Med & Health Jan 2026; 21(1): 557-562 https://doi.org/10.17576/MH.2026.2101.38

CASE REPORT

Recurrent Kimura Disease of the Submandibular Region After Prolonged Remission to Radiotherapy and Its Challenges

NUR FA'IZAH AB MUIN[1]*, ADZIM POH YUEN WEN[2], REENA RAHAYU MD ZIN[3]

[1]Department of Radiotherapy & Oncology, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia
[2]Plastic & Reconstructive Surgeon, Surgical Department, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia
[3]Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia

Received: 16 September 2024 / Accepted: 24 October 2024

ABSTRAK

Penyakit Kimura ialah keadaan keradangan kronik yang jarang berlaku, dan lazimnya memberi kesan kepada golongan dewasa muda, terutamanya dalam kalangan individu berketurunan Asia. Penyakit ini biasanya muncul dalam bentuk nodul subkutaneus dan limfadenopati setempat. Walaupun bukan kanser, ia boleh menyebabkan kecacatan yang ketara dan masalah yang berulang. Seorang lelaki berumur 56 tahun berketurunan Cina dengan sejarah penyakit Kimura menghadapi masalah ketulan berulang di kawasan infraaurikular kanan, yang pertama kali dikesan pada tahun 1987. Walaupun telah menjalani pembedahan dan terapi steroid yang berpanjangan, penyakit itu tetap berulang. Pesakit kemudian menjalani radioterapi di bahagian pipi kanan dan rahang bawah. Kawalan penyakit yang baik dirasai selama 12 tahun. Walau bagaimanapun, pada tahun 2022, penyakit Kimura kembali berulang. Rawatan ulangan radioterapi ada dipertimbangkan memandangkan tindak balas sebelumnya terhadap radioterapi, tetapi terapi ini disimpan sebagai pilihan terakhir kerana risiko yang mungkin timbul akibat radiasi berulang. Sebaliknya, suntikan triamcinolone acetonide diberikan yang membawa kepada kawalan simptom yang ketara dan kawalan saiz ketulan. Pengurusan penyakit Kimura adalah mencabar disebabkan oleh kadar sakit berulang yang tinggi. Kes ini menonjolkan kesukaran dalam menguruskan penyakit Kimura yang berulang selepas radioterapi dan menunjukkan keberkesanan terapi steroid intralesi sebagai rawatan alternatif.

Kata kunci: *Ganjil; keradangan kronik; penyakit Kimura*

ABSTRACT

Kimura disease is a rare, chronic inflammatory condition predominantly affecting young adults, particularly those of Asian descent. It presents with subcutaneous nodules and regional lymphadenopathy, and while benign, it can cause significant disfigurement and recurrent issues. A 56-year-old male of Chinese descent with a history of Kimura disease presented with a recurrent mass in the right infraauricular area, initially diagnosed in 1987. Despite surgical resections and extended steroid therapy, disease recurrence

Correspondence: Nur Fa'izah Binti Ab Muin. Department of Radiotherapy & Oncology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +601128388054 E-mail: drfaizah_abmuin@ukm.edu.my

persisted. The patient then underwent radiotherapy targeting the right cheek and mandible. He experienced excellent disease control for 12 years. However, in 2022, the patient experienced a relapse. Given the recurrence and prior response to radiotherapy, re-irradiation was considered but reserved as a last option due to potential risks. Instead, triamcinolone acetonide injections were administered, resulting in significant symptom improvement and control of the lesion. Management of Kimura disease remains challenging due to high recurrence rates. This case highlights the difficulties in managing recurrent Kimura disease after radiation and demonstrates the effectiveness of intralesional steroid therapy as an alternative treatment option.

Keywords: Chronic inflammatory; Kimura disease; rare

INTRODUCTION

Kimura disease is a rare chronic inflammatory disease of unknown etiology (Kim & Szeto 1937; Medeiros 2021). It typically manifests with subcutaneous nodules in the head and neck area, often accompanied by enlarged regional lymph nodes or swelling of the salivary glands (Abhange et al. 2018). While it primarily affects individuals of Asian descent, sporadic cases have been reported in other racial groups as well (Fouda et al. 2011). The condition is more prevalent among young adults, with the majority of patients falling between the ages of 20 and 40; men are affected more commonly than women (Fouda et al. 2011; Tseng et al. 2005). Although benign, Kimura disease can cause disfigurement and tends to progress slowly without evidence of turning malignant (Chang et al. 2006; Rahman et al. 2005).

CASE REPORT

A 56-year-old male of Chinese descent, with a medical history including hypertension, dyslipidemia and a previous cataract in his right eye, was diagnosed with Kimura disease in the right infraauricular area at the age of 20 in 1987. Initial presentation involved a painless lump that exhibited chronic growth. The patient underwent resection procedures in both 1987 and 1992.

Prednisolone therapy was administered for 15 years to manage the condition, but concerns about side effects led to its discontinuation in December 2008. Upon cessation, the mass measured 8 cm x 6 cm. Subsequent biopsy findings demonstrated histological features consistent with fibro-collagenous and fibrofatty tissue infiltrated by chronic inflammatory cells in the pattern of perivascular lymphoid aggregates. The infiltrate predominantly comprised small lymphocytes and eosinophils, with some lymphoid aggregates exhibiting prominent germinal centers. Surgery was performed; however, despite resection, the mass recurred after the procedure

He was subsequently referred to our department, where a follow-up computed tomography (CT) scan was performed in March 2010. The scan revealed an ill-defined, heterogeneous soft tissue density in the right submandibular region, which remained stable in size at 2.3 cm x 5.6 cm x 3.7 cm compared to the scan conducted in June 2009. Additionally, multiple cervical lymphadenopathies were noted bilaterally at levels I and II, as well as in the right levels III and IV. The largest lymph node in the right level I measured 1.0 cm, showing no significant change in size compared to the previous CT scan in June 2009.

In April 2010, he underwent radiotherapy targeting the right cheek and mandible, receiving a dose of 30Gy in 15 fractions with 12MeV, followed by a boost of 8Gy in 4 fractions. He experienced excellent disease control and remained free from flare-ups for 12 years. Unfortunately, in 2022, he encountered a relapse in his right ear and the surrounding periauricular region. He exhibited swelling around the right earlobe starting in September 2022, along with itching, occasionally resulting in bleeding following intense scratching.

Due to the COVID-19 pandemic, there was a postponement of the patient's visit to the clinic. A punch biopsy of the right cheek was conducted in January 2023 revealing scattered perivascular lympho-histiocytic infiltration extending into the subcutaneous tissue (Figure 1a & b). Lymphocytic aggregation with germinal centers was observed, comprising a heterogeneous population of lymphocytes, histiocytes, and degranulated eosinophils. No intraepidermal atypia or evidence of malignancy was detected (Figure 1c & d). Immunohistochemistry revealed a mixed population, predominantly B lymphocytes highlighted by CD20, along with a significant presence of T lymphocytes highlighted by CD3, and histiocytes highlighted by CD68 (Figure 1e-

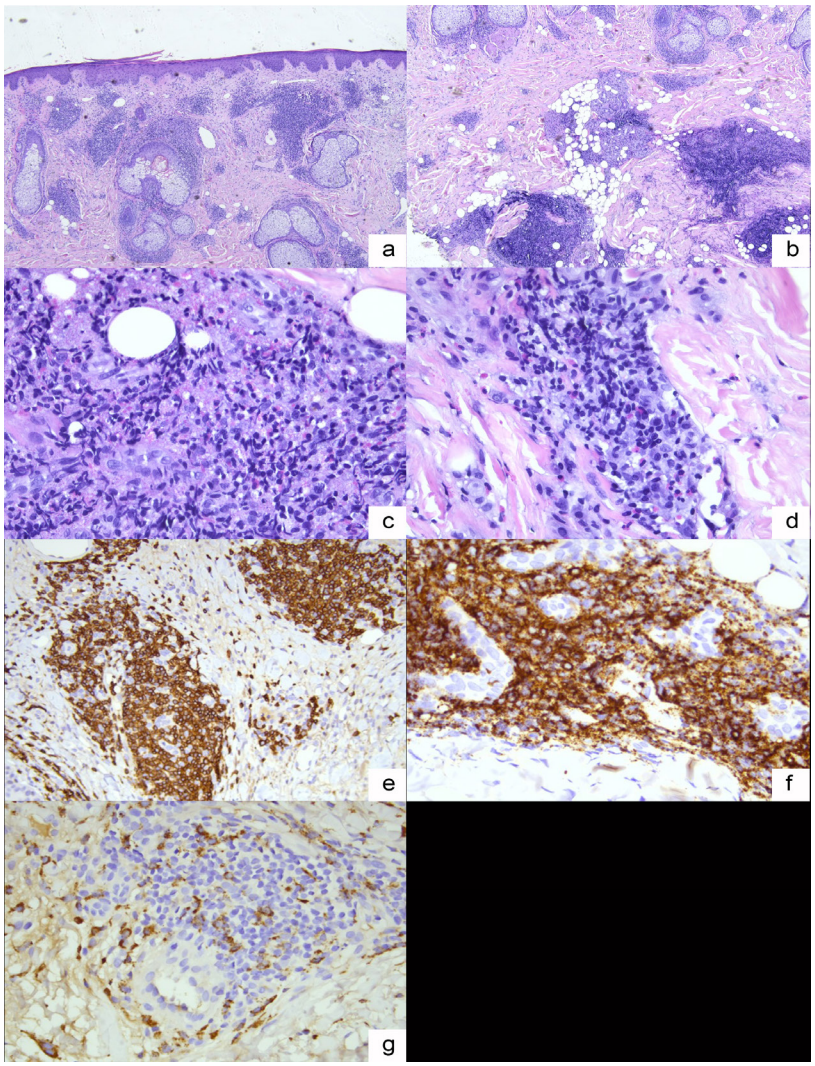

FIGURE 1: Histopathological slides showed the (a) presence of scattered perivascular lympho-histiocytic infiltrates within the dermis; (b) extending into the subcutis; (c-d) aggregates of lymphoid tissue consisting of a heterogeneous population of lymphocytes, histiocytes and degranulated eosinophils; (e-g) and immunostaining highlighting a mixed population of predominantly B lymphocytes, T lymphocytes and histiocytes, as indicated by CD20, CD3, and CD68, respectively

g). The pathologist characterised the specimen as consistent with reactive lymphoid hyperplasia, suggesting a departure from typical Kimura disease but advising clinical correlation.

In June 2023, a magnetic resonance imaging (MRI) scan (Figure 2) revealed a well-defined lobulated soft tissue mass measuring 2.6 x 4.9 x 6.3 cm in the right pre- and postauricular space. Enlarged and enhancing lymph nodes were noted in levels 2, 3 and 4 of the right cervical neck regions, with the largest nodes measuring 10 x 11 mm and 11 x 17 mm.

He was subsequently referred to our clinic to explore the possibility of re-irradiation, considering his prior favourable and lasting response. The case was presented at a multidisciplinary meeting, where surgical intervention was not recommended due to the involvement of the earlobe, which poses challenges for surgical intervention unless reconstructive options are feasible. Radiotherapy was considered a last resort due to concerns about the risks associated with re-irradiation, particularly given the benign nature of the disease and the potential for radiation exposure to a significant area.

Subsequently, he began receiving triamcinolone acetonide injections administered by the plastic surgeon in the post-auricular area, starting in July 2023. These injections are administered 4-6 weekly. A mixture of steroid (triamcinolone 40 mg/ml) and 2% lignocaine in a 1:1 ratio, totaling 2 ml, was injected intralesionally, with equal distribution in the areas of induration. Significant improvement in symptoms was noted, with reduced itchiness and swelling reported by the patient in the post-auricular area. The practitioner also noticed reduction in size, induration, erythema, pliability and vascularity of the lesion. His symptoms remained under control until his recent follow-up in July 2024.

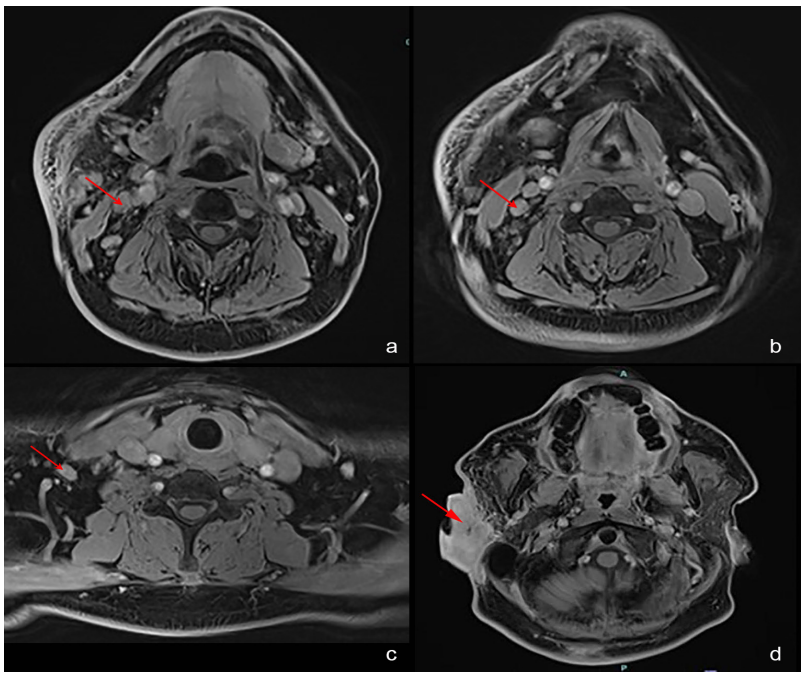

FIGURE 2: MRI images showed (a-c) enlarged and enhancing lymph nodes at levels 2, 3, and 4 of the right cervical neck regions; (d) lobulated soft tissue mass measuring 2.6 cm x 4.9 cm x 6.3 cm in the right pre- and postauricular space

DISCUSSION

There is currently no universally agreed-upon optimal treatment strategy for Kimura disease. Treatment options typically encompass surgical excision, steroid therapy and radiation. Initially, a combination of surgical excision and/or systemic steroid therapy is often pursued, with radiotherapy primarily reserved for cases of residual or recurrent disease (Hareyama et al. 1998).

Due to the absence of consensus regarding the optimal treatment approach, our patient initially underwent surgical excisions. Regrettably, disease recurrence was observed following each resection, which aligns with findings from the literatures indicating the challenging nature in managing these lesions due to their high recurrence rates. Recurrence rates have been reported to range from 25% to above 60% following local excision (Day et al. 1995; Rajpoot et al. 2000). This challenge may be attributed to the difficulty in achieving complete excision during surgery, given the infiltrative nature of the lesion and associated swelling of the regional lymph nodes (Rajpoot et al. 2000).

The patient underwent extended steroid therapy for a period of 15 years; nevertheless, it failed to offer sustained control. This was partly due to the possibility of low compliance owing to Cushing's side effects, such as buffalo hump, moon facies and truncal obesity reported by the patient. This observation is consistent with literature findings that highlight the limited effectiveness of systemic steroid therapy in achieving enduring control. Despite the beneficial effects of systemic steroids, withdrawal frequently triggers relapse (Chen et al. 2004).

This patient was offered radiotherapy because of multiple recurrences even after surgery and medical treatment. Studies suggest that radiotherapy can effectively control recurring and persistent lesions, with a good success rate in controlling the problem area; thus, it's recommended for patients who have positive surgical margins and repeated postoperative recurrences (Hareyama et al. 1998; Muangwong et al. 2021; Zhang & Jiao 2019). A retrospective study also found that radiotherapy is more effective compared to local excision or systemic steroids. The radiotherapy group showed a local control rate of 64.3%, whereas the non-radiotherapy group had a rate of 22.2%, with no secondary malignancies detected (Chang et al. 2006). The radiation field should be limited to the lesion and any associated swollen lymph nodes, with a typical dosage ranging from 26 to 30 Gy, regardless of the tumor's size (Hareyama et al. 1998). It was noted that radiotherapy offered local control for up to 68 months (Hareyama et al. 1998).

Re-irradiation in benign conditions such as Kimura disease presents challenges, primarily due to concerns about the heightened risk of malignancy, and therefore should be thoroughly discussed. For this patient, re-irradiation was discussed upon during the multidisciplinary team clinic consultation, which the patient elected to undergo a trial of triamcinolone acetonide injections, which have demonstrated efficacy thus far.

Based on the literature search, there is no standardised method for steroid administration. In our experience, the intralesional steroid was administered with a standardised dosage. We found this approach to be effective and it did not require systemic steroid adjuncts. The patient did not develop any cushingoid symptoms or signs. In the future, we may consider adding antihistamines or monoclonal targeted therapy in combination.

CONCLUSION

Given the rarity of Kimura disease, effective management strategies-especially for recurrence after prolonged remission following radiation-are limited. At first diagnosis, we treated the patient with surgical excision and a prolonged course of steroids. When steroid treatment failed, radiation therapy was administered, which proved effective for 12 years. Upon recurrence, intralesional triamcinolone was administered to avoid systemic steroids and mitigate the risks associated with re-irradiation. This approach

effectively controlled symptoms, and the patient remained stable through his last follow-up in July 2024.

Author contributions: All authors contributed to manuscript drafting, patient management, literature review, critical revision of the manuscript, reviewed and approved the manuscript for submission.

Conflict of interest: The authors declare no conflicts of interest.

Funding: This research received no external funding.

Acknowledgement: Not applicable

Ethical statement: Written informed consent was obtained from the patient for publication of this case report.

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