Tacrolimus on Kimura's disease: a case report

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Objective. We report preliminary results of an ongoing study that assesses the efficacy of tacrolimus on Kimura's disease (KD).
Study Design. A patient with refractory KD after surgery and treatment with prednisone was treated with tacrolimus. Tacrolimus (FK-506) was administered at an initial dosage of 1 mg every 12 hours, and FK-506 concentration in the blood was monitored monthly. FK-506 blood concentration was controlled within 5 to 15 μg/L. After 6 months, the dosage of tacrolimus was reduced to 0.5 mg daily for another 2 months and then treatment was stopped.
Results. Swelling of the bilateral salivary glands disappeared within the first week. No serious side effects were noted and the disease has not recurred in the 2 years of follow-up.
Conclusions. Tacrolimus may be an effective treatment for patients with KD, but more research is needed to determine its long-term efficacy and safety as well as its mechanism of action. (Oral Surg Oral Med Oral Pathol Oral Radiol 2014;117: e74-e78)

Kimura's disease (KD) is a chronic inflammatory condition that occurs mainly in the Asian population. The etiology of KD remains uncertain to date. KD involves the soft tissues of the head and neck region. Patients with KD often complain about nontender lumps or enlarged soft tissues and present with subcutaneous nodules, predominantly in the head and neck region, with peripheral blood eosinophilia and elevated serum levels of immunoglobulin (Ig) E.

Surgery, drug treatment, and radiation are used for the management of KD. Resection is the most effective and preferred method for the treatment of this disease, but complete resection is often unattainable because of the diffuse characteristics of KD. Steroid treatment is the main drug regimen, but is associated with a high rate of recurrence and high rate of morbidity after long-term treatment. In this study, the authors administered tacrolimus (FK-506) to a patient with KD and achieved good results. Swelling of the bilateral salivary glands disappeared within the first week of treatment and has not recurred to date.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent form is available for review by the editor-in-chief of this journal.
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Received for publication Feb 21, 2012; returned for revision Mar 28, 2012; accepted for publication Apr 3, 2012.

2212-4403/$ - see front matter
http://dx.doi.org/10.1016/j.oooo.2012.04.022

MATERIAL AND METHODS

Clinical data

A 30-year-old man with nontender swelling of the bilateral salivary gland regions for a period of 6 years was referred to our hospital. The lesions had recurred following 2 previous resections. The swelling involved the area of the bilateral salivary glands, with poorly defined margins. The swelling on the right salivary gland area measured approximately 4.0 × 3.0 cm and that on the left measured approximately 2.0 × 2.5 cm. Palpation revealed that the lesions were firm but mobile. The skin over the lesions was darker than the surrounding skin. Eosinophil count was 5.91×10^9 cells/L, which was about 12 times the upper limit of normal (ULN). The percentage of eosinophils was 0.507%, which was 10 times the ULN. Serum IgE concentration was 2100 IU/mL, which was 17.5 times the ULN. Multiple soft tissue lesions were seen on the bilateral salivary gland region by magnetic resonance imaging (MRI) (Fig. 1). Findings on the remainder of the oral and maxillofacial region and on general physical examination were normal. The patient's blood pressure, blood test, urine test, and chest x-ray results were also within the normal range.

Treatment

A parotidectomy procedure was performed under general anesthesia, and the lesion on the right parotid gland was resected. Palpation of the resected specimen revealed that it was firm. The specimen was sectioned and stained with hematoxylin and eosin (H&E). Immunohistochemical analysis for S100 protein and CD1a was also conducted.

Following diagnosis of KD, the patient refused further resection and received prednisone at a dosage of 10 mg daily for 3 months but then stopped treatment. One

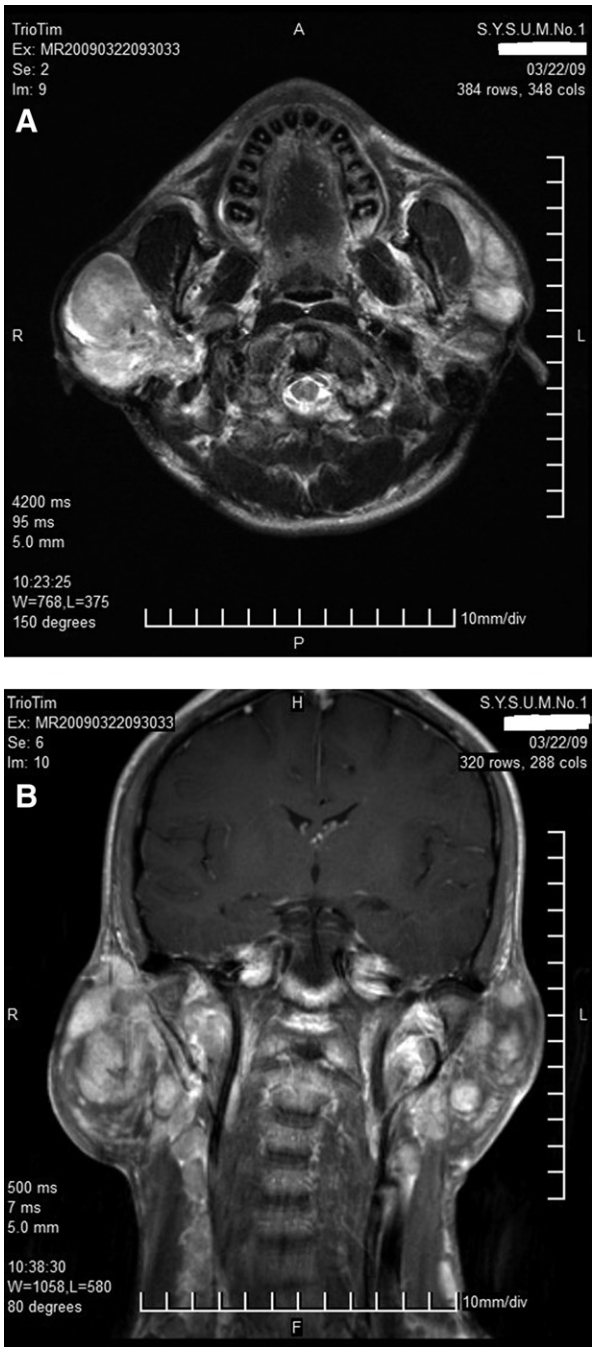

Fig. 1. Transectional view **(A)** and coronal view **(B)** of preoperative MRI: multiple soft tissue lesions can be seen on the bilateral parotideomasseteric region.

month after steroid treatment termination, the lesion on both sides of the glands had recurred. Following informed consent, the patient was administered tacrolimus. Tacrolimus (FK-506; Fujisawa Group, Japan) was administered at an initial dosage of 1 mg every 12 hours, and the drug concentration in blood was monitored monthly. The concentration of FK-506 in the blood was controlled to within 5 to 15 μg/L by adjusting the dosage of tacrolimus. Plasma creatinine and amylopsin levels were measured to assess the patient's renal and pancreatic function, respectively. The patient was advised to stop tacrolimus treatment and contact his physician if an infection or serious side effects occurred. After 6 months, the dosage of tacrolimus was reduced to 0.5 mg daily for another 2 months and then treatment was stopped.

RESULTS

Postoperative histopathologic examination revealed multiple lymphoid follicles with distinct germinal centers. Multinucleate cells were also found. Eosinophilic infiltrates were found in the lymphoid follicles and the interfollicular areas. Fine irregular fibrosis was also noted. Fibrotic changes were seen within the interfollicular zones and around blood vessels. No evidence of malignancy was found.

On immunohistochemical analysis, cells expressing S100 protein and CD1a, which were thought to be dendritic cells (DCs), were found throughout the lymphoid tissue (Fig. 2).

Based on these characteristic histopathologic and clinical findings, the patient was diagnosed with KD.

Swelling on the bilateral salivary glands disappeared within the first week of tacrolimus treatment, which was given at a dosage of 1 mg every 12 hours. The dosage of tacrolimus was adjusted according to the blood concentration of FK-506. Tacrolimus treatment was stopped after 8 months. The patient was followed for another 2 years and no recurrence has been observed (Fig. 3). At the end of the 2-year follow-up, eosinophil count decreased to 1.42×10^9 cells/L, which was about 3 times the ULN. The percentage of eosinophils decreased to 0.188%, which was 4 times the ULN. The serum IgE concentration decreased to 643 IU/mL, which was about 5 times the ULN. No serious side effects were reported. Neither renal nor pancreatic dysfunction was found to occur with tacrolimus therapy.

DISCUSSION

KD was first reported by a Chinese author named Kim in 1937 as eosinophilic hyperplastic lymphogranuloma, and was named after the Japanese author Kimura, who described the disease in 1948. KD is commonly found in the Asian population, such as in China and Japan, but can be also found in whites. The disease is mainly diagnosed in Asian men in their 30s. KD is a rare chronic inflammatory disease that mainly affects the soft tissues of the head and neck region and surrounding area and lymph nodes. Patients mainly present with a mass in the affected area, such as the neck, retroau-