ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA – A RARE ENTITY

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ABSTRACT

Background and Objective: Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare, benign, vasoproliferative entity of unknown etiology. It is said to be more frequent in Asians and Caucasians with a predilection to involve the head and neck area. These cases are reported here, with the objective, to share our experience with others. The diagnosis was made by routine histopathological procedures.

Methods: Three cases of ALHE were recently diagnosed. Case 1 was a 60-year-old male with multiple nodules in the peri-auricula area. He was a teacher by profession. Case 2 was a 29-year-old male with recurrent swelling in the left temporal area. He worked in a pesticide factory. Case 3 was a 77-year-old male with a slow growing swelling on left cheek for 15 years. He was a farmer in his active years.

Results: Microscopic examination of all the cases revealed lesions comprised of vascular and inflammatory components. The vascular channels were lined by plump and prominent endothelial cells. The inflammatory cells included lymphocytes, plasma cells, hemosiderin eaden macrophages and numerous eosinophils.

Conclusion: ALHE is said to be more frequent in Asians and Caucasians. Awareness of the entity can help prevent the diagnosis being missed. Correct diagnosis would prompt appropriate therapy, which is vital keeping in view the multifocal and recurrent nature of the disease.

Key words: Angiolymphoid Hyperplasia with Eosinophilia, Kimura Disease, histiocytoid endothelial cell, painless nodule.

INTRODUCTION

Angiolymphoid Hyperplasia with Eosinophilia (ALHE) is a rare benign, vasoproliferative entity of unknown etiology. It is said to be more frequent in Asians and Caucasians.[1] It is most commonly seen in the head and neck region with a special propensity to involve the peri-auricular areas. Some other affected areas have been reported to be the oral cavity, trunk, extremities and genitilia.[2] The exact cause is unknown but immunologic factors, trauma, insect bites, vaccination and hormonal factors have been implicated.[3-5] Three cases of ALHE were recently encountered and are being reported here to share the experience of others.

METHODS AND PATIENTS

All cases presented in Jinnah Hospital, Lahore and the resected specimens were submitted to Pathology Department of Allama Iqbal Medical, Lahore where they were diagnosed by subjecting them to routine histopathology procedures for tissue diagnosis.

CASE REPORTS

Case 1: A 60-year-old male, a teacher by profession, presented with itchy and painful papulonodular lesions in right auricular area. Multiple lesions were seen involving the ear lobe, concha, external auditory canal and retro-auricular area. The provisional diagnosis was ALHE. Blood examination of the patient revealed normal eosinophilic counts.

The lesion was excised and submitted for histopathological examination. On gross examination, it consisted of a skin covered nodule measuring 0.5 × 0.4 × 0.2 cm.

Microscopic examination revealed a dermal lesion covered over by epidermis. There were numerous vascular channels lined by plump eosinophilic endothelial cells with prominent nuclei. There were several cytoplasmic vacuoles in these cells. The surrounding vascular wall revealed mucin and fibrosis (Fig. 1). The intervening stroma was infiltrated by inflammatory cells mainly lymphocytes and eosinophils (Fig. 2). No well-formed lymphoid follicles were seen. The features concurred with the clinical diagnosis of ALHE.

Case 2: A 29-year-old male presented with a painless swelling in left temporal region for one year. The swelling had gradually increased in size and was 3×2.5×2 cm at the time of presentation. There was no history of itching or bleeding from the lesion. The overlying skin was intact. There were no constitutional symptoms.

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The patient worked in a pesticide factory. He gave past history of similar swelling in the scalp one year back which had been excised and diagnosed as a lipoma.

On examination, the swelling was non tender. Laboratory workup revealed normal blood eosinophil counts. The provisional diagnosis was lipoma.

The swelling was excised and was received in the laboratory as a 3×2×2 cm nodular mass. Cut surface was grey white and firm. Microscopic examination revealed a circumscribed mass with numerous vessels lined by eosinophilic cells with prominent nuclei. These cells exhibited cytoplasmic vacuoles as in Case 1. The intervening fibrous tissue was intiltrated by numerous lymphocytes and scattered eosinophils. Few hemosiderin laden macrophages were also seen (Fig. 3, 4).

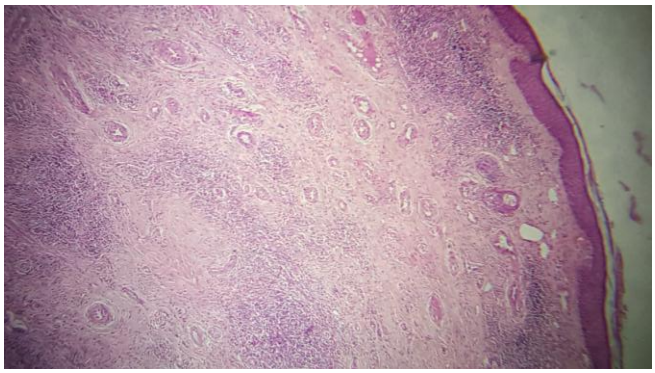

Fig. 1: *Photomicrograph of Case 1, showing an epidermis covered dermal lesion comprised of both vascular and inflammatory components (H&E, ×40).*

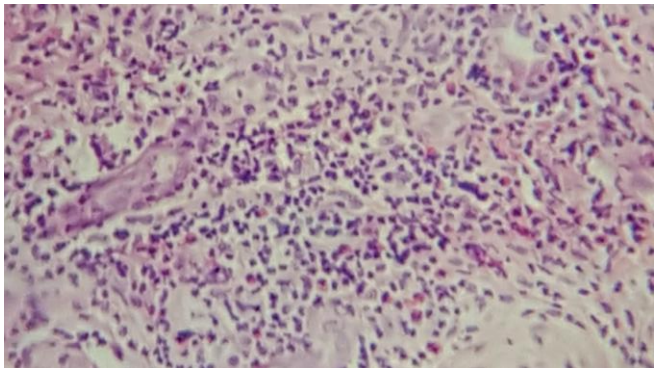

Fig. 2: *Photomicrograph of the same case as Fig. 1. At a higher magnification, the plump, histiocytoid endothelial cells and eosinophils are obvious (H & E, ×40).*

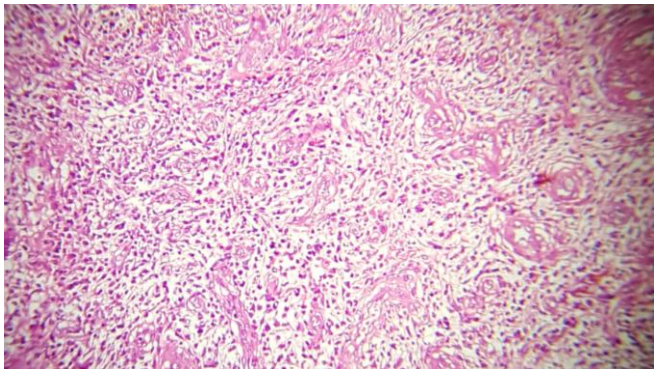

Fig. 3: *Photomicrograph from Case 2. The vascular and inflammatory components are well visualized. (H&E, ×200).*

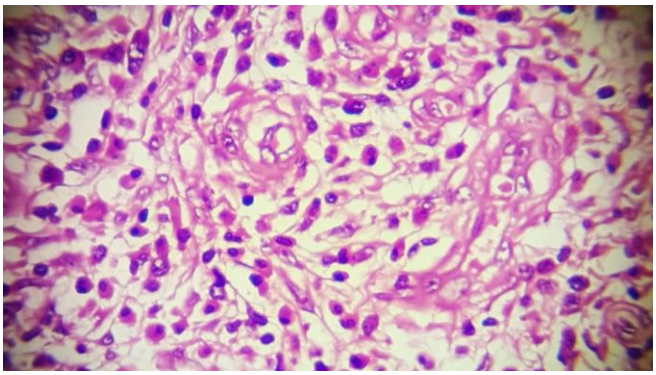

Fig. 4: *Photomicrograph from Case 2, showing in greater detail the prominent endothelial cells, cytoplasmic vacuoles, fibrosis and the surrounding infiltrate containing numerous eosinophils as well as lymphocytes and plasma cells (H&E, ×400).*

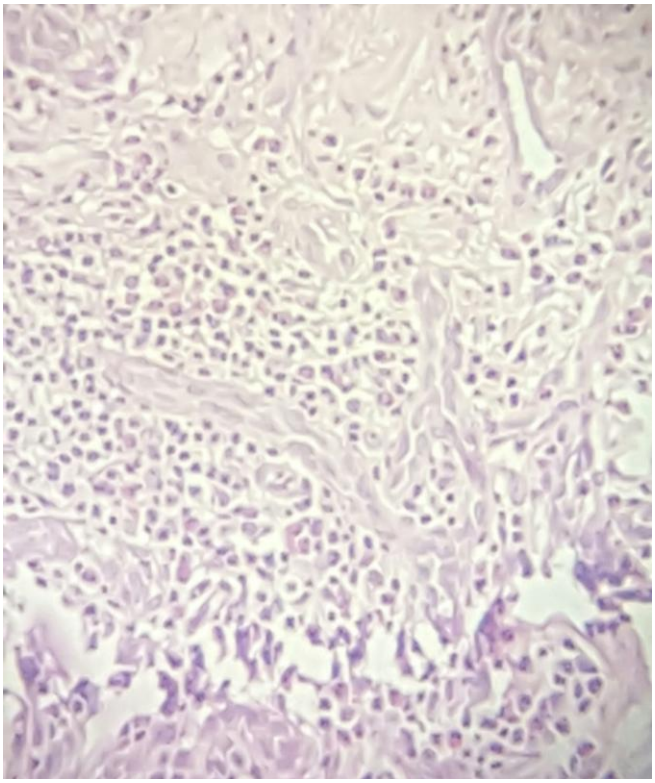

Fig. 5: *Photomicrograph of Case 3. Plump endothelial cells with vacuolation line blood vessels which are surrounded by an inflammatory infiltrate with a heavy component of eosinophils (H&E, ×400).*

Table 1: *Distinguishing clinicopathological features of Angiolymphoid Hyperplasia with Eosinophilia and Kimura Disease.*

Feature	*Angiolymphoid Hyperplasia with Eosinophilia*	*Kumura Disease*
Race(s) more effected	Asians and Caucasians	Orientals
Blood eosinophilia	+/0	++
Serum IgE levels	Usually normal	Usually raised
Predominant tissue of origin	Blood vessels	Lymphoid tissue
Similarity to lymphoid tissue at low power magnification	-	++
Blood vessels	Thick walled, irregularly shaped, dilated	Thin walled with regular lumina
Plump, histiocytoid endothelial cells	++	-
Presence of one or more vacuoles in the endothelial cells	+	-
Lymphoid follicles with active germinal centers	+/-	+
Smooth muscle in vascular walls	+	-
Mucin in vascular walls	++	-
Eosinophils in infiltrate around vessels	+	++
Fibrosis	+/-	+

The diagnosis was ALHE.

Case 3: A 77-year-old male was brought with a swelling over right cheek. It had been present for the last 15 years and had grown to a size of 5×5 cm at the time of presentation. An incisional biopsy measuring 0.5× 0.4×0.4 cm was submitted. On microscopic examination, a skin covered lesion comprised of numerous vascular channeld was seen. These channels were lined by plump endothelial cells similar to those already described in previous cases. The surrounding stroma contained a mixed inflammatory infiltrate with a prominent component of eosinophils (Fig. 5).

Verbal consent for publication was obtained from the patients.

DISCUSSION

ALHE was first described in 1969 by Wells and Whimister[6] who believed it to be one end of a spectrum, with Kimura disease representing the other end. Kumura disease was reported earlier by Kimm and Satzo from China[7] and soon afterwards by Kimura from Japan.[8] The two share several clinicopathological features. Both are comprised of vascular proliferations and inflammatory cells with a predilection for the head and neck region. Both show a variable degree of fibrosis and spare skin adnexal structures.[9,10] Later Rosai et al[11] delineated ALHE better. Still later workers began to report differences between the two conditions and currently these two are thought to be distinct, unrelated entities. The definitional criteria for Kimura disease is well established. It is now said to be a triad of painless nodules in the head and neck region, eosinophilia in peripheral blood as well as tissues, and increased serum levels of immunoglobulin E (IgE). The last two features are not seen in ALHE. Other important differences are listed in Table 1.[9,10,12]

As already started ALHE is commonly seen in the head and neck region.[13] All our patients had nodules in this area. The peri-auricular area is especially likely to harbour such nodules.[1] Our first patient had a nodule near his ear. Swelling in case 3 was also close to the ear. Only two Case reports could be accessed describing ALHE in Pakistan. One of these was in the peri-auricular region[4] and the other one in the scalp.[14] Search of literature from neighboring geographic areas revealed most of the reported cases to be similarly located with only one report describing a nodule in the arm.[2,5,9,15] It should also be noted that patient in Case 2 gave a history of a similar swelling close to the one he now had, a year ago. It had been excised and reported as a lipoma. While no record could be obtained to support it, the possibility of that too having been the same lesion remains worthy of consideration.

The type of vessels involved in proliferation is an active area of research today. Most workers report the vascular lining cells to stain with Factor VIII and CD 34, confirming the vascular lineage of these cells. One recent study describes the highlighting of these cells by D2-40 hinting that the vessels are of a lymphatic lineage.[16]

The main therapeutic options include surgery, cryotherapy, radiation, injection of steroids, oral retinoids and chemotherapy. Surgical excision remains the treatment of choice especially for single lesions.[1,2] Patient education is important as the condition has a tendency to recur.[1,17]

It is ***concluded*** that ALHE though rare, has a predilection for Asians and Caucasians. This is why it must be considered in the differential diagnosis in painless nodules in the head and neck region especially the peri-auricular area. Correct diagnosis is crucial keeping in view its tendency to recur. The fact that most cases reported in Pakistan as well a elsewhere in the subcontinent were seen in classic location of head and neck especially peri-auricular area, is also noteworthy.

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Author's Contribution

AAI &AA: Did the diagnostic work and prepared the manuscript. TR: Made clinical diagnosis. SM & ST: Were in-charge of Case 1, 2 and 3 respectively as clinical residents.

REFERENCES

1. Limbo S, Balato A, Cirillo T, Balato N. A Long-Term Follow-up of Angiolymphoid Hyperplasia with Eosinophilia Treated by Corticosteroids: When a Traditional Therapy is Still Up-to-Date. Case Rep Dermatol. 2011; 3: 64-7.
2. Ahmad SM, Ahmad SM, Wani GM, Khursheed B, Qayoom S. Angiolymphoid hyperplasia with eosinophilia mimicking multiple cylindromas: a rare case report. Indian J Dermatol. 2014; 59: 423.
3. Jeon EK, Cho AY, Kim MY, Lee Y, Seo YJ, Pak JK, Lee JH. Angiolymphoid hyperplasia with eosinophilia that was possibly induced by vaccination in a child. Ann Dermatol. 2009; 21: 71-4.
4. Rehman A, Asad Shabbir SM, Tabassum S, Hafeez J. Auricular angiolymphoid hyperplasia with eosinophilia. J Coll Physicians Surg Pak. 2011; 21: 623-5.
5. Aggarwal A, Keluskar V. Epithelioid hemangioma (angiolymphoid hyperplasia with eosinophilia) in the oral mucosa. Indian J Dent Res. 2012; 23: 271-274.
6. Wells GC, Whimster IW. Subcutaneous angiolymphoid hyperplasia with eosinophilia. Br J Dermatol. 1969; 81: 1-14.
7. Kimm HT, Szeto C. Eosinophilic hyperplastic lymphogranuloma, comparison with Mikulicz's disease. Proc Chin Med Soc. 1937; 1: 329.
8. Kimura T, Yoshimura S, Ishikawa E. On the unusual granulation combined with hyperplastic changes of lymphatic tissues. Trans Soc Pathol Jpn. 1948; 37: 179-80.
9. Maheshwari V, Sharma R, Alam K, Khan A. Angiolymphoid hyperplasia with eosinophilia (alhe) versus kimura's disease: Changing concepts. Indian J Dermatol Venereol Leprol. 1999; 65: 186-8.
10. Briggs PL. Kimura disease is not angiolymphoid hyperplasia with eosinophilia: clinical and pathological correlation with literature review and definition of diagnostic criteria. An Bras Dermatol. 2006; 2: 167-73.
11. Rosai J, Gold J, Landy R. The histiocytoid hemangiomas. A unifying concept embracing several previously described entities of skin, soft tissue, large vessels, bone, and heart. Hum Pathol. 1979; 707:30.
12. Suzuki H, Hatamochi A, Horie M, Suzuki T, Yamazaki S. A case of angiolymphoid hyperplasia with eosinophilia (ALHE) of the upper lip. J Dermatol. 2005; 32: 991-5.
13. Pettinato G, Insabato L, De Chiara A, Ruocco V, Bucci L. Fine-needle aspiration cytology of angiolymphoid hyperplasia with eosinophilia: a case report with electron microscopy and immunohistochemistry. Diagn Cytopathol. 1989; 5: 88-94.
14. Muzaffar M, Mamoon N, Mushtaq S, Tahir M. Angiolymphoid hyperplasia with eosinophilia. Pak Armed Forces Med J. 1997; 47: 30-2.
15. Amin A, Umashankar T, Dsouza CO. Intra-Arterial Angiolymphoid Hyperplasia with Eosinophilia: A Rare Case Report of Peripheral Medium Sized Muscular Artery Involvement. J Clin Diagn Res. 2015; 9: 16-7.
16. Miteva M, Galimberti ML, Ricotti C, Breza T, Kirsner R, Romanelli P. D2-40 highlights lymphati vessels proliferation of angiolymphoid hyperplasia with eosinophilia. J Cutan Pathol. 2009; 36: 1316-22.
17. Chitrapu P, Patel M, Readinger A, Menter A. Angiolymphoid hyperplasia with eosinophilia. Proceedings (Baylor University Medical Center), 2014; 27: 336-337.