

Kimura's Disease: Diagnostic Challenge and Treatment Modalities

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SUMMARY

Case Report: Five cases of Kimura's disease had been treated in our centre from year 2003 to 2010. All cases were presented with head and neck mass with cervical lymphadenopathy. Surgical excision was performed for all cases. Definite diagnosis was made by histopathological examination of the resected specimens. One out of five cases developed tumour recurrence four years after resection.

Conclusion: Surgical excision is our choice of treatment because the outcome is immediate and definite tissue diagnosis is feasible after resection. Oral corticosteroid could be considered as an option in advanced disease. However, tumour recurrence is common after cessation of steroid therapy.

KEY WORDS:

Kimura's disease, eosinophilia, lymphadenopathy

INTRODUCTION

Kimura's disease is a rare immune-mediated inflammatory disorder, primarily is seen in Asian males in the second and third decades of life. It is characterized by painless head and neck mass, regional lymphadenopathy, blood and tissue eosinophilia and elevated serum Immunoglobulin E level. We report a case series of Kimura's disease that were seen in our centre from year 2003 to 2010.

RESULTS

Clinical findings: Majority of the cases were male with age ranging from 16 to 52-year-old. All cases were presented to us with a mass in the head and neck region, involving subcutaneous tissue or salivary glands. Regional lymph nodal involvement was observed in all cases. There was no significant ENT endoscopic finding in all patients. The duration from onset of disease to treatment was ranging from 6 to 36 months.

Haematology and blood chemistry: Peripheral blood eosinophilia was observed in all patients during the initial presentation. IgE level was not measured.

Diagnostic imaging findings: Computed tomography scan was performed in four cases. A submandibular mass was excised without imaging study.

Treatment: All cases were treated with surgical excision. Superficial parotidectomy was performed for two patients who had parotid gland involvement. One of the parotid cases was advised for surgery after a poor response to ten-week course of oral corticosteroid. There was no post-resection adjuvant therapy given to all patients.

Microscopic features: All resected specimens were sent for histopathological examination. In overall, all specimens showed lymphoid follicles with formation of various sizes germinal centres. There were polyclonal plasma cells and numerous eosinophils in inter-follicular areas, forming occasional eosinophilic abscesses. The background showed vascular proliferation with plentiful thin-walled post-capillary venules. The vessels were lined by flattened endothelium. There was no morphological or immunohistochemical evidence of Hodgkin lymphoma. The salivary gland tissue appeared to be normal in two of the parotid cases.

Follow-up: In the period of two to eight years follow-up, four patients were relapse-free with good outcome. One of the patients developed tongue spindle cell carcinoma five years after left superficial parotidectomy. He had undergone left hemiglossectomy and neck dissection. A patient developed relapse of disease at right level II region four years after surgical excision. He is relapse-free after a second excision.

DISCUSSION

Kimura's disease was first described by Kim and Szeto in 1937 as 'eosinophilic hyperplastic lymphogranuloma'. It was named as Kimura's disease after a detailed description by Kimura *et al* in 1948.¹ It is a rare, benign, immune-mediated chronic inflammatory disorder. It is characterized by lymphoid hyperplasia, eosinophilic infiltration and elevated serum IgE level. Kimura's disease predominantly manifests as a mass in head and neck region, commonly involving major salivary glands and lymph nodes. Less frequently, axillary, inguinal and epitrochlear nodes involvement had been reported as well.

This article was accepted: 23 September 2014

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Table I: Clinical Profiles of Five Kimura's Disease Cases in Sarawak General Hospital in year 2003-2010.

No.	Age (Yr) / Sex	Main lesion	Size (cm)	Duration of Symptoms (Months)	Blood Eosinophilia (X10 ⁹ /L)	Treatment	Outcome (Years of Follow-up)
1	52/F	Right parotid mass	6	36	7.2	Superficial parotidectomy	2, no rec
2	38/M	Left submandibular mass	3	10	4.5	Excision	3, no rec
3	24/M	Left parotid mass	3	6	3.7	Oral steroid followed by superficial parotidectomy	8, no rec. Developed tongue spindle cell ca 5 years after surgery
4	16/M	Right level II mass	4.5	12	2.0	Excision	6, rec X1
5	23/M	Left retroauricular mass	3.5	6	3.9	Excision	4, no rec

Abbreviation: rec - recurrence



Fig. 1: Enhanced axial cervical computed tomography (Case 4) shows a homogeneously enhancing, well demarcated right level II mass with adjacent ipsilateral subcentimetre lymph nodes.

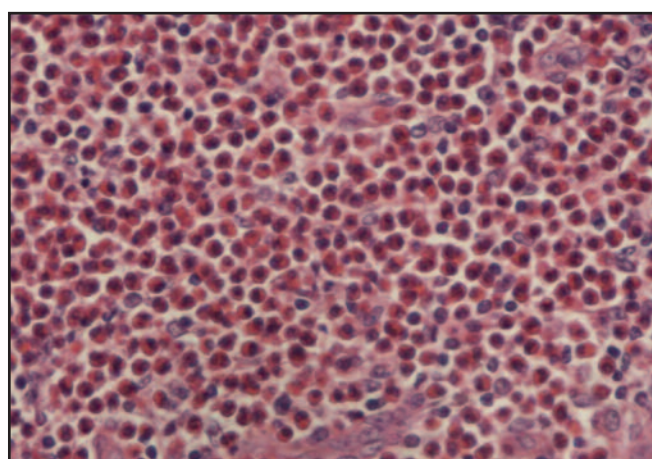


Fig. 2: Photomicrograph of right level II mass (Case 4) shows lymph node architecture with abundant eosinophils and larger activated lymphoid cells in inter-follicular areas. (Haematoxylin & eosin X 400).

The histological characteristics of Kimura's disease are eosinophilic tissue infiltration, lymphatic follicular hyperplasia, fibro-collagenous deposition and vascular proliferation. Its additional features include prominent germinal centres, folliculolysis and marked fibrosis. Fine needle aspiration and biopsy are of limited value because there is lack of pathognomonic feature in the histopathological and cytological examinations. Substantial amount of tissue specimen is required for confirmation of diagnosis. Therefore, haematological, serological and imaging studies are valuable for a provisional diagnosis before a definite histological diagnosis is obtained from the resected specimen.

Blood eosinophilia and elevated serum IgE level are the important markers in Kimura's disease. Hiroshi et al had described blood eosinophilia at mean count of 35.2 % with elevated IgE in all Kimura's cases.² In a study of parotid mass, there was significant difference in eosinophil count between Kimura's disease and parotid malignancy. Blood eosinophilia was exclusively observed in Kimura's disease. This remarkable finding is useful in determining the nature of parotid mass at the preliminary stage of investigation. All of our cases showed blood eosinophilia as described.

Several studies had described the findings of Kimura's disease in computed tomography, magnetic resonance imaging and ultrasonography.³ However, even with the combination of multiple radiological modalities, diagnosis is not feasible with the imaging solely. Kimura's disease displays non-specific intensity and signal change on computed tomography and magnetic resonance imaging due to its varied degree of inflammation process. It always exhibits ill-defined margin, heterogenous intensity, subcutaneous infiltration and enlarged draining lymphadenopathy.³ Nevertheless, it could manifest as a well-demarcated and homogeneously enhanced lesion as well (Figure 2). Malignancy could hardly be excluded with these ambiguous findings. Thus, the role of imaging is practically more useful in delineating the tumour extension for resectability.

Kimura's disease is difficult to be eradicated because it is a systemic immune-mediated disorder with local infiltrative behaviour. Multimodal treatment has been studied with limited success, hampered by the unwanted side effects of treatment or tumour recurrence. The treatment options include surgical excision, radiotherapy, oral corticosteroid and cytotoxic therapy. Complete surgical excision is preferable to others because its outcome is immediate and definite diagnosis can be made from histopathological

examination of the tumour. Furthermore, patients are spared from potential harmful side effects of radiotherapy or cytotoxic therapy. However, surgery is plagued by a few problems: (1) Frequent tumour recurrence; (2) Difficult complete resection because of its infiltrative nature; (3) Multiplicity of tumour and associated draining lymphadenopathy. Tumour recurrence is not uncommon even after complete resection. In our series, a case of tumour recurrence occurred in total five cases.

Corticosteroid therapy has not shown convincing results so far because its effect is transient. Tumour recurrence is common after termination of steroid. One of our cases showed limited response to oral steroid which resort to surgical excision eventually. The side effects of long-term steroid administration discourages us from continuing steroid therapy. Several reports demonstrated satisfactory results with long term oral cyclosporine A. Beccastrini E *et al* had described a case in complete remission for eight years with long term low dose cyclosporine A therapy. The regression of tumour was accompanied by reduction of IgE and eosinophilia. However, the patient developed relapse soon after the cytotoxic agent was withheld.⁴

Chang AR *et al* had described the application of low-dose radiotherapy as a primary treatment for Kimura's disease. In a mean duration of 65 month follow-up, complete remission was observed in 64% of the cases.⁵ Nevertheless, radiotherapy is not routinely practised as primary treatment. Others have described radiotherapy as an effective adjuvant therapy for incomplete resection cases or salvage treatment for recurrence cases.⁵ In a study of salvage treatment for post-resection recurrence, radiotherapy had been proven to be superior to corticosteroid with lower second recurrence rate. The potential complications of radiotherapy deferred us from delivering radiotherapy to our recurrence case. We believe that the risk of radiation-induced malignancy is more hazardous to patient with this benign condition. More comprehensive studies are required to determine the safety and therapeutic dosage of radiotherapy in this scenario.

CONCLUSION

Kimura's disease is a rare clinical entity. Surgical excision is the choice of treatment in our setting because the outcome of treatment is immediate and definitive tissue diagnosis is feasible after resection. Oral corticosteroid could be considered as an option in advanced disease. However, tumour recurrence is common after cessation of steroid therapy.

ACKNOWLEDGEMENT

We would like to express our gratitude to Dr. Tan Suzet, Consultant Radiologist, Dr. Jacqueline Wong Oy Leng and Dr Joseph ak Uchang, Consultant Pathologists, Sarawak General Hospital for contributing the CT scan photograph and photomicrograph in this manuscript.

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