Bilateral orbital Kimura's disease: A case report and brief review of literature

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Key words: Autoimmune orbital disease, hypereosinophilia, inflammatory orbital disease, Kimura's disease, proptosis

A 17-year-old male presented with complaints of gradually progressive painless swelling of both upper eyelids for the past 2 years [Fig. 1a]. There was no history of any trauma or other systemic illness. He gave a history of oral steroid intake 4 months back advised by a local practicing ophthalmologist, which led to complete remission of the swelling. However, it recurred within 2 weeks of stopping oral steroids.

On general physical examination, bilateral cervical lymphadenopathy was noted. Ocular examination was within normal limits. There was diffuse bilateral swelling of the upper eyelids with palpable bilateral orbital masses, which were nontender, firm in consistency, not fixed to overlying skin, not compressible, and mobile.

A contrast-enhanced computerized tomography of head and orbit showed ill-defined lesions in both upper eyelids with moderate postcontrast enhancement [Fig. 1b]. Lab investigations including anti-dsDNA, c3 complement, c4, c-ANCA, p-ANCA, ANA, serum ACE all were within normal limits. However, blood counts revealed absolute eosinophil count of 12 cells per microliter, erythrocyte sedimentation rate – 9 mm/h, C-reactive protein – 1.92, and a 1.67 serum IgG4 levels. Based on the clinical picture, differential diagnoses of Kimura's disease (KD), angiolymphoid hyperplasia with eosinophilia, IgG4 orbitopathy, and leukemic infiltrates were made.

The patient underwent an incisional biopsy. The histopathology revealed a tissue with proliferating capillaries and lymphatic channels infiltrated with lymphoid follicles and numerous eosinophils. These features were compatible with KD [Fig. 1c]. The patient was prescribed oral corticosteroids and a remarkable reduction was noted by 3 weeks [Fig. 1d]. The patient has been on follow-up ever since and is doing well even after 6 months. The oral steroids have been slowly tapered.

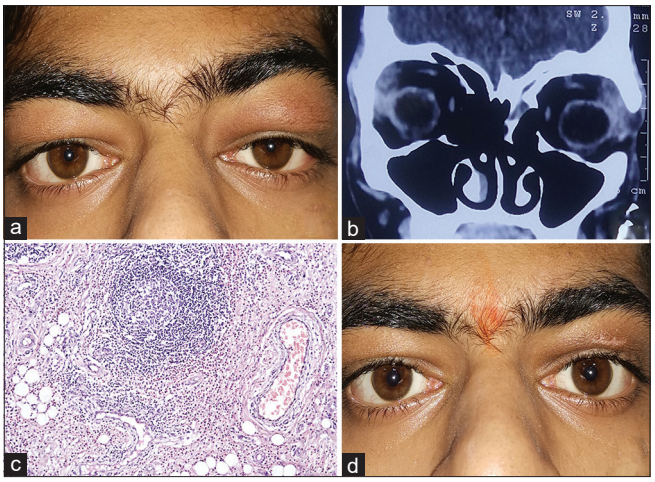

Figure 1: a: Clinical picture of the patient showing bilateral upper eyelid swelling. b: CECT head and orbit showing bilateral homogenous mildly enhancing soft tissue lesion in the upper eyelid region. c: Histopathological slides showing proliferating capillaries and lymphatic channels infiltrated with lymphoid follicles and numerous eosinophils. d: Clinical picture of the patient showing remarkable response to oral steroids after 3 weeks

Discussion

KD is a chronic inflammatory disorder of unknown etiology, which presents with tumor-like swellings and frequently affects young male adults in the Asian population.[1]

It was first described in Chinese literature as "eosinophilic hyperplastic lymphogranuloma" by HT Kimm and C Szeto *et al*. in 1937.[2] The histological description was published by Kimura *et al*.[3] in 1948, and hence, the disease has borne his name. Wells and Whimster named the disease subcutaneous angiolymphoid hyperplasia with eosinophilia (ALHE) in 1969.[4] They had suggested that the two diseases were the same, subcutaneous ALHE representing any earlier stage which with time progressed to KD.[4] However, later studies divided the diseases into two separate categories based on histopathology findings.

It occurs commonly in the second to fourth decades of life (70–80%).[1] The clinical picture is usually painless, sometimes disfiguring subcutaneous nodules are present predominantly in the head-and-neck region.[1]

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Although certain infectious etiologies have been postulated, KD is now believed to be related to an autoimmune or a delayed hypersensitivity reaction. An aberrant allergic response is further supported by the association with asthma, allergic rhinitis and conjunctivitis, atopic dermatitis, and peripheral hypereosinophilia, as well as raised serum IgE levels.[1] In 2018, Lee *et al*.[5] have reported a case of KD in a 30-year-old individual who also had a high-serum IgG4 level.

Most cases have been reported in the dermatology, oral surgery, and pathology literature.[6] It is usually a localized process without many systemic manifestations; however, few associated conditions have been reported, namely, nephrotic syndrome, asthma, tuberculosis, proteinuria, Loeffler syndrome, and even allergy to fungal infections like candida.[4] Regional lymph node involvement occurs in up to 75% of cases.[7]

The disease rarely affects the ocular system. The first reported case with orbital involvement was by Nakai *et al*.[15] in 1966.[8] In the review of the literature we performed, we found a total of 49 cases of orbital KD [Supplementary Table 1]. The skin and lymph nodes of the postauricular and parotid gland region tend to be affected before the orbital involvement (superior orbit and lacrimal gland).[4] The condition is largely asymptomatic.[9] It may mimic nonspecific inflammations of the orbit, certain neoplasias, and even Graves' orbitopathy. In 2014, Li *et al*.[10] reported a 47-year-old Chinese male with orbital KD affecting the lacrimal gland mimicking IgG4 orbitopathy. At times, the disease may present with bilateral extraocular muscle enlargement, as documented by Gonçalves *et al*. in 2016.[11] In 2017, Francis *et al*.[12] have reported a recurrent KD limited to the inner canthus, which was not associated with any lymphadenopathy. At times, the disease may involve multiple structures in the orbital along with regional lymph nodes, as described by Chakraborti *et al*. in 2019.[13]

Computed tomography scan findings are nonspecific and consist of homogeneously enhancing lesions. On MRI studies, KD usually presents hypointense areas on T1 and varying intensity on T2 weighted and postcontrast images.[14] A proliferation of lymphoid follicles, dense fibrosis, capillary proliferation, and germinal centers are typically noted on histopathological examination, showing interfollicular infiltration by eosinophils.

The treatment modalities for KD include observation, surgical excision, oral corticosteroid, cytotoxic drugs, and radiation therapy or any combination.[8] Corticosteroids remain the primary medical therapy. However, the disease mostly recurs once the steroid is weaned off where surgical excision then can be performed. In our case, the patient was explained regarding all the treatment options and started on oral corticosteroid 0.5 mg/kg. There has been a marked reduction in the swelling, and the patient has been on follow-up.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Review of literature since year 2000

Author/Journal	Patient details	Management and outcome
Edward Yip Yeung, and Lih Ma. Bilateral orbital Kimura's disease. Chang Gung Med J Vol. 2002 January (25)	16-year-old Asian male with bilateral eyelid swelling for 1 year	Underwent surgical removal of lesions. 7 months follow-up had satisfactory results
Yeung EY, Ma L. Bilateral orbital Kimura's disease in a young Asian man. Chang Gung Med J. 2002 Jan; 25 (1):45-50	16-year-old Asian man with bilateral eyelid swelling with multiple palpable mass lesions, which waned after treatment with corticosteroids. The lesions waxed after medications were discontinued, for about 1 year. Associated bilateral postauricular lymphadenopathy was present for about 9 years	The tumor mass in the right orbit excised No evidence of recurrence was noted after follow-up for 7 months
Yoganathan P, Meyer DR, Farber MG. Bilateral lacrimal gland involvement with Kimura's disease in an African American male. Arch Ophthalmol. 2004;122:917-9	24-year-old urban African American man with bilateral upper eyelid swelling, discomfort, and intermittent vertical diplopia for 1 year.	Managed with cyclosporine and prednisolone combination which resulted in moderate reduction of symptoms
Prabhakaran, Venkatesh C; Sachdev, Arun; Cheung, David *et al.* Kimura Disease of the Eyelid: A Clinicopathologic Study With Electron Microscopic Observations, Ophthalmic Plastic & Reconstructive Surgery: Nov-Dec 2006; 22 (6): 495-8	70 year old white man presented with a solitary eyelid nodule of 6 months' duration.	Studied histopathology of the eyelid sample and documented a few Weibel Palade bodies.
Lee JK, Almousa R, Thamboo TP, Amrith S. Kimura disease of the eyelid in an Indian man. Clin Exp Ophthalmol. 2009 May; 37 (4):412-4	50-year-old Indian man with eosinophilia, a slow-growing, painless lump in the left upper eyelid	Excisional biopsy was carried out. The lesion was noted to be infiltrating the orbicularis and subcutaneous tissue. Last follow up of the patient 6 weeks following surgery showed no recurrence
Lee SJ, Song JH, Kim SD. Kimura's disease involving the ipsilateral face and extraocular muscles. Korean J Ophthalmol. 2009 Sep; 23 (3):219-23	13-year-old male with a 2-year history of exophthalmos of the left eye and facial swelling	A lateral rectus muscle incisional biopsy of the left eye was performed. Oral methylprednisolone therapy was initiated and tapered following the incisional biopsy After oral steroid therapy was tapered for about 2 months, the exophthalmos of the left eye and facial swelling had substantially subsided though there was a recurrence post tapering
Monzen Y, Kiya K, Nishisaka T. Kimura's Disease of the Orbit Successfully Treated with Radiotherapy Alone: A Case Report. Case Rep Ophthalmol. 2014 Mar 13;5 (1):87-91	28-year-old male history of blepharoptosis, exophthalmos, a reduction of visual acuity as well as a visual field defect in the right eye Inferior hemianopsia with a scotoma in the center was present. Double vision and disturbance of the lateral gaze in the right eye were also pointed out. A mass on the right side of the neck had been observed 19 years earlier	An incisional biopsy of the mass of the right orbit was performed by a neurosurgeon Irradiation with 21.6 Gy was administered to the tumor bed in a single dose of 1.8 Gy in 5 weekly fractions via a high-energy linear accelerator (6-MV X-ray). The tumor gradually diminished and ultimately disappeared. Four months after the completion of radiotherapy, improved visual acuity, and inferior visual field as well as the disappearance of the scotoma in the center
Li J, Ge X, Ma J, Li M, Li J. Kimura's disease of the lacrimal gland mimicking IgG4-related orbital disease. BMC Ophthalmol. 2014;14:158	47 year old Chinese man presented with history of 26 months swelling and redness left upper eyelid. On biopsy found to have Kimura's disease occurring in the left lacrimal gland with increased serum levels of IgG4 mimicking IgG4-related disease	Surgical excision with oral steroids had satisfactory outcome on follow-up

Contd...

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Author/Journal	Patient details	Management and outcome
Praeger AJ, Tsui A, Hardy TG. Kimura disease: rare cause of a slowly progressive orbital mass. Clin Exp Ophthalmol. 2014 May-Jun; 42 (4):385-7	20-year-old male with left upper lid swelling since 5 year. He had known history of associated nephrotic syndrome, a sub mandibular lump for which he had underwent excisional biopsy at age of 10 and a left elbow mass excised at age of 19 years	He underwent orbitotomy through a lid crease incision. Postoperatively 5 months, he had normal vision and a good cosmetic result
Gonçalves AP, Moritz RB, Aldred VL, Monteiro MR. Bilateral extraocular muscles enlargement from Kimura's disease of the orbit. Indian J Ophthalmol 2016;64:538-40	44 year old male with bilateral extraocular muscles enlargement	Managed with oral prednisolone for 6 months with slow tapering
Francis, Irimpan L.; Ramalingam, Mohan; Ali, Nadir A. M.; Telisinghe, Pemasari U. Recurrent Kimura Disease of the Inner Canthus With No Lymphadenopathy, Ophthalmic Plastic and Reconstructive Surgery: May/June 2017; 33 (3S) : S45-7	39-year-old male from Malaysia presented with swelling in his left inner canthus for 3 months	Surgical excision was done with 1 year follow-up with no recurrence
Lee JH, Kim JH, Lee SU, Kim SC. Orbital Mass With Features of Both Kimura Disease and Immunoglobulin G4-Related Disease. Ophthalmic Plast Reconstr Surg. 2018 Jul/ Aug; 34 (4)	30-year-old man with a 3-month history of protrusion and conjunctival injection of the right eye	After surgical resection (orbitotomy), protrusion and conjunctival hyperemia of the right eye improved. The patient was prescribed oral steroids for 1 week to reduce postoperative orbital inflammation and was observed, without recurrence or complications, for 3 months postoperatively
Chakraborti C, Saha AK, Bhattacharjee A, Lakra R. Kimura's disease involving bilateral lacrimal glands and extraocular muscles along with ipsilateral face: A unique case report. Indian J Ophthalmol 2019;67:2107-9	23-year female presented with bilateral recurrent swelling of eyelids along with ptosis and proptosis for last 3 year	Responded well to systemic cortico-steroids
Carrera W, Silkiss RZ. Kimura's disease of the lacrimal gland with concomitant chronic sinusitis. Orbit. 2021 Apr; 40 (2):169-170	18-year-old man of Filipino ancestry with firm swelling of his left upper eyelid for 3 years. He had a history of nephrotic syndrome as a toddler	The lacrimal lesion was successfully treated with partial excision, and the sinusitis resolved with oral doxycycline and intranasal corticosteroid