ISSN: 2395-6429

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170323

RESEARCH ARTICLE

KIMURA DISEASE: A RARE CAUSE OF LYMPHADENOPATHY

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ARTICLE INFO

Article History:
Received 11th September, 2017
Received in revised form 5th October, 2017
Accepted 16th November, 2017
Published online 28th December, 2017

ABSTRACT

Kimura disease is a rare but distinctive chronic eosinophilic inflammatory disorder that is characterized by tumor-like lesions in the soft tissue and enlargement of nodes of the head and neck. Here we present the case of a 16 years male patient with low grade intermittent fever with generalized lymphadenopathy without any pallor or hepatosplenomegaly. On investigation there was very high leukocyte count with eosinophilic predominence. Lymph node biopsy revealed features consistent with Kimura's disease. The patient recovered spontaneously. The diagnosis of Kimura Disease can be difficult and misleading as patients with this disease are often misdiagnosed as lymphoid malignancies.

INTRODUCTION

Kimura disease is a chronic disorder with angiolymphatic proliferation. It is endemic in Asia particularly the Far East occurring in the 3rd decade with a 3.5-7:1 strong male predilection. It presents with a plethora of symptoms but commonly with triad of subcutaneous swellings in the head and neck region, blood and tissue eosinophilia, and raised IgE levels. It's a great mimicker like in our case clinical examination and initial biochemical tests can be suggestive of a lymphoproliferative disorder but biopsy from lymph node proving otherwise. There are different modalities of treatment but as in our case spontaneous resolution may also occur.

Case presentation

A 16 year old male patient, student by occupation, presented to us with chief complaints of fever for last 20 days. Fever was low grade, intermittent in nature. There was dry cough for the same duration. It was not associated with any shortness of breath, wheezing, rash, joint pain, pain abdomen, jaundice or bleeding from any site. There was no significant past history of any medical or surgical illness. His mother suffered from pulmonary tuberculosis six years back for which she was adequately treated. He had no history of addiction or high risk behavior. There was no history of similar or any major illness in his family. His sleep was normal but appetite was decreased.

On examination, the patient was alert, conscious, co-operative, built was below average with BMI of 15.9. Pallor, clubbing, jaundice, cyanosis were absent, pulse was of 100/m, regular, blood pressure was of 100/70 mm Hg. No significant skin, hair, nail changes were found. JVP was not elevated. There were enlarged upper cervical lymph nodes, three in number, largest one measuring about 1x1.5 cm, in right axilla one central group of lymph node about 2x1cm was palpable, multiple enlarged right sided inguinal nodes with largest one measuring 2x1.5cm, right epitrochlear lymph node was also enlarged(1x1cm). There was no sternal tenderness and no organomegaly. Other systemic examinations were also within normal limit. On routine investigations, Hemoglobin was 12.2gm/dl, Total leukocyte count-68000/dl, Platelet-2.32lakhs/dl and on Differential count-Neutrophil 15%Lymphocyte 08%Monocyte 6%Eosinophil 71%. ESR was 42mm in 1st hour and MCV/MCH/MCHC was 83/28.6/34.4 respectively. Urea and Creatinine were - 23mg/dl and 0.5mg/dl. Uric acid was 3.3 mg/dl. Serum LDH was elevated-582mg/dl. Serum Sodium was134 mEq/Lt and Potassium-4.3mEq/Lt. Liver function test showed transaminitis -Total bilirubin-0.36mg/dl, Direct bilirubin-0.09mg/dl,AST-71U/Lt,ALT-122U/Lt, ALP-631U/Lt. Total serum protein-7.9gm/dl along with altered albumin: globulin ratio-3.7:4.2. Urine for routine examination revealed-pH 6.5, sugar, albumin. casts or crystal was absent. ICTC was non reactive. Chest X-ray revealed no significant abnormality. Ultrasonography of abdomen showed borderline enlarged liver with normal echotexture, mildly raised cortical echo texture of right kidney with few enlarged pre and Para aortic lymph node. FNAC from lymph node was done which showed predominantly small mature lymphocytes admixed with centroblast, centrocyte and immunoblasts; fair number of eosinophils were also seen; no granuloma or evidence of malignancy was seen. Impression was reactive hyperplasia of lymph node.

So for confirmation excisional lymph node biopsy was done which showed lymphoid follicles with expansion of interfollicular areas and infiltration by large number of eosinophils admixed with histiocyte and lymphocytes. Proliferated vascular channels lined by epithelioid endothelial cells were also present. No granuloma or RS cell was present. Features are consistent with Kimura's disease.

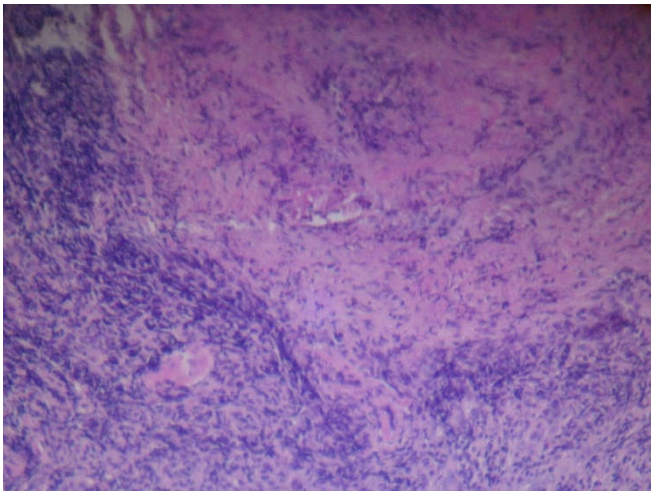

Figure 1 Histopathology of Lymph Node

The patient was treated symptomatically with antipyretics on as and when required basis. The patient became afebrile after a week and was discharged. He is on regular follow-up on OPD basis for past 6 months and is totally asymptomatic with no recurrence of fever, lymphadenopathy or blood eosinophilia.

DISCUSSION

Kimura disease is a benign, chronic inflammatory disorder of unknown etiology that commonly presents as multiple lymph node enlargement or subcutaneous masses in the head and neck region. It was first described in Chinese patients in 1937 as eosinophilic hyperplastic lymphogranuloma and the current nomenclature is in vogue since 1948[(1)]. The disease has been described in all races and ethnic groups with an increased prevalence in south-east Asia. Very few cases have been reported till date from India. There is a male preponderance with most studies show a ratio of 3.5:1 to 7:1 and the usual age of presentation is in the third decade[(2)].

Patients with Kimura disease typically present with nontender, pruritic subcutaneous nodules and masses in the head and neck, especially in the parotid and submandibular regions. These lesions are often associated with lymphadenopathy. Less frequently, the orbit (including the eyelids, conjunctiva, and lacrimal glands), paranasal sinuses, epiglottis, tympanic membrane, parotid gland, and parapharyngeal space may be involved. Although Kimura disease mainly affects the head and neck, involvement of the trunk, extremities and inguinal lymph nodes has been reported [(3)]. In addition, a presentation of Kimura disease as a pulmonary hilar mass has recently been described [(4)]. In 20% cases there is an association with nephrotic syndrome. Laboratory tests have shown peripheral eosinophilia with increased serum IgE. Serum urea and creatinine may also be elevated in cases with nephrotic syndrome which was not so in our case(5).

The appearance of Kimura disease on imaging modalities, including CT scanning and MRI, is variable and is thought to be due, at least in part, to the variable degrees of vascular proliferation and fibrosis within individual lesions. One of the largest case series to date notes the characteristic findings to be multiple ill-defined, enhancing lesions around the parotid gland, with associated lymphadenopathy[(6)].

Biopsy and histopathological examination is the keystone for accurate diagnosis.

Lymphoid nodules with discrete germinal centers with Warthin-Finkeldy type polykaryocytes, vascularisation of germinal centres increased post-capillary venules in the paracortex occupy an area extending from the reticular dermis to the fascia and muscle. A marked eosinophilic infiltrate and eosinophilic abscesses are present. Immunoperoxidase studies show IgE reticular networks in germinal centers. Nondegranulated surface IgE-positive mast cells are present in the paracortex. Kimura's disease may represent an aberrant immune reaction to an as yet unknown stimulus. Although the individual histological features are nonspecific, the constellation of features is highly characteristic of Kimura's disease [(7)].

There is no consensus yet on effective treatment of the disease. In some cases there may be spontaneous regression of the masses as it was in our case but generally local recurrence is the rule. Corticosteroids are the first line of treatment, short course for 12 weeks orally or intralesional therapy is recommended [(8)]. Cyclosporine has been reported to induce remission in patients with Kimura disease [(9)]. A dose of 5 mg/kg/d was effective, but, in most cases, the lesions recurred upon cessation of therapy [(10)]. In one study a combination of cyclosporine and steroids has been used with better results [(11)]. Intravenous immunoglobulin (IVIG) was used in one patient as a steroid-sparing agent, and he remained disease free more than 6 years after follow-up [(12)].

Oral pentoxifylline has been reported to be effective in one patient with Kimura disease; however, the lesions relapsed after discontinuation of therapy [(13)].

All trans -retinoic acid in combination with prednisone has resulted in remission of Kimura disease in one patient, and he remained disease free 12 months after discontinuation of all therapy [(14)].

Imatinib may be an effective treatment for Kimura disease, based on advances in research for therapy in hypereosinophilic syndrome, but further investigation is necessary [(15)].

A novel mode of therapy which has been tried is intra-lesional pulse dye laser. The rationale for using the 595-nm ultra-long PDL in KD, is that it is possible selectively to target the haemoglobin within the increased vascular structures of these condition and eliminate the lesion without scarring. The ultra-long pulse width delivers greater energy to targeted blood vessels over longer periods of time to enable effective destruction of larger vessels, avoiding the photo-acoustic response. In addition, the dynamic cooling device allows the safe use of higher frequency and wavelength of 595 nm penetrates deeper into the dermal tissue [(16)].

Surgical excision has been the mode of choice of treatment both for primary disfiguring facial lesions and in recurrent or resistant cases [(17)].

Radiotherapy has occasionally been used to treat recurrent or persistent Kimura disease lesions. A report by Hareyama *et al* [(18)] reported on the use of radiotherapy at dosages of 26-30 Gy; local control was achieved in 74% of lesions. Another study

demonstrated that radiotherapy (21.6-45 Gy) was more effective than local excision and steroid treatment, with local response rates of 64.3% versus 22.2%, respectively. No adverse effects were observed during a mean follow-up period of 65 months [19]. However, considering the benign nature of Kimura disease, further investigation may be required, and caution using radiation outside of recurrent, disfiguring lesions is required.

In earlier literature Kimura's disease was used synonymously with Angiolymphoid hyperplasia with eosinophilia (ALHE) but different clinicopathological evidence has been to the contrary. The common features shared by both conditions included 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 individuals for a longer duration and occurred as a deeply seated, large soft-tissue mass, without significant change of the overlying skin initially. In addition, it was often accompanied by peripheral blood eosinophilia and elevated serum IgE. In contrast, ALHE lesions were multiple small dermal papular or nodular eruptions observed in older patients and present for a shorter duration; they were less frequently accompanied by peripheral blood eosinophilia. The main histopathological difference was the presence of "histiocytoid" or "epithelioid" blood vessels in ALHE but not in Kimura's disease. Kimura's disease was further characterized by eosinophilic folliculolysis; IgE deposits in the germinal centers; and frequent involvement of regional lymph nodes, salivary glands, and skeletal muscles. The eosinophilic infiltration, especially the formation of eosinophilic microabscesses, along with increased number of small blood vessels, perinodal eosinophilic infiltration, and eosinophilic folliculolysis characterized the nodal involvement by Kimura's disease [20].

CONCLUSION

Kimura's Disease is a chronic benign inflammatory condition endemic to Asians. If not properly diagnosed, the cervical lymphadenopathy in Kimura's disease may be initially mistaken for a malignancy. However, due to a well-obtained clinical history and histopathologic awareness a proper diagnosis has been established in this case. Surgical excision is the treatment of choice and it is notorious for its high rate of recurrence but our patient has been asymptomatic for the last 6 months without any relapse.

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