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CASE REPORT

# Radiotherapy for Kimura's disease: case report and review of the literature

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## Summary

*Kimura's disease is a chronic inflammatory disease of uncertain etiology which involves subcutaneous tissue, presents as a tumor-like lesion and predominantly occurs in the head and neck region. Radiotherapy has been used for treating unresectable or recurrent lesions. We report a 32-year-old male who presented with a mass on the right side of the neck. The mass measured 52×40 mm. Peripheral eosinophilia and 5-fold increase in serum IgE level were found. Pathological evaluation following subtotal excision of the mass confirmed Kimura's disease and the patient was given prednisolone p.o. Local recurrence was observed one month later for which the patient received local radiotherapy. No recurrence has been observed up to 30 months in the post-radiotherapy period. Effective radiotherapy given in a favorable schedule and dosage could be a highly effective alternative when other treatment modalities are unsuccessful.*

**Key words:** Kimura's disease, eosinophilic hyperplastic lymphogranuloma, surgery, radiotherapy, head and neck

## Introduction

Chinese authors Kimm and Szeto had first reported Kimura's disease in 1937 and a Japanese author, Kimura, first published its descriptive definition in 1948 [1,2]. It is usually reported as eosinophilic granuloma of the soft tissue, eosinophilic hyperplastic lymphogranuloma and eosinophilic lymphoid granuloma [3].

Kimura's disease is a chronic inflammatory condition of unknown etiology involving subcutaneous tissue [4]. It is thought to be a manifestation of an allergic response [5] and presents as a tumoral lesion with a predilection for the head and neck region. Clinically it is often confused with parotid tumor with lymph node metastasis [4].

The disease is most prevalent in Asia and 85% of the cases occur in men. The typical presentation is a young oriental male with non-tender subcutaneous swellings in the head and neck region, lymphadenopathy, peripheral eosinophilia and elevated serum IgE. The parotid gland may be involved and there may also be proteinurea [5]. Pathological examination reveals typically a dense inflammatory infiltrate characterized by proliferating lymphoid tissue with germinal centers, basophilic microabscesses and fibrosis. The lesion needs to be distinguished pathologically from angiolymphoid hyperplasia with eosinophilia (ALHE) [6,7]. Several studies report development of regional lymphadenopathy in approximately 67-100% of patients which, in longstanding disease, may become generalized [8].

Follow up is acceptable if the lesions are neither symptomatic nor disfiguring [3]. Surgical excision is preferred in localized disease. Intralesional or oral steroids can shrink the nodules but seldom result in cure. Cyclosporine is also used [9]. Recurrence rates

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are high [3]. Radiotherapy has been used to treat unresectable and recurrent lesions or for patients who have failed to achieve local control by steroid therapy. The prescribed radiation doses vary from 20-45 Gy [10-12]. Our case demonstrates the effectiveness of radiotherapy in a patient with recurrent disease, previously treated by surgery and steroids.

## Case presentation

A 32-year-old male presented with swelling on the right side of his neck. This finding was first observed 3 months ago after a tooth extraction. On physical examination a painless fixed right submandibular mass with skin-like color measuring 5×5 cm, and 2 enlarged lymph nodes on the right sternocleidomastoid muscle measuring 2×2 cm each were observed. Computerized tomography (CT) scan of the head and neck disclosed a mass of 52×40 mm in the right submandibular region along with conglomerated lymphadenopathy (LAP). The mass invaded the submandibular gland and the parotid (Figure 1).

Complete blood count indicated eosinophilia (eosinophils 2.94%) whereas routine blood chemistry investigations were within normal limits. Brucella Group Agglutination Test (Wright) and Infectious Mononucleosis Test (Monospot) were negative. Peripheral eosinophils rose to 6% 20 days later, and serum IgE was elevated to 242 IU/ml (normal up to 87). The results of fine needle aspiration cytology revealed reactive lymphoid tissue. Due to the higly fibrotic texture and adherence to the internal jugular vein, a surgical excision excluding the posterior and superior part of the mass was performed. Microscopic study revealed vascularization at the germinal centers of the lymph nodes, folliculosis, eosinophilic microabscesses in follicles and eosinophilic infiltration of fibrotic areas. There were irregular inflammatory areas, glandular destruction of different grades, fibrosis and intense eosinophilic, lymphocytic and plasmacytic infiltration at subcutaneous lesions. Reticular deposits were observed in the centers of follicles by anti IgE tests. All pathological (Figures 2, 3) and clinical findings were consistent with the diagnosis of Kimura's disease.

Following subtotal excision of the mass prednisolone p.o. 1 mg/kg/day was administered for a week. Local recurrence was detected one month after the pa-

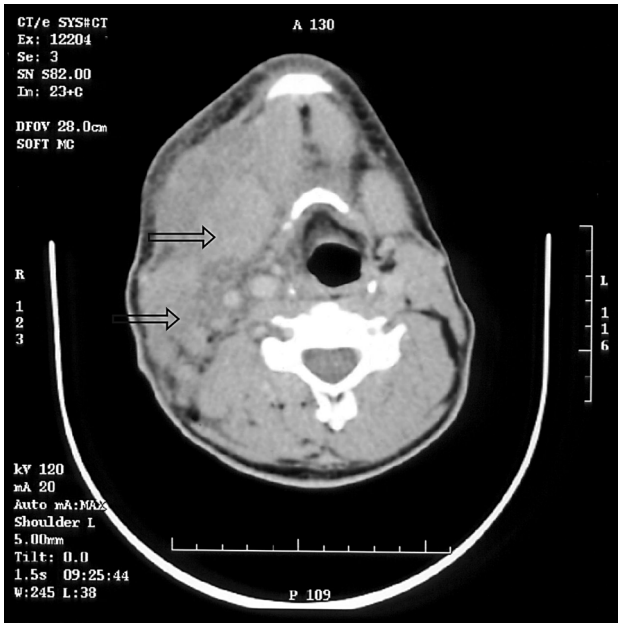


**Figure 1.** Preoperative CT revealed a mass in the right submandibular region (arrows).

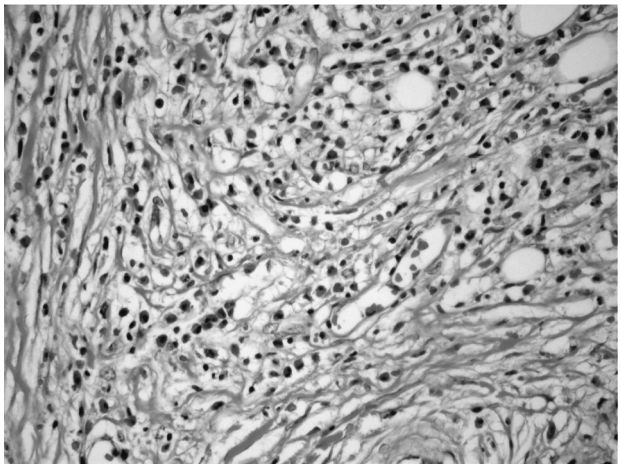

**Figure 2.** Histopathological examination of excision specimen revealed vascular hyperplasia, mostly of post capillary venules and diffuse eosinophilia (H&E×440).

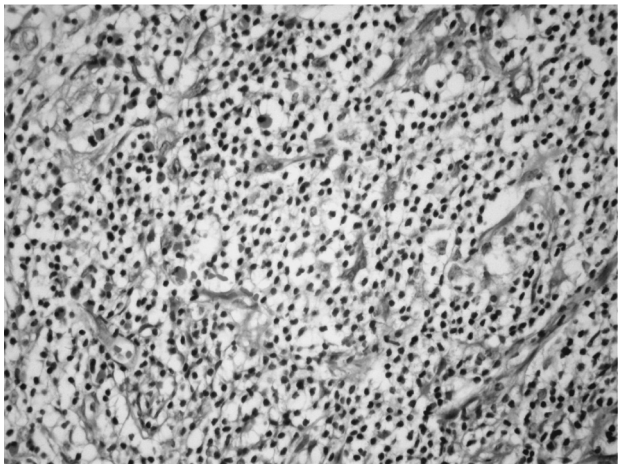

**Figure 3.** Histopathological examination of excision specimen revealed diffuse eosinophilia (H&E×440).

tient's discharge from the hospital. Conglomerated LAP infiltrated the sternocleidomastoid muscle and carotid artery. CT scan showed the mass invaded the right parotid and submandibular gland on the right side of his neck (Figure 4).

Multiple LAP was present at the right supraclavicular region and the other parts of the right side of the neck. LAP up to 2 cm in diameter was observed on the left side of the neck along with right tonsillar hypertrophy secondary to infiltration. Postero-anterior (PA) chest radiographs and abdominal ultrasonography (US) were normal.

Due to disease progression the patient was scheduled to receive radiotherapy at a dose of 44 Gy in 22 fractions administered locoregionally by Cobalt-60 teletherapy machine. Irradiation was given through bilateral cervical opposite parallel fields and one anterior supraclavicular field. No acute side effect were observed, except grade 1 (RTOG) mucositis. On completion of radiotherapy complete response was achieved on the left side of the neck, whereas two lymph nodes (the largest one was 3 cm in diameter) at the superior and medial jugular region of the right side of the neck persisted.

CT scan performed 3 months after the completion of radiotherapy disclosed continuation of complete response (Figure 5). CT scan of the thorax, abdomen and head/neck performed 6 months after completion of radiotherapy were normal.

Milimeter-sized lymph nodules were present in the neck at the 13th month post-radiotherapy. However,

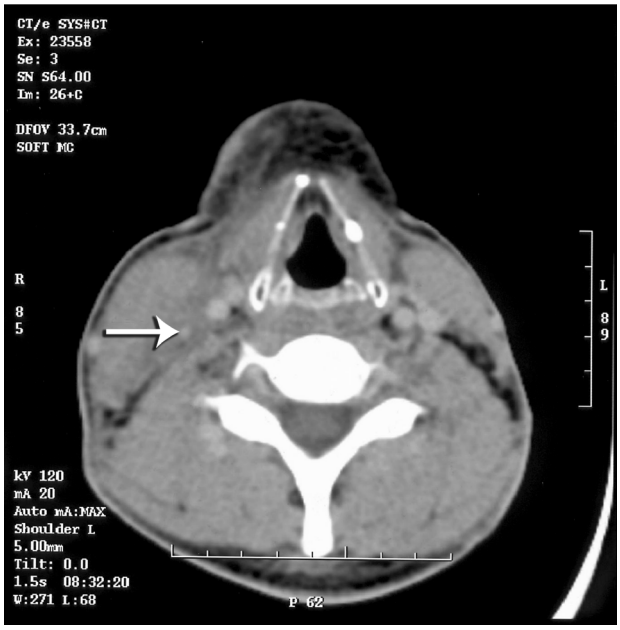


**Figure 5.** CT performed 3 months after the completion of radiotherapy disclosed an excellent local control (arrow).

multiple bilateral pulmonary hilar LAP and what was interpreted as bilateral lung interstitial lymphangiitic invasion were present on CT scan. Abdominal US was normal. Upon consultation with the Thoracic Surgery department it was decided to keep the asymptomatic patient under observation only. At that time point peripheral eosinophils were 1.87%.

At the 30th month post-radiotherapy the patient had neither complaints nor symptoms. Physical exami-

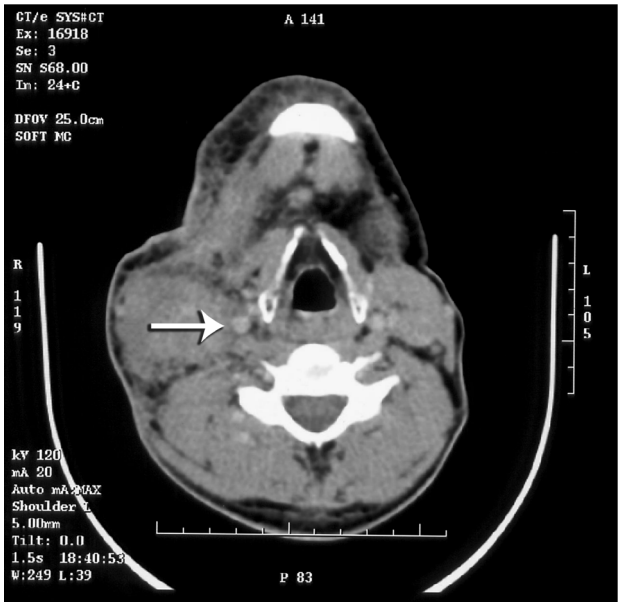


**Figure 4.** Postoperative CT revealed gross residual mass with invasion of the right parotid and submandibular gland (arrow).

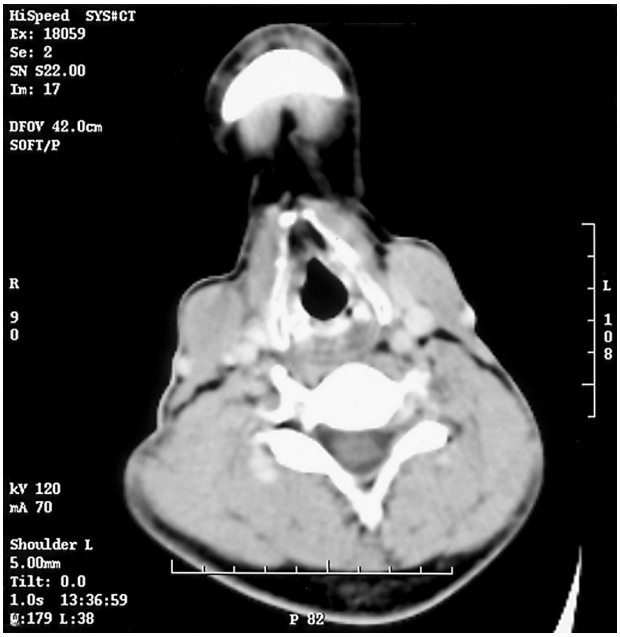


**Figure 6.** CT at the 30th month after radiotherapy revealed complete response.

nation was free of LAP and mass. Cervical (Figure 6) and thoracic CT scans revealed no LAP in the neck, mediastinal and axillary regions but fibrotic alterations located at the right paracardiac region. Abdominal CT scan was also normal.

A complete response was attained and neither recurrence nor late complication were detected up to 30 months. The patient is still under regular follow up.

## Discussion

In Kimura's disease, which is considered as a benign illness, radiotherapy has been used to treat patients not amenable to or failing after surgical excision or steroid therapy [1,3]. In the literature, a wide range of radiotherapy doses (20-44 Gy) has been administered to the lesion and the adjacent enlarged lymph nodes in a small number of patients [10-12]. The rarity of Kimura's disease led to a wide range of radiotherapy schedules but local control rate was above 90% with radiation doses of 25 Gy or higher [10,12]. Itami et al. reported 79% local control rate in 10 patients who received radiation therapy to a total dose of 25-30 Gy [12]. In the Hareyama et al. series with 20 patients, local control was obtained in 25%, 90% and 92.3% of the patients at dosages of < 25 Gy, 26-30 Gy and >30 Gy, respectively [10]. Kim et al. divided 17 recurrent patients who had local excision and/or systemic steroids as their first-line treatment into 2 treatment groups: 8 of the patients were treated with systemic steroids alone while the remaining 9 were treated with external beam irradiation at a dosage of 21.6-45 Gy. Six of the 8 patients treated with steroids alone experienced rapid recurrence. On the contrary, 8 of 9 patients in the radiation group achieved complete response. The recurrence rates were 11% and 75% in their irradiated and nonirradiated group, respectively. No secondary malignancy was observed in the radiation group [11]. In our case relatively higher dose (44 Gy) was delivered due to the rapid progression of the mass, invasion of the parotid, tonsil, large vessels and the regional lymphoid tissue. Whether we would have been able to obtain the same local control with a lower dose will remain speculative, since doses in the literature are not suggestive about the optimal dose [10-12].

The presence of the hilar LAP rose suspicion about generalization of the disease, regarding cases mentioned in the literature [2,8], thus the asymptomatic patient was kept under regular follow up.

Radiotherapy given in a favorable schedule and dosage could be a highly effective alternative where other treatment modalities are unsuccessful. Radiotherapy can be primary therapy, alternative for cases in which surgical excision may cause high morbidity due to the lesion's anatomical location and steroid therapy can not be administered. The side effects of radiotherapy will be minimized by the improvements in radiotherapy techniques such as 3D conformal radiotherapy and intensity-modulated radiotherapy. Although it is accustomed to prefer surgical excision as the principal therapeutic modality, we believe that radiotherapy should be considered as a first-choice treatment instead of surgery in some selected cases. With increased clinical experience by employing multidisciplinary approaches in patients with Kimura's disease there will be a chance for determining the optimal treatment planning.

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