EPITHELIOID HEMANGIOMA OF THE ORBIT: CASE REPORT

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SUMMARY – Epithelioid hemangioma (EH) and Kimura's disease (KD) were once considered different stages of the same disease, as they share many clinical and histopathologic similarities. Nowadays, they are considered as two different entities, but some authors still confuse these terms. Our objective is to present a case of EH occurring in a very uncommon location and to emphasize the microscopic and clinical differences between EH and KD. We present a case of EH of the orbit in an 83-year-old man diagnosed after histopathologic evaluation of a mass that was surgically removed from the orbit. The tumor showed typical microscopic appearance with pathognomonic epithelioid endothelial cells. The diagnosis was also confirmed by immunohistochemical analysis. Our case clearly illustrates typical appearance of EH and the main differences between EH and KD are thoroughly discussed.

Key words: *Angiolymphoid hyperplasia with eosinophilia – pathology; Hemangioma; Diagnosis, differential; Kimura's disease; Orbital diseases; Case reports*

Introduction

Epithelioid hemangioma (EH) is an uncommon vascular tumor with peculiar histopathologic findings that occurs in the orbit extremely rarely. Wells and Whimster[1] were the first to describe it and they used the term angiolymphoid hyperplasia with eosinophilia (ALHE) for this condition[1]. Some other terms such as inflammatory angiomatous nodule, histiocytoid hemangioma and atypical or pseudopyogenic granuloma could also be found in the literature[2-5]. It typically occurs during early to mid-adult life (20-40 years of age) and women are affected more commonly than men. In most cases, EH develops in the head and neck area, particularly around the ear and because of this they are usually detected early. EH usually presents as small, red, pruritic plaques in the subcutis or dermis, while crusting, excoriation and bleeding of these plaques can also be present. Systemic symptoms are absent in most cases, although very rarely peripheral blood eosinophilia and regional lymph node enlargement may occur[6]. Kimura's disease (KD) is the main differential diagnosis and for a long time these two entities were considered as different stages of the same disease because of many clinical and histologic similarities[6]. Nevertheless, significant differences do exist. We present a case of EH of the orbit and discuss the main differences between EH and KD.

Case Report

An 83-year-old male patient presented with a subcutaneous mass of the left lower eyelid. He underwent surgical procedure of his left eye 5 years prior to the current state, when the cataract was removed. Magnetic resonance imaging revealed a homogeneous tumor mass in the left orbit and lower eyelid. Inferior orbitotomy was performed with tumor excision. Macroscopic inspection of the mass revealed a lobulated,

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white tumor measuring 2.5x2x0.8 cm. Examination under the light microscope revealed a tumor composed of proliferating blood vessels of varying caliber, lined by plump endothelial cells with large cytoplasmic vacuoles (Figs. 1 and 2). Immunohistochemically, endothelial cells showed positive reaction for CD31. The stroma around vascular spaces contained numerous lymphatic follicles with germinal centers and a large proportion of eosinophils. Eosinophilia was not present in peripheral blood. After medical data evaluation, microscopic and immunohistochemical examination, the diagnosis of EH was established.

Discussion

Epithelioid hemangioma and KD share many features. However, there are also many clinical and histopathologic differences. Ahn and Lee[7] made a comparison of patients suffering from EH and KD[7], which showed some significant differences between the two conditions. Duration of KD (mean duration 7.4 years) was much longer than duration of EH (mean duration 3-6 months). KD also presented with much larger lesions (5.6 cm) compared to those in EH (0.3-1 cm). Considering the affected regions, EH affected the head and neck region in more than 80% of cases, whereas KD was present in more than 50% of cases in the regions other than head and neck. Peripheral blood eosinophilia was detected in nearly 70% of patients with KD as compared to less than 20% of those with EH. An increased level of serum immunoglobulin E (IgE), proteinuria and nephrotic syndrome may also occur in KD. More than half of patients with KD also had regional lymphadenopathy. Even though Ahn and Lee[7] did not find it in patients with EH, other researchers report that regional lymphadenopathy may be found in up to 10% of patients[7,8]. This difference in its incidence makes regional lymphadenopathy clinically important in distinguishing KD and EH. The most important microscopic difference is the presence of epithelioid or histiocytoid endothelial cells which contain vacuolated cytoplasm and rounded or lobulated nuclei. Occasionally, these endothelial cells protrude deeply into the lumen and can even occlude it. Blood vessels in KD are lined with either flattened or low cuboidal endothelial cells. The most prominent component in KD is inflammatory infiltrate; in most cases the entire lesion is infiltrated by lymphocytes and eosinophils which can form eosinophilic microabscesses. Plasma cells and mast cells are also present and all cases display lymphoid follicles with germinal centers. Infiltrates in EH lesions are of similar composition but with a significantly less intensity. Fibrosis in EH is minimal and mostly perivascular, in contrast to KD where fibrosis is interstitial and in more severe cases hyalinization can also be seen. Lymphoid follicles with germinal centers may occur in EH and are considered to be the result of a specific host re-

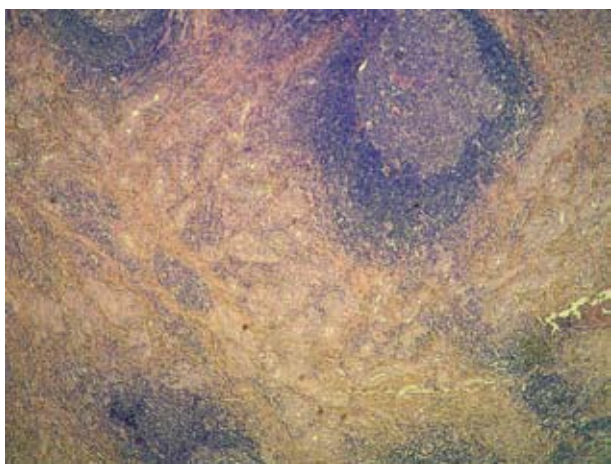

Fig. 1. Low-power photomicrograph showing structures resembling lymphoid follicles and blood vessels of varying calibers (HE, X40).

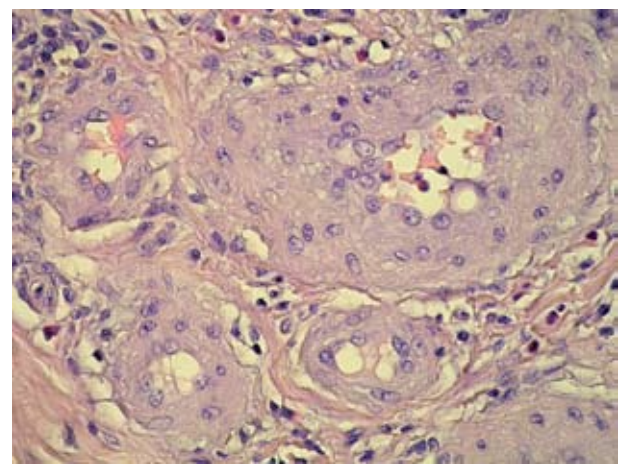

Fig. 2. Blood vessels lined by plump endothelial cells with large cytoplasmic vacuoles (HE, X400).

Table 1. Main clinical and microscopic findings in epithelioid hemangioma and Kimura's disease[7,8]

	Epithelioid hemangioma	Kimura's disease
Clinical feature		
Sex	Women more often	Male predominance
Race	All races	More common in Orientals
Age	Young to middle (30-60)	Young adulthood (20-40)
Presentation	Small, dull red plaques	Discrete subcutaneous mass
Size	<2 cm (1 cm on average)	>2 cm (3 cm on average)
Location	Head and neck almost regularly	Head and neck, elbow, thigh also possible
Number	Multiple	Single more common
Lymphadenopathy	Uncommon	Common
Duration	3 months to 2 years on average	>5 years on average
Pruritus	No	Occasionally, possibly severe
Overlying skin	Erythematous	Normal
Blood eosinophilia	Less than 20% of patients	Almost regularly present
Serum IgE	Normal	Usually elevated
Glomerulonephritis, proteinuria	Rare	Occasional
Histopathologic		
Depth	Dermis, subcutaneous	Subcutaneous, muscle
Endothelium	Cuboid, 'epithelioid'	Flat to low cuboidal
Inflammation	Sparse to heavy infiltrate of plasma cells and lymphocytes	Abundant infiltrate of plasma cells and lymphocytes
Lymphoid follicles	May be present, rarely	Always found
Eosinophils	Sparse	Abundant
Eosinophilic abscesses	Rare	Present
Sclerosis	Not a prominent feature	Significant at all stages

sponse[7,8]. The main clinical and microscopic findings in EH and KD are summarized in Table 1[7,8].

Reed and Terazakis[9] report a case in which EH gave microscopic metastases to regional lymph node but this is so far a unique event although one-third of these lesions do recur[9]. There were cases with spontaneous regression but the lesion is usually surgically removed. Complete or at least partial response to superficial radiotherapy is reported in 80% of patients. There were some attempts with cryotherapy and intralesional steroids but without success[10].

Opinions regarding the basic nature and pathophysiology of EH are still divided. Some authors consider them neoplastic and the others reactive. Some data indicate that 60% of EH lesions are associated with large vessel damage and many authors also report the presence of arteriovenous shunts, especially in deeply situated EH[11]. However, EH can be multifocal and recur and extremely rarely can give metastases. It is possible that this entity is a heterogeneous disorder characterized by epithelioid change of the endothelium[9,12]. According to Seregard,[13] EH is less frequently found in the orbit and periocular region than KD[13].

It is essential to differentiate between EH and KD, as they may have different clinical courses and require different therapy. For EH patients, surgical excision of the lesion is, in the vast majority of cases, sufficient. On the other hand, KD patients may develop nephrotic syndrome, which is very important to recognize and treat appropriately. As some clinical findings may overlap between these two entities, microscopic confirmation of the presence of epithelioid endothelial cells in EH still remains the major factor for distinguishing EH from KD.

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Sažetak

EPITELIOIDNI HEMANGIOM ORBITE: PRIKAZ SLUČAJA

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Epitelioidni hemangiom (EH) i Kimurina bolest (KD) su zbog mnogih kliničkih i histopatoloških sličnosti smatrani različitim stadijima iste bolesti. Danas se smatraju dvama različitim entitetima, ali neki autori još uvijek poistovjećuju ova dva pojma. Naš cilj je predstaviti slučaj EH koji se pojavio na vrlo neuobičajenom mjestu te naglasiti mikroskopske i kliničke razlike između EH i KD. Predstavljamo slučaj EH orbite koji se pojavio kod 83-godišnjeg muškarca. Dijagnoza EH potvrđena je patohistološkom analizom kirurški uklonjenog tumora iz orbite u kojem su nađene specifične epitelioidne endotelne stanice koje nikad nisu prisutne kod oboljelih od KD. Dijagnoza je potvrđena imunohistokemijskom analizom. Opisani slučaj rijetkog orbitalnog tumora jasno pokazuje značajke specifične za EH, uz podrobno prikazane razlike između EH i KD.

Ključne riječi: *Angiolimfoidna hiperplazija s eozinofilijom; Hemangiom; Dijagnoza, diferencijalna; Kimurina bolest; Orbitalne, bolesti; Prikazi slučaja*