

Kimura's Disease: An Unusual Cause of Cervical Tumor

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Summary

Kimura's disease (KD) is an angiolymphoid proliferative disease of soft tissue with peripheral blood eosinophilia and elevated serum immunoglobulin (Ig) E. The treatment options range from conservative observation for the asymptomatic patient to surgical excision, steroid therapy and radiotherapy for symptomatic patients. Surgical excision is the most common diagnostic measure and is the treatment of choice. A case of KD in a 13-year-old Malay girl is presented. Clinically there was painless right jugular digastric mass measuring 3cm by 3cm. Her blood investigation showed pronounced eosinophilia. She underwent excision biopsy uneventfully. The biopsy from the swelling showed reactive follicular hyperplasia with prominent eosinophilia. There was no evidence of malignant change. Postoperatively after 3 years follow up, she was asymptomatic and no signs of tumor recurrence.

Key Words: Angiolymphoid hyperplasia, Cervical lymphadenopathy

Introduction

Kimura's disease is a chronic inflammatory disorder of unknown etiology. H. T Kimm and C. Szeto first described investigation of benign lymph node mass with eosinophilic infiltration in China in 1937¹. In 1948, Kimura et al published a paper describing unusual granulation and hyperplastic changes of lymphatic tissue². Since then the disease became known as Kimura's disease. It can involve subcutaneous tissue of major salivary glands and lymph nodes mainly in head and neck region^{3,4}. Other sites of presentations are oral cavity, groin, trunk and limbs.

It is primarily seen in Asian male. Although the disease can become apparent at any age, most cases have been reported in the second and third decade of life. It is male predominance (M: F=5:1). Kimura's disease is endemic in the Far East but only a few cases have been reported in non- Oriental⁴.

Case Report

A 13-year-old Malay girl presented with three years history of painless right jugular digastric swelling. There was no ear, nose and throat symptom. There was no history of fever, night sweat, loss of weight and loss of appetite. Physical examination revealed a right jugular digastric mass. It was non-tender, firm on palpation, measuring 3cm by 3cm with normal overlying skin. No other lymphadenopathy was noted. Other systemic examinations were unremarkable. Her fine needle aspiration cytology (FNAC) was inconclusive. The ear, nose and throat examination was unremarkable.

A full blood count demonstrated a white cell count (WBC) of 19.5×10^9 /l with eosinophilia of absolute count of 5.38×10^9 /l (32.4%). Her renal profile result was within normal limit. Her urine analysis result was also normal. There was no evidence of focal lesion on

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CASE REPORT

chest radiograph. Her erythrocyte sedimentation rate (ESR) was 20 mm/hr. The immunoglobulin (Ig) E concentration was markedly increased. The titers for Toxoplasmosis gondii, rubella and cytomegalovirus were non reactive. Urine analysis was normal.

Computed tomography (CT) scan of the neck revealed a benign swelling over the right jugular digastric region. There was no other cervical lymphadenopathy. The patient underwent excision of the mass under general anesthesia. Intra-operatively the nodes were easily removed from other surrounding tissue. Histological

report of her neck node showed hyperplastic follicles prominent germinal centers. There was abundant eosinophilia infiltration within the germinal centers (Fig.1). Thin wall capillaries were also present. These finding were consistent with Kimura's disease. The biopsy did not demonstrate any malignant cell including Reed Steenberg cell. These finding were important to exclude embryonic malignant tumor as well as Hodgkin lymphoma. She was well after three years post operation and there was no node swelling to suggest recurrence.

Table I: Summary of clinical differences between Kimura's disease and angiolymphoid hyperplasia with eosinophilia

	Kimura's disease	ALHE
Nationality	Oriental	Western
Age of incidence	2nd to 3rd decade	3rd to 5th decade
Gender preference	Male predominance	Equal
Lesion	Large nodule or tumor (Usually > 2cm and deep)	Papule or nodule (Usually < 2cm)
Overlying skin	Normal	Erythematous to brown
Lymphadenopathy	Common	Uncommon
Duration of history	2/12 to 10 year	3/52 to 12 year
Serum Ig E	Usually elevated	Usually normal

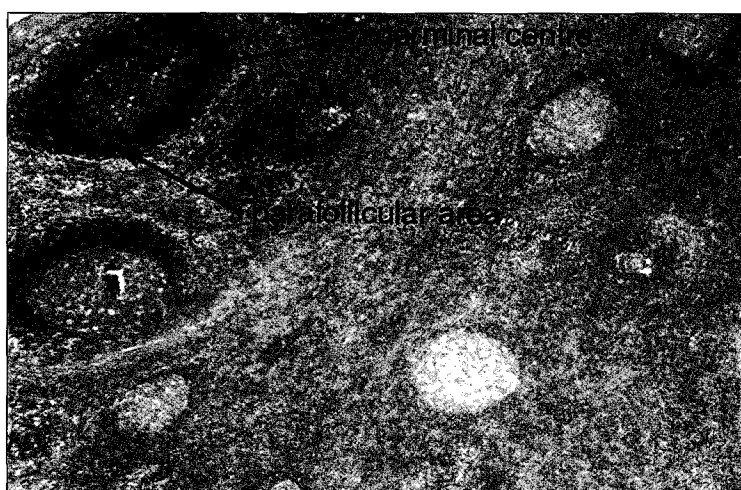


Fig. 1: Histology of Kimura's disease. Involved germinal centre with eosinophilic infiltrate within parafollicular area (H & E, original x2).

Discussion

The usual presentation in KD is with discrete nodules or a localized swelling with diffuse margin. The onset is insidious often of long duration (years). Superficial dermal and visceral involvements are rare. The systemic manifestation has been renal involvement (proliferative glomerulonephritis and marginal proliferative glomerulonephritis) leading to the nephrotic syndrome in up to 60% of patients. The pathophysiology of KD is not well understood, but it may be related to a disturbance in the normal rate of production of eosinophils and IgE^{1,4}. Currently the disease is believed to be a product of an interaction between types 1 and types 2 T helper cells. Kimura's disease may be a disease in which activated lymphocytes release cytokines and these releasing cytokines such as granulocyte macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor alpha (TNF- α) and SIL-2R caused eosinophil activation.

The mechanism of renal disease is also being investigated. The elevated serum Ig E, lymph node proliferation and eosinophilia could all account for glomerulopathy⁴. Ig E deposits along the glomerular capillary wall will cause epithelial damage in renal glomerular resulting proteinuria. Ig E deposits also have been reported by immunofluorescent along the capillary wall and paramesangial area.

On histology, several entities may mimic KD and a differential diagnosis should include angiolymphoid hyperplasia with eosinophilia (ALHE), tuberculosis, nodal metastasis, hamartoma and epithelioid hemangioma⁴. On the most controversial differential diagnosis in the literature has been between ALHE and KD. ALHE is a true vascular neoplasm whereas KD is a localized manifestation of a systemic reaction. The clinical differences are summarized in Table I⁴.

Distinct histology differences between KD and ALHE can be noted. "Histiocytoid" blood vessels are present in ALHE and have never been found in KD^{1,4}. These are described as containing hypertrophy endothelial cell with eosinophilic cytoplasm. Some of them are characteristically vacuolated. Vacuolated endothelial cells are never seen in KD^{1,4}. Other differences are the lysis of follicles. It can be found in almost every case of KD but never been seen in ALHE. The third

difference is that immuno-histochemical stains have shown Ig E in the germinal center of KD but not ALHE¹. On histology, in Kimura's disease there are occasional eosinophilic micro-abscesses.

Computed tomography (CT scan) and magnetic resonance imaging (MRI) have been useful in the investigation of the Kimura's disease⁴. A CT scan showed contrast intensity in the neck node. On MRI the involved neck nodes demonstrated high T 1 and T 2 weighted signal intensity⁴. A CT scan is useful in delineating the site of lesion separating it from the surrounding abnormal tissue. It is also important in defining the extent of the disease before any surgical intervention. An ultra-sonographic features are non-specific. It only can show variable characteristics from pure necrosis to a rather heterogeneous echo texture. Surgical excision is the most common diagnostic measure and is often therapeutic. Management options for Kimura's disease are surgical excision, systemic steroid therapy, radiotherapy and observation⁴. The treatment outcome is variable. The recurrence is common, occurring in up to 25% of cases treated with surgical excision alone⁴. After surgical excision, if there are recurrent masses, it can be managed with steroid therapy. The patient will be given a high dose of prednisolone and the dose is tapered to the minimal dose. A long-term steroid treatment can have many side effects especially among younger age group of patient.

Concern for secondary malignancy has dampened enthusiasm for the use of radiotherapy for this disease. However, 80% control (8 months to 13 years) with 25 to 30 Gy of local irradiation has been reported⁵. Indications for radiotherapy are for the patient who failed medical management or tumor relapse after steroid treatment. Moderate doses of radiation provide local control⁴.

Local initial recurrence can often be managed by local excision. If recurrence becomes frequent or patient developed symptomatic nephrotic syndrome, medical management with steroid should be initiated. For patient who failed medical management of nephrotic syndrome or with tumor that failed to regress, radiotherapy should be considered. Patient who has severe renal involvement, an aggressive treatment with corticosteroid and cyclophosphamide is advocated.

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