneous lesions have more

florid vascular proliferation than cellular infiltrate. [8] Stroma may be fibrotic or myxoid.

On immunohistochemistry, endothelial cells stain positive for CD 31, CD 34, Von Willebrand factor and D2-40 and negative for cytokeratin (CK) and epithelial membrane antigen (EMA). Lymphocytes being T-helper cells, express CD3, CD4, CD43 and CD45RO. [9] The close differential diagnosis includes Kimura's disease, lymphoma cutis, pyogenic granuloma, Kaposi's sarcoma, epithelioid haemangioendothelioma, epithelioid angiosarcoma and retiform haemangioendothelioma. [8,9] Among all these conditions, Kimura's disease is the closest one distinguishable by its large size, deeper subcutaneous location, frequent involvement of salivary glands and regional lymph nodes, characteristic lymphoid follicles with germinal centres, less marked vascular proliferation with flat endothelial cells and markedly raised blood eosinophils and IgE levels [4,8,9] The coexistence of ALHE and Kimura disease has also been reported in literature. [10]

Being a benign disease with spontaneous regression in some smaller lesions, ALHE may be kept under observation for years if there are no complications. For obvious reasons such as increase in size, bleeding or ulceration, treatment is warranted. Currently, there are many treatment modalities among which Mohs micrographic surgery, pulsed dye laser and Nd:Yag laser ablation and intralesional triamcinolone and vinblastine injection has been most effective for most of the cases [8,9,11] Chances of recurrence even after surgical excision cannot be completely avoided. Other options include CO2 laser, electrodesiccation, cry therapy, radiotherapy, and topical application of imiquimod and tacrolimus, isotretinoin and interferon α -2a and oral administration of isotretinoin, indometacin farnesil, pentoxifylline and mepolizumab (interleukin-5 inhibitor). [12,13]



Figure 1: a. Multiple grouped erythematous and violaceous papulo-nodular lesions over the cavum conchae and external meatus of right ear.

b. Clusters of proliferating plump endothelial cells surrounded by diffuse lymphocytic and eosinophilic infiltrate (H & E, X 200).

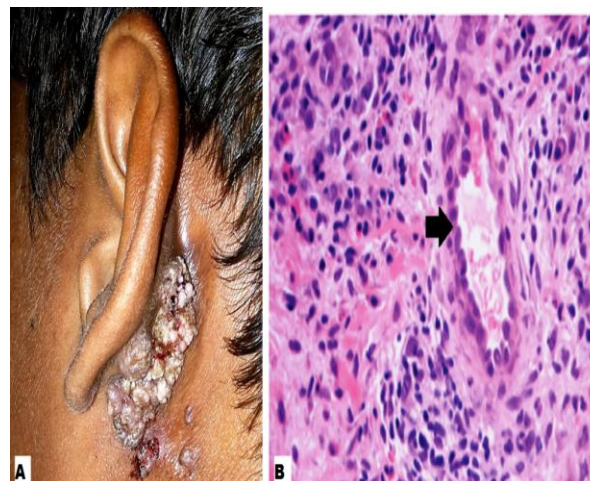


Figure 2: a. Multiple grouped reddish-brown nodules forming plaques on lower half of retroauricular groove of left ear. Blood clots are also seen.

b. Plump endothelial cell proliferation with dense infiltration of lymphocytes and eosinophils (H & E, X 400).

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