Recurrent Kimura’s Disease: Excellent Response To Cyclosporine

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Abstract
Kimura’s disease is a chronic inflammatory disorder involving the skin, subcutaneous tissues and lymph nodes, predominantly in the head and neck region. Though surgery, intralesional or systemic steroids or radiation therapy have been the mainstay of treatment recurrence is a common problem. On the basis of occasional case report of Kimura’s disease responding to cyclosporine, we attempted oral cyclosporine in our patient with dramatic improvement.

INTRODUCTION
Kimura’s disease, also known as epithelioid hemangioma or atypical pyogenic granuloma was first described as an independent entity by Kimura et al in Japan. The first description of similar cases however was by Chinese authors Kimm and Szeto in 1937 with a clear predominance in Asian population or those with Asian ancestry.

CASE REPORT
A 43-year old executive presented to us with a gradually progressive swelling of the left cheek extending up to the left ear pinna and part of the neck since the last 18 months. He did not have any history of fever, weight loss, or tobacco and alcohol addiction. The patient did not have any dry mouth, sialhorrhea, change in the size of the swelling with the sight or smell of food or pain on chewing. There was a past history of recurrent such swellings four times in the past: once on the same side behind the ear, twice on right side in the parotid region and in the neck, on different occasions all over a period of last 10 years. Each time, the swelling had been surgically excised. The patient had two pre-surgical cytology and two excision biopsy reports with him all suggesting varied inflammatory tissue and on one occasion reactive lymphadenitis. One of the reports suggested an eosinophilic infiltration.

On examination the patient had normal vital parameters, good oral hygiene and no evidence of any generalized lymphadenopathy. The left sided swelling was soft, lobulated with ill-defined margins about 10 x 10 cms in size, non-tender, freely movable and overlying skin was not separable [Fig. 1a]. He also had a small similar swelling on the right retroauricular lesion. Investigations revealed a normal blood count with a marked eosinophilia of 45% and an absolute eosinophil count of 3150 cells per cu mm. Biochemical parameters, and radiographs of the chest as well as cervical spine were normal. In view of the recurrent history and high eosinophil count a possible differential of eosinophilic leukemia, angiolymphatic hyperplasia with eosinophilia, and Kimura’s disease were considered. Normal hematological parameters, with absence of systemic features made eosinophilic leukemia unlikely. As the patient was reluctant for a biopsy, aspiration cytology of the affected lesion was performed and was suggestive of Kimura’s disease.

As the patient had already had recurrent surgeries, on the basis of a case report from Japan available in literature, we decided to give the patient a trial of oral cyclosporine at a dose of 5 mg/kg/day in two divided doses. Renal function tests and blood counts were monitored weekly. The patient responded remarkably with an approximate 80% reduction in size of lesion within two weeks of therapy. We continued therapy for 4 weeks [Fig. 1b] and then tapered by halving the dose every four weeks, total therapy lasting for 14 weeks. The patient has been off the drug for nearly 6 weeks now and asymptomatic so far.

DISCUSSION
Kimura’s disease is essentially a benign disease predominantly affecting the head and neck region, major salivary glands and lymph nodes though variable involvement of oral cavity, trunk, groin and limbs as
also various lymph nodes have already been described.\textsuperscript{1,5} The differential diagnosis includes malignant lymphoma, eosinophilic granuloma, Mikulicz disease and angioimmunoblastic lymphadenopathy, though the closest differential is probably angiolymphatic hyperplasia with eosinophilia (ALHE).\textsuperscript{5} The two are different disease entities with a number of features in common like male predominance, predilection for the head and neck regions, tendency to recur, and vascular nature of the lesion with lymphoid and eosinophilic infiltrates. However, Kimura’s disease was usually seen in younger Asian individuals for a longer duration.\textsuperscript{4} The main histopathological difference is the presence of “histiocytoid” or “epithelioid” blood vessels with vacuolated endothelial cells and intact germinal centers in ALHE while in Kimura’s disease, germinal centers are destroyed due to heavy infiltration of eosinophils, rarely even forming microabcesses and vascular channels may be seen, but vacuolated endothelial cells are absent.\textsuperscript{1,6} IgE deposits in the germinal centers are also characteristic though this test could not be done as the patient was unwilling for excision biopsy again and FNAC had to be used.

The etiology of Kimura’s disease is uncertain, but many theories have been suggested including sub clinical parasitic or candida infection to an abnormal atopic response in view of the high peripheral eosinophilia.\textsuperscript{1}

Recurrence is known in Kimura’s disease to the extent of about 25 to 40%.\textsuperscript{1,8} Management guidelines for recurrent disease are unclear, but steroids or intralesional irradiation have been attempted without much of a satisfactory response.\textsuperscript{1} Overactivity of the helper T-cells (Th2) and Th 2 cytokines in Kimura’s disease has been suggested with a subsequent suppression of these cytokines by cyclosporine-A.\textsuperscript{7} Cyclosporine has also been tried in a patient of Kimura’s disease in Japan with complete resolution.\textsuperscript{2} On this basis we attempted a similar therapy in our patient with excellent results.

The recommended dose of cyclosporine is about 5 mg/kg/day and though the duration is uncertain we gave the therapy for about four weeks though excellent
response was obtained within the initial two weeks. A slow taper of dose is advisable to prevent recurrence. No adverse effects were noted during therapy. Ideally monitoring of cyclosporine levels is recommended, though we could not do the same and only renal and hematological parameters were measured. The eosinophil count dropped markedly from 45% at the start of therapy to 11% within two weeks and 4% at four weeks [Fig 1.b]. Even now the eosinophil count remains within normal and may serve as a useful test to predict a likely recurrence.

To the best of our knowledge this is the first such reported case from the Indian subcontinent and the excellent response to cyclosporine is very encouraging, though further studies and observations may be required.

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References

Announcement
Echo and Color Doppler Centre, Sunder Lal Jain Hospital Complex, Ashok Vihar, Phase III, Delhi is organizing the XIIIth Comprehensive Course on Echocardiography from 2nd April to 7th April 2006. The course is absolutely based on American and European standards with emphasis on “Hand’s-on Training programme”. The course is accredited by IMA Academy of Medical Specialties, Indian Academy of Echocardiography and Delhi Medical Council.

A limited number of participants with Hands on Training Programme shall be enrolled as in previous courses. An accredited certificate shall be issued to each participant.

For further details contact: Dr. Rakesh Gupta, Organizing Secretary Cum Course Director, Echo & Color Doppler Centre, Sunder Lal Jain Hospital, Ashok Vihar III, Delhi - 110 052.

Announcement
One Year Fellowship in Infectious Disease at the PD Hinduja National Hospital and Medical Research Centre, Mumbai. 1st April 2006 to 31st March 2007

No. of fellowships : 2
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Interested candidates may send their complete CV (please mark the envelope “for ID fellowship”) Mr. AK Menon, Manager Personnel, PD Hinduja National Hospital and Medical Research Centre, Veer Savarkar Marg, Mahim, Mumbai 16.

Suitable candidates will be called for an interview. Selected candidates will be required to pay a non-refundable deposit and will be entitled to a course stipend and hostel accommodation.

Last date for receipt of application: 1st March, 2006

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