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Comparative Analysis of Angiolymphoid Hyperplasia with Eosinophilia (ALHE) and Kimura Disease: Case Series and Clinical Insights

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Abstract
Angiolymphoid hyperplasia with eosinophilia (ALHE) and Kimura disease are both rare benign vascular disorders characterized by vascular proliferation and inflammatory infiltrate, but they exhibit distinct clinical and histopathological features. Herein, we present a series of 5 cases of ALHE initially misdiagnosed as multiple pyogenic granulomas and acne keloidalis nuchae highlighting the importance of accurate diagnosis and differential consideration, particularly in unusual clinical presentations. We compare ALHE with Kimura disease, emphasizing their differences in clinical presentation, histopathological findings and management strategies.

INTRODUCTION

Angiolymphoid Hyperplasia with Eosinophilia (ALHE), also known as epithelioid hemangioma, is characterized by vascular proliferation and eosinophilic infiltration, typically presenting as red to violaceous papules or nodules. It predominantly affects middle-aged adults and commonly involves the earlobe and scalp. The etiology of ALHE remains elusive, although it is postulated to arise from reactive responses to various stimuli, including trauma or inflammatory triggers. Histopathologically, ALHE is distinguished by dilated capillary-sized vessels lined by hobnail endothelial cells and a prominent inflammatory infiltrate comprising lymphocytes and eosinophils[1,2].

In contrast, Kimura disease is a chronic inflammatory disorder characterized by painless subcutaneous masses, lymphadenopathy and peripheral eosinophilia. It primarily affects young Asian males, with a predilection for the head and neck region. Histologically, Kimura disease exhibits lymphoid follicles with germinal centers, eosinophilic infiltrate and proliferation of postcapillary venules. While the exact pathogenesis remains uncertain, it is believed to involve dysregulated immune responses and chronic antigenic stimulation[3,4].

This case series highlights the importance of understanding ALHE and Kimura disease, particularly in their differential diagnosis and management. Despite their distinct clinical presentations, these conditions can lead to misinterpretation and delayed treatment initiation. This emphasizes the need for histopathological examination and comprehensive evaluation for accurate diagnosis. Comparative analysis of ALHE and Kimura disease offers insights into their overlapping features, such as vascular proliferation and eosinophilic infiltration. The therapeutic approach to both conditions differs based on the extent of involvement and associated complications. Surgical excision is the primary treatment for localized ALHE lesions, aiming for complete removal to prevent recurrence. In contrast, Kimura disease may require systemic corticosteroids or immunomodulatory agents to alleviate symptoms and prevent disease progression. The case report provides clinicians with practical guidance for optimizing patient care. This also enhances our understanding of these rare vascular disorders, emphasizing the importance of accurate diagnosis and tailored management.

Learning Objectives:

- To differentiate between Angiolymphoid Hyperplasia with Eosinophilia (ALHE) and Kimura disease based on their distinct clinical presentations, including the morphology and distribution of cutaneous lesions and associated symptoms such as pruritus or lymphadenopathy.
- To analyze the histopathological features of ALHE and Kimura disease, including vascular proliferation, inflammatory infiltrate composition, and characteristic immunohistochemical staining patterns, to facilitate accurate diagnosis and differential consideration
- To evaluate the treatment modalities for ALHE and Kimura disease, including surgical excision, systemic corticosteroids and adjuvant therapies, based on disease severity, extent of involvement, and potential for recurrence, to optimize patient management and outcomes

Case 1: A 38-year-old male presented with multiple solid black lesions over the left back of the ear, which had been progressively enlarging over the past five years. The lesions were associated with intermittent pruritus and occasional bleeding upon scratching. There was no significant medical history or family history of similar lesions. On physical examination, multiple firm, non-tender, well-defined, dome-shaped lesions ranging from 3-10mm in diameter were noted on the left back of the ear (Fig. 1). Some lesions exhibited a black coloration, while others appeared skin-colored. There were no signs of inflammation or ulceration. The rest of the physical examination was unremarkable.

Clinical Diagnosis: Based on the clinical presentation, the differential diagnosis included angiolymphoid hyperplasia, kimura, multiple pyogenic granulomas, and other benign vascular tumors.

Investigations: A punch biopsy of the lesion was performed and histopathological examination revealed a well-circumscribed vascular proliferation composed of dilated capillary-sized vessels lined by endothelial cells with hobnail appearance (Fig. 2). Additionally, there was a prominent inflammatory infiltrate consisting of lymphocytes, eosinophils and occasional histiocytes in the stroma surrounding the vessels. Immunohistochemical staining showed positive staining for CD31 and CD34, confirming the vascular nature of the lesion. Based on these findings, a diagnosis of angiolymphoid hyperplasia with eosinophilia (ALHE) was made.

Treatment: Following the histopathological diagnosis of angiolymphoid hyperplasia with eosinophilia, the patient was counseled regarding the benign nature of the condition. Given the chronicity and cosmetic concerns associated with the lesions, the patient opted for surgical excision of the remaining lesions. Complete excision of the lesions was performed under local anesthesia and the postoperative course was uneventful. The patient was followed up regularly to monitor for recurrence.

After discussing the treatment options with the patient, surgical excision of the lesion was performed

under local anesthesia. The nodule was completely excised with a 2-mm margin of normal tissue. Hemostasis was achieved and the wound was closed primarily. The postoperative course was uneventful, and the patient was discharged home with instructions for wound care.

Outcome: Histopathological examination of the excised specimen confirmed the diagnosis of ALHE, with clear surgical margins. The patient was followed up regularly in the outpatient clinic and there was no evidence of recurrence during the 6 months follow-up period.

Case 2: A 32-year-old male presented with multiple solid lesions over the scalp at the nape of neck, which had been progressively enlarging over the past I year. The patient complained of tendency of bleeding while itching. There is history of similar illness in the family members. On physical examination, multiple, non-tender, well-defined, dome-shaped lesions ranging from 3-5mm in diameter were noted on the occipital region (Fig. 3). No signs of ulceration present. The rest of the physical examination was unremarkable.

Clinical Diagnosis: Based on the clinical presentation, the differential diagnosis included angiolymphoid hyperplasia, Acne keloidalis nuchae, multiple pyogenic granulomas and other benign vascular tumors.

Investigations: A punch biopsy of the lesion was performed and histopathological examination favoured the diagnosis of angiolymphoid hyperplasia with eosinophilia (ALHE).

Treatment: The patient was counseled regarding the treatment modalities but however the patient was lost followup.

RESULTS AND DISCUSSIONS

Angiolymphoid Hyperplasia with Eosinophilia (ALHE) is a rare vascular lesion that often poses diagnostic challenges due to its variable clinical presentation and histological features. The differential diagnosis includes other vascular tumors such as pyogenic granuloma, Kaposi sarcoma and Kimura disease, as well as inflammatory conditions like lupus erythematosus and granuloma faciale. Histopathological examination remains the gold standard for diagnosis, typically demonstrating a combination of vascular proliferation and inflammatory infiltrate, including eosinophils[5].

Surgical excision is the treatment of choice for ALHE, aiming for complete removal of the lesion with clear margins to minimize the risk of recurrence. Other treatment modalities such as laser therapy, cryotherapy and systemic corticosteroids have been used with variable success, particularly in cases where surgery is not feasible or as adjuvant therapy for recurrent lesions[6].

These tables provide a comparative analysis of the clinical and histopathological features of Angiolymphoid Hyperplasia with Eosinophilia (ALHE) and Kimura Disease, aiding in the differentiation and understanding of these rare benign vascular disorders.

Epidemiologically, ALHE is considered rare benign vasoproliferative disorder characterized by the presence of solitary or multiple pink to red-brown dome-shaped papules or nodules, primarily occurring on the head and neck region. While ALHE is uncommon, its exact prevalence remains unclear due to its infrequent occurrence and variability in reporting. However, it typically affects adults in their third to fifth decades of life, with no significant sex predominance reported. The incidence of ALHE appears to be higher in certain ethnic groups, particularly individuals of Asian descent. Despite its rarity, ALHE can have a significant impact on patients' quality of life, necessitating appropriate diagnosis and management strategies to optimize outcomes[1].

In contrast, Kimura disease is a rare chronic inflammatory disorder of unknown etiology, predominantly observed in young adults aged 20-40 years, with a male predominance (3:1 ratio). While endemic in Asian populations, KD occurs sporadically in

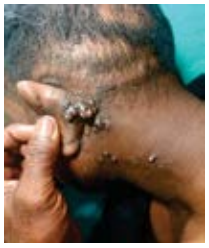

Fig. 1: Visual inspection of the lesion

Fig. 2: Picture showing the area of lesion after excision

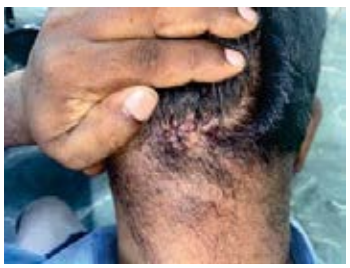

Fig. 3: Diagnosis included angiolymphoid hyperplasia, acne keloidalis nuchae and multiple pyogenic

Table:1 Summary of findings of case series

Case	Age	Sex	Onset of skin lesions	Clinical features	Diagnosis	Treated with	Prognosis
1	38	M	5 years	Multiple solid black lesions over the left back of the ear,	ALHE	Surgical excision	Good
2	35	M	1 year	Multiple solid lesions over the scalp at the nape of neck	ALHE	Nil	-
3	42	F	8 months	Multiple red- brown papules of size 2-4mm over the periauricular region	ALHE	Electro cautery	Good
4	37	F	1 year	Multiple hyperpigmented nodules of size 2-3 cm present over the temporal scalp	ALHE	Surgical excision	Good
5	26	F	5 months	Multiple hyperpigmented discrete papules of varying size over the right post auricular area	ALHE	Cryotherapy	Better

Table 2: Clinical characteristics of angiolymphoid hyperplasia with eosinophilia (ALHE) and kimura disease

Clinical Features	Angiolymphoid Hyperplasia with Eosinophilia (ALHE)	Kimura Disease
Age at Presentation	Middle-aged adults	Young to middle-aged adults
Gender Predilection	Equal distribution	Male predominance
Location	Head and neck region, particularly around ears	Head and neck region, especially parotid
Lesion Appearance	Red to violaceous papules or nodules	Painless subcutaneous masses
Associated Symptoms	Pruritus, occasional bleeding	Lymphadenopathy, allergic rhinitis
Progression	Slowly enlarging over years	Gradual growth over months to years
Histopathological Findings	Vascular proliferation, eosinophilic infiltrate	Lymphoid follicles, eosinophilic infiltrate
Treatment	Surgical excision	Systemic corticosteroids, surgical excision
Recurrence Rate	Low	Moderate to high
Prognosis	Generally favorable	Variable

Table 3: Histopathological features of angiolymphoid hyperplasia with eosinophilia (ALHE) and kimura disease

Histopathological Features	Angiolymphoid Hyperplasia with Eosinophilia (ALHE)	Kimura Disease
Vascular Proliferation	Dilated capillary-sized vessels, hobnail endothelial cells	Lymphoid follicles with germinal centers
Inflammatory Infiltrate	Eosinophils, lymphocytes, occasional histiocytes	Eosinophils, lymphocytes
Presence of Germinal Centers (if applicable)	Absent	Present
Stromal Components	Connective tissue stroma	Fibrous tissue
Immunohistochemical Staining (if applicable)	Positive for CD31, CD34	Positive for CD3, CD20
Association with Eosinophilic Granuloma (if present)	May coexist with eosinophilic granuloma	Rarely associated

other racial groups. In India, only around 200 cases have been reported worldwide since its histopathological diagnosis. The exact prevalence of Kimura disease is not well-established, but it is believed to be more common in endemic regions such as China and Japan. Peripheral blood eosinophilia and elevated serum immunoglobulin E (IgE) levels are consistent features of KD, with coexisting renal disease observed in a significant proportion of cases, ranging from 10-60%[7].

Clinically, ALHE typically presents as solitary or multiple erythematous to violaceous papules or nodules, often associated with pruritus or tenderness[8]. These lesions may vary in size and distribution but commonly occur on the head and neck region, including the earlobe, scalp and periauricular area[9]. In contrast, Kimura disease presents as painless subcutaneous masses or nodules, usually involving the parotid gland, submandibular region, or cervical lymph nodes[7]. Patients with Kimura disease may also present with regional lymphadenopathy and peripheral blood eosinophilia[3].

Histopathologically, ALHE is characterized by a proliferation of dilated capillary-sized vessels lined by endothelial cells with a hobnail appearance, accompanied by a dense inflammatory infiltrate composed of lymphocytes, eosinophils and occasional histiocytes[10]. Immunohistochemical staining typically demonstrates positive expression for CD31 and CD34, confirming the vascular nature of the lesion[11]. In contrast, Kimura disease is characterized by lymphoid follicles with germinal centers, accompanied by eosinophilic infiltrate and prominent vascular proliferation[12]. Immunohistochemical analysis may reveal positivity for CD3, CD20 and CD68, reflecting the lymphocytic and histiocytic components of the lesion.

Management strategies for ALHE primarily involve surgical excision, aiming for complete removal with clear margins to minimize the risk of recurrence[6]. Other treatment modalities, including laser therapy, cryotherapy and systemic corticosteroids, have been utilized with variable success, particularly in cases of extensive or recurrent lesions[13]. In contrast, management of Kimura disease often entails a combination of surgical excision, systemic corticosteroids and immunomodulatory agents[14]. Systemic corticosteroids are typically employed to reduce inflammatory response and control disease progression, while surgical excision may be indicated for symptomatic or cosmetically bothersome lesions[15].

Despite advances in diagnostic modalities and therapeutic interventions, both ALHE and Kimura disease remain challenging entities to manage clinically. Differential diagnosis between these conditions can be particularly challenging due to overlapping clinical and histopathological features. Moreover, misdiagnosis or delay in diagnosis may lead to inappropriate management and suboptimal outcomes.

CONCLUSION

In conclusion, our case series highlights the importance of a thorough comparative analysis between Angiolymphoid Hyperplasia with Eosinophilia (ALHE) and Kimura Disease, two rare benign vascular disorders. Despite sharing similarities in vascular

proliferation and inflammatory infiltrate, they exhibit distinct clinical presentations and histopathological features. Accurate diagnosis is paramount to guide appropriate management strategies and ensure favorable outcomes. In clinical practice, awareness of these distinctive features facilitates accurate diagnosis and appropriate therapeutic interventions. Long-term follow-up is essential to monitor for recurrence and ensure optimal patient care.

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