

## Kimura Disease: A differential diagnosis in a nephrotic child

Aziz A, Mohamad I, Zawawi N

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### Authors:

#### Azliana Aziz

(Corresponding author)

MB Bch BAO

Department of Otorhinolaryngology-

Head & Neck Surgery, School of

Medical Sciences, Universiti Sains

Malaysia, 16150 Kota Bharu

Kelantan, Malaysia.

Email: az.aziz21@yahoo.com

#### Irfan Mohamad

MMed ORL-HNS

Department of Pathology, School

of Medical Sciences, Universiti

Sains Malaysia, 16150 Kota Bharu

Kelantan, Malaysia.

#### Norzaliana Zawawi

MPath

School of Dental Sciences, Universiti

Sains Malaysia, 16150 Kota Bharu

Kelantan, Malaysia

### Abstract

Kimura disease presents as benign lesion and is commonly present among the Asian population. It is a disease with a favourable prognosis and a peak age of onset in the third decade. It is a chronic inflammatory disorder of unknown etiology that involves the lymph nodes and subcutaneous tissues of the head and neck region. We report a case of a 15-year-old boy with multiple Kimura lymphadenopathies involving the left posterior auricular region as well as the anterior and posterior triangles of the neck.

### Introduction

Patients with head and neck lesions can present to primary care for initial investigation and are commonly referred to otorhinolaryngologists. The involvement can be a single or multiple and painful or painless enlarging pathology. The most common neck mass is a cervical lymphadenopathy for which a variety of causes or disorders including infectious, autoimmune, and allergic diseases as well as benign and malignant neoplasms have been reported. Others may present with masses such as keloids, osteomas and cysts. Less commonly, a Kimura lymphadenopathy case may present. Kimura lymphadenopathy most typically affects young Asian males with an incidence of coexisting renal disease ranging from 10% to 60%.<sup>1</sup>

### Case report

A 15-year-old boy, with an underlying steroid-resistant nephrotic syndrome, was referred to us for a painless left posterior auricular lesion of more than 5 years in duration. The lesion was gradually increasing in size with rapid enlargement within the past 2 months. There was no history of otalgia, otorrhoea, hearing impairment, trauma or insect bites to the area. He had no significant nose or throat symptoms, no constitutional symptoms or contact with any tuberculosis patients. He was diagnosed with nephrotic syndrome at the age of 7. However, he developed a resistance to steroid treatment and had a number of relapses prior to referral to our clinic. The renal biopsy done was inconclusive. He was treated with high dose of oral prednisolone and oral

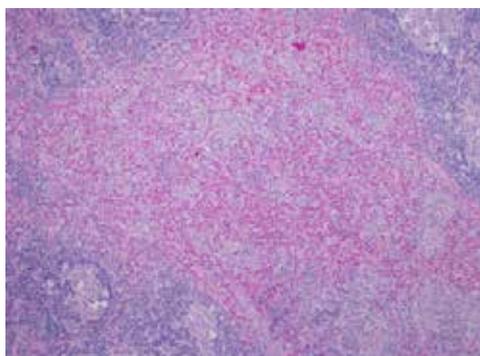
Cyclosporin A. The patient was non-compliant to medications. Prior to his referral to our service, he had an excisional biopsy done by the Surgical Department for a similar lesion at the left posterior triangle of the neck.

On examination, there was a smooth-surfaced left posterior auricular lesion measuring 4cm x 2cm in size, which was non-tender, fixed and fluctuant in consistency. On neck palpation, there were also multiple small lymph nodes present in the anterior and posterior triangles of varying sizes. The largest node was at posterior triangle measuring 1cm x 2cm. Examination of the ears was normal.

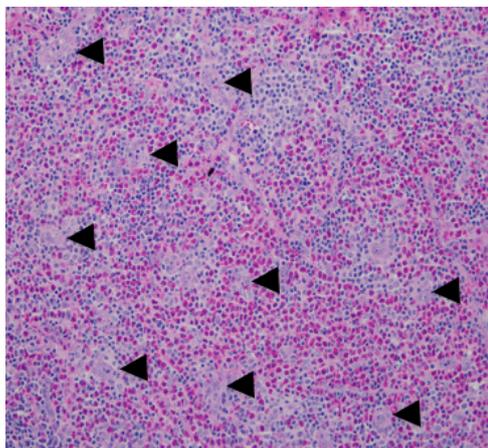
An ultrasonography of the neck revealed multiple cervical lymphadenopathies in the left posterior auricular region, and the anterior and posterior triangles with the left posterior auricular nodes homogenously hyperechoic. It also demonstrated increased vascularity. Other enlarged nodes in the anterior and posterior triangles varied in sizes contained multiple target signs and showed increased vascularity.

Subsequently, an excisional biopsy of the left posterior auricular swelling was done. A 4cm x 3cm mass was completely excised. The histological examination revealed lymph nodes composed of variable sizes of lymphoid follicles with prominent germinal centers. The parafollicular cortex (**Figure 1**) area was heavily infiltrated by eosinophils with areas of eosinophilic abscess formation. Interstitial fibrosis and hyalinized vessels were present however no Warthin-Finkeldey polykaryocytes or folliculolysis were noted (**Figure 2**). Features of Hodgkin's lymphoma are not readily identified either

morphologically or immunohistochemically. This finding is consistent with Kimura Disease. A similar pathology was reported from the excisional biopsy done earlier by the surgical team. The patient was reviewed for the next 6-month period and no recurrence was noted at the site of the excision. However, after approximately a year, the patient developed a similar new lesion on the neck but further surgical intervention was not contemplated. The patient continues to attend his regular pediatric medical follow-ups and reviews.



**Figure 1:** The parafollicular cortex area shows intense infiltration by eosinophils and capillary hyperplasia with reactive lymphoid follicles seen at the periphery of this figure. (Hematoxylin and eosin, 10X)



**Figure 2:** Eosinophilia and capillary hyperplasia (arrows). (Hematoxylin and eosin, 20X)

### Discussion

The general presentation of head and neck masses in the primary care setting may vary, ranging from benign lesions to nodal metastasis. Other common head and neck lesions may include cervical lymphadenopathy caused by infections such as tuberculosis, lymphoma and allergic and autoimmune diseases.

Kimura disease, which was first reported in 1937<sup>2</sup> by Kimm and Szeto, is a cause of cervical lymphadenopathy which most often involving the cervical and posterior auricular lymph nodes. It is a common disease in the East Asian population with a higher preponderance of the disease in males. It also has a favorable prognosis and a peak age of onset in the third decade.<sup>3</sup>

Kimura disease is characterized by painless subcutaneous masses in the head and neck region occurring commonly in the pre-auricular area. In our case, the patient presented with a painless site in the left posterior auricular region. It is not known why the disease commonly occurs at this site. It may also affect axillary, epitrochlear and inguinal lymph nodes, as well as submandibular salivary glands.<sup>4</sup> Rarely does it involve nasal sinuses, the oral cavity, the orbit and median nerves or the lacrimal glands.

It is an inflammatory condition which is often associated with elevations in serum immunoglobulin E levels and eosinophilia.<sup>5</sup> In our case, there was the presence of tissue eosinophilia. The tissue obtained was heavily infiltrated by eosinophils with areas of eosinophilic abscess formation present. This is consistent with a study done in the United States involving a series of 21 cases of Kimura disease in which the majority had eosinophilia. Other histological features include follicular hyperplasia, eosinophilic infiltrates and the proliferation of post-capillary venules.<sup>6</sup>

Interestingly, 12 percent of patients with Kimura disease have proteinuria<sup>7</sup> and nearly half of the cases have nephrotic syndrome. A steroid-resistant nephrotic syndrome associated with Kimura disease has been reported. Hung et al also reported a case similar to ours in which a 3-year-old boy with Kimura disease-associated nephrotic syndrome initially responded well to steroid treatment.

However, he suffered frequent relapse until finally, he became steroid resistant and a progressive decline in renal function occurred.<sup>8</sup> In our patient, the nephrotic syndrome was diagnosed earlier than the Kimura disease and was treated with high doses of oral prednisolone and oral Cyclosporin A. Non-compliance with medications can also lead to the recurrence of the Kimura lymphadenopathy despite recent evidence showing a positive result with low-dose Cyclosporin A.<sup>8</sup>

The approach to the clinical problem involves a complete history and examination. The features that are strongly suggestive of Kimura disease include a painless, subcutaneous mass in the pre-auricular region, a patient of East Asian descent and a male in his third decade.

For further workup, blood tests, a radiological investigation and a biopsy are required.

A definitive diagnosis is based on the histopathological evaluation of the resected lesion. It should be noted that no pathognomonic features have been recognized for Kimura disease.<sup>9</sup> The most common histological features found in Kimura disease include reactive follicular hyperplasia, eosinophilic infiltration and postcapillary venules proliferation were found in the presented case. Other features which are frequently present such as fibrosis, polykaryocytes, eosinophilic abscesses and vascularization of the germinal centres as described by Hui et al<sup>10</sup> were not identified in our case.

Multiple treatment methods have been proposed for Kimura but surgical resection is the most common. However, the recurrence rate remains high at approximately 60 percent after local excision of the lesion. Recurrence has been reported in one of the five cases which have undergone complete resection.<sup>11</sup> Our patient also had a recurrence of the disease at location other than the excision site.

Particularly for a recurrence of the disease, some case reports suggest benefit from corticosteroids, the usage of the selective H1 receptor antagonist cetirizine<sup>12</sup> or radiotherapy.<sup>13</sup> Others propose the use of low-dose Imatinib for an excellent outcome in Kimura disease treatment.<sup>4</sup>

However, it was found that tumor recurrence is common after the cessation of steroid therapy<sup>11</sup>. The successful complete remission with cetirizine for 6 months has been reported. Cetirizine in this case acts as anti-inflammatory agent apart from inhibiting eosinophil chemotaxis and adhesion to endothelial cells.<sup>12</sup>

As for radiotherapy, its promising role has been highlighted when compared to local excision and systemic steroid therapy. A study showed

local response rates of 64.3% and 22.2%, respectively, for the two types of treatment. There were no side effects with a mean time of 65 months of follow-up in the radiotherapy group.<sup>13</sup> The effectiveness of radiotherapy has been supported by a few case studies using an effective total dose of radiation between 20 Gy to 45 Gy of radiotherapy. There were no adverse effects observed during a mean follow-up period of 65 months<sup>14</sup> and there have been no documented malignant transformations to date.

In selected cases, conservative management may be an option. It may be wise to leave the lesion alone due to frequent tumor recurrence, and the difficulty in obtaining a complete resection due to the infiltrative nature and multiplicity of the tumor and the associated draining lymphadenopathy.<sup>11</sup> We opted for surgical excision in this case, as the lesion was accessible and could be excised safely for histopathological confirmation of the diagnosis. The patient was spared from the potentially harmful side effects of radiotherapy or cytotoxic therapy.

Currently, there is no proposed duration of follow up. However, a tumor recurrence four years after resection has been reported<sup>11</sup>. No case of malignant transformation of the Kimura Lymphadenopathy has been reported in the literature.

### Conclusion

Diagnoses of head and neck masses are challenging to the Primary Care Practitioner as there can be multiple differential diagnoses. Occasionally, rare diseases such as Kimura Lymphadenopathy may be present. In such instances, referral to a specialist is in order. Strong indications of Kimura disease include a painless, subcutaneous mass in the pre-auricular region involving a male patient of East Asian descent in his third decade. Apart from a clinical determination, the diagnosis of Kimura disease can be made from radiological and most importantly histopathological examinations. Challenges remain in the management and treatment of the disease. However, the disease is fortunately benign as no malignant transformation has yet been described.

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