

Kimura's disease: case report of an Italian young male and response to oral cyclosporine A in an 8 years follow-up

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Abstract Kimura's disease is a benign chronic inflammatory disease, common in Asian males and rare in Western people. Clinically, Kimura's disease is characterized by subcutaneous nodular lesions, usually localised in head and neck, often associated with regional lymphadenopathy. Peripheral blood eosinophilia and elevated serum IgE are often observed. We report a case of a 40-year-old Italian patient presenting with nodular subcutaneous lesions and peripheral eosinophilia. Based on clinical, histopathological and laboratory findings, a diagnosis of Kimura's disease was made. The patient was treated with very low doses of cyclosporine A with no evidence of disease recurrence over the following 8 years. However, the discontinuation of cyclosporine A determined a relapse of the disease. The relevance of this case is due to the rarity of the disease in Italy, to its peculiar clinical presentation and, moreover, it is the first case in literature that has a good response to treatment with low doses of cyclosporine A, documented in an 8-year follow-up.

Keywords Cyclosporine A · Eosinophilia · Kimura's disease · Lymphadenopathy

Introduction

Kimura's disease (KD) is a rare chronic inflammatory disease with unknown aetiology. It is endemic in Asian countries, and typically affects young and adult males [1]. In Europe, it is rarely diagnosed probably due to the several clinical features shared with the more widely spread angiolymphoid hyperplasia with eosinophilia. This determines the need of a specific differential diagnosis [2] (Table 1).

Clinically, KD is characterized by nodular subcutaneous masses, typically localised to the neck and the head, and seldom reported involvement of parotid glands [3]. Localizations on trunk, limbs and oral cavity are uncommon. Lymphadenopathy is another common clinical finding in KD [2].

Peripheral blood eosinophilia and increased IgE serum levels are frequently encountered. Nephrotic syndrome has also been reported in association with KD.

Histopathologically, KD is characterized by tissue infiltration of eosinophils and lymphocytes as well as eosinophilic abscesses. Other common findings include lymphoid follicles with germinal centres and venular hyperplasia with flat or cuboidal endothelium [2, 4].

Several therapeutic approaches have been pursued, including, among the others, surgical excision, radiotherapy and medical therapy [5, 6]. KD has been successfully treated with systemic corticosteroids although relapse of the disease is often observed after discontinuation of treatment [7].

Literature reports cases of KD successfully treated with cyclosporine A (CSA) at dose of 3–5 mg/kg/day, combined or not with corticosteroids. In these cases, no relapses have been observed even 18 months after treatment suspension [8]. Treatments with pentoxifylline, nonsteroidal anti-inflammatory drugs and oral retinoids are rarely reported.

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Table 1 Clinical, laboratory and histopathological features of KD and ALHE

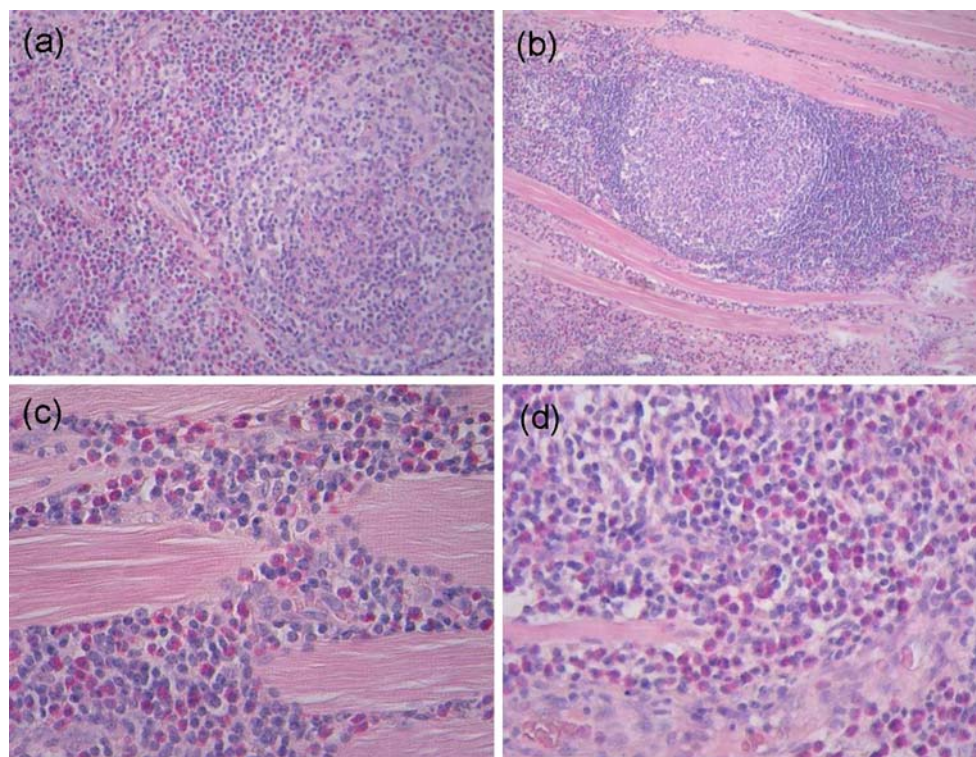
	KD	ALHE
Clinic		
Age	20-30 years	30-50 years
Sex	Male predominance	Female predominance
Race	More frequent in Oriental people	All races
Presentation	Deep single or multiple sub-cutaneous mass (>2 cm)	Superficial multiple erythematous dermal papules or nodules (<2 cm)
Location	Head, neck, documented also trunk, limbs, parotid glands, oral cavity	Head and neck
Lymphadenopathy	Common	Uncommon
Laboratory		
Blood eosinophilia	Present	Uncommon
Serum IgE	Usually elevated	Usually normal
Histology		
Vessels	Vascular hyperplasia	Vascular hyperplasia
Lymphoid follicles	Always present	Rare
Eosinophils and eosinophilic abscesses	Present	Rare
Endothelium	Flat to low cuboidal	Cuboidal to dome-shaped epithelioid or histiocytoid

Case report

A 40-year-old Italian male has been treated in our centre since September 1999 for the appearance of peripheral eosinophilia and nodular subcutaneous lesions on trunk, right elbow, right wrist and left hip, associated with pain and pruritus. The overlying skin colour was almost normal

with mild erythema. The nodules were of elastic consistence, movable and non-tender. The imaging findings of the trunk lesion revealed a diameter of 9 cm, with eco-doppler evidence for vascularization. A right side axillary lymphadenopathy was also found. The lymph node, less than 2 cm in diameter, was elastic, movable on palpation and not painful.

Fig. 1 **a** Dense mononuclear infiltrate with numerous eosinophils (original magnification $\times 20$); **b** lymphoid follicles with germinal centres (original magnification $\times 10$); **c** prominent eosinophilic infiltration (original magnification $\times 40$); **d** venular hyperplasia with flat endothelium (asterisks, original magnification $\times 20$)



Laboratory data revealed peripheral blood eosinophilia ($1,900 \text{ cells/mm}^3$), increased serum IgE levels ($1,578 \text{ KU/L}$) and high serum levels of cationic eosinophil protein (180 mcg/L).

Histological examination of a subcutaneous nodule from the wrist showed a dense infiltration of mononuclear cells with numerous eosinophils involving the connective and muscle tissues. Lymphoid follicles with germinative centres as well as venular hyperplasia with flat endothelium were appreciated (Fig. 1).

Based on clinical, histopathological and laboratory findings, a diagnosis of Kimura's disease was made. The patient was treated with prednisone (25 mg/day), progressively tapered over 3 months and then discontinued. At the same time, treatment with CSA was started at initial dose of 3 mg/kg/day . After 6 months, clinical examination and imaging findings showed complete regression of the nodular lesions. Eosinophilia and overproduction of IgE were both suppressed.

The CSA dose was, therefore, reduced to 2.5 mg/Kg/day and treatment was discontinued after 14 months. The discontinuation of CSA determined a relapse of the disease after 3 months. Reappearance of lesions on right axilla, right hip, and right wrist was found. Blood eosinophilia ($1,400 \text{ cells/mm}^3$) was also encountered. Once again, the patient was treated with glucocorticoids at the same doses and a rapid improvement and eosinophilic blood levels normalisation were observed. After about 1 month, CSA was reintroduced as maintenance treatment at a dose of 3 mg/kg/day , while the steroid therapy was gradually tapered and discontinued. This treatment was continued for 3 years with no relapse or evidence of disease recurrence. Later, a new CSA tapering attempt to the dose of 1.5 mg/kg/day was performed. Though evidence of relapse of subcutaneous lesions, without hypereosinophilia was observed. The CSA was therefore increased to 2 mg/kg/day , with no evidence of disease recurrence over the following 5 years and in the absence of side effects related to CSA.

Discussion

The most peculiar aspect of this report is the rarity of KD in Western countries [1] and the clinical features of the subcutaneous lesions on trunk, elbow, wrist and hip, with no involvement of the more typical sites: head and neck [3]. Moreover, the long-term treatment with CSA at the maintenance dose of 2 mg/kg/day , in an 8 years follow-up, has not been described in literature. In fact, only 15 months free from disease period, during CSA 4 mg/kg/day therapy, is documented [9]. Other studies report an improvement of the lesions after 1 month of treatment with CSA 5 mg/kg/day

[10]. Finally, Kaneko et al. report a follow-up of 18 months without relapse of disease, after CSA was discontinued. In the present study, we describe a therapy with CSA at the maintenance dose of 2 mg/kg/day , with no relapse of disease over a 5 years follow-up. On the other hand, the lesions began to appear again when the treatment with CSA was stopped or reduced.

Therefore, our data confirm the efficacy of steroids in inducing remission of disease and the long-term efficacy of very low doses of CSA in maintaining such a result. Therefore, we can infer that a lower maintenance dose of CSA is well tolerated, exposing the patient to less side effects. Although once it is suspended, it may enhance a more rapid onset of disease relapse.

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Disclosures None

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