

# Kimura's disease

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[Abstract](#)

[Keywords](#)

[Name of the disease and its synonyms](#)

[Epidemiology](#)

[Clinical, biological and anatomopathological description](#)

[Outcome](#)

[Etiology](#)

[Therapeutic management](#)

[References](#)

## Abstract

*Kimura's disease, a rare entity in the West but endemic in Asia, manifests as solitary or multiple subcutaneous nodules, primarily located in the cervical region. They are often accompanied by local adenopathies and/or salivary gland hypertrophy. Histologically, the lesions are characterized by hyperplastic lymphoid tissue, an inflammatory infiltrate rich in eosinophils and a proliferation of postcapillary venules. Hypereosinophilia in the blood and elevated levels of circulating IgE are found. A nephrotic syndrome must be systematically sought. The etiology of this chronic inflammatory disease is unknown. An aberrant immune reaction to an unknown antigenic stimulus has been suggested. Treatment consists of surgical excision of the lesion(s) and corticotherapy is prescribed for relapsing forms and when renal involvement is present. The prognosis is good and no malignant transformation has ever been observed. Other drug classes have been tried with some success.*

## Keywords

Kimura, eosinophilic lymphogranuloma, subcutaneous nodules, local adenopathies, salivary gland hypertrophy, glomerulonephritis.

## Name of the disease and its synonyms

Kimura's disease or eosinophilic lymphogranuloma

features. There is a marked male predominance with a M/F sex ratio of 3.5 to 7. The peak age of onset is during the third decade.

## Epidemiology

The disease was first described in 1937 in the Chinese literature by HT Kimm and C Szeto. The definitive histological description was published by Kimura et al. in 1948 and, henceforth, the disease has borne his name. This disease is endemic in Asia (especially China and Japan) but rare, with about 200 reported cases since its histological description, and sporadic in the rest of the world. Non Asian patients have similar clinical and histological

## Clinical, biological and anatomopathological description

The usual clinical presentation consists of one or several subcutaneous, indolent nodules, that slowly increase in volume, located in the head and neck, accompanied by satellite adenopathies and/or increased volume of the salivary glands (mainly the parotid and submaxillary glands). The nodules can be pruritic and painful but the overlying skin is normal. Epitrochlear, axillary, inguinal and

popliteal localizations have been described. The eyes, ears, sperm ducts and nerves are rarely affected. Renal involvement, usually extramembranous glomerulonephritis, is found in half patients. Cutaneous eosinophilic vasculitis has been described. Laboratory analyses detect peripheral blood eosinophilia and increased serum total IgE concentrations. Proteinuria, demonstrating a nephrotic syndrome, must be systematically evaluated.

Histological examination of the excised lesions shows hyperplastic lymphoid tissue with proliferating germinal centers, moderate-to-massive infiltration by eosinophils in their interfollicular and perivascular zones sometimes forming an eosinophil 'abscess' and a proliferation of postcapillary venules. Folliculolysis is possible. Fibrosis is more severe in subcutaneous nodules and salivary glands than in enlarged lymph nodes.

#### Comments on the main differential diagnoses

Angiofollicular hyperplasia with eosinophilia, described by GC Wells *et al.* should no longer be confused with Kimura's disease. Their characteristics are given in the following table.

Kimura's disease	Angiofollicular hyperplasia with eosinophilia
Young man (2nd-3rd decade) Oriental	Middle-aged woman (3rd-5th decade) Westerner
Voluminous subcutaneous mass(es), adenopathy(ies), salivary gland involvement	Subcutaneous or dermal cervical papules or nodules; overlying skin is erythematous or pigmented; rare adenopathies
Follicular hyperplasia, eosinophil infiltration of interfollicular and perivascular zones with abscess formation and lysis, postcapillary venule proliferation	Same aspect. Histiocytoid vessels with particular endothelial cells (different sized nuclei and protrusion into the vessel lumen)
Elevated total IgE, hypereosinophilia Benign pathology	No increase of IgE, hypereosinophilia Benign form of a group of vascular proliferation diseases ranging from hemangioendothelioma to epithelioid angiosarcoma

#### Outcome

The prognosis of Kimura's disease is good and no malignant transformation has been reported. The evolution is characterized by spontaneous remission but also relapses in 25% of the patients treated with surgery alone.

#### Etiology

The etiology of this chronic inflammatory disease is unknown. An aberrant immune reaction to an unknown antigenic stimulus has been suggested, perhaps implicating a role for *Candida albicans*, but no formal demonstration has been made to date. No clonal rearrangement of TCH- $\delta$ , TCR- $\gamma$ , and IgH genes were founded, except in one case with TCH- $\delta$  gene rearrangement. It can be suggested that prolonged immunologic stimulation can lead to clonal lymphoid proliferation in occasional cases. Mast cells, a major source of interleukin 4 and 5, and RANTES, might play an important role in the pathogenesis of Kimura's disease, by regulating IgE synthesis and orchestrating eosinophilic infiltration.

#### Therapeutic management

Treatment of Kimura's disease is not codified. Surgical excision of the lesion(s) is the first-line therapy, but relapses are frequent. Systemic corticotherapy with prednisone is prescribed for relapsing forms and when renal involvement is present, and has been shown to have good efficacy, but with a risk of relapse when treatment is withdrawn. Local radiation therapy (25-30 Gy) is prescribed for lesions refractory to corticotherapy or when surgery is not possible but sequelae (especially xerostomia) must be considered in making this therapeutic decision. In a 34-yr-old man with relapsing Kimura's disease despite prednisone, a combination of all-trans-Retinoic acid with low dose prednisone lead to complete remission. Pranlukast, a leukotriene receptor antagonist, (450 mg/day) has been tried in 2 patients with success after respectively 2 years and 2 months of treatment, without side-effects. Cetirizine (histamine (H-1) receptor blockers) induced a complete remission (CR) in a corticosteroid dependant patient within 2 months of treatment. Despite steroid discontinuation, this patient is still in CR 6 months later.

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