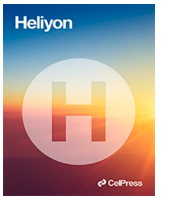
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Case report

Kimura disease, a rare Ethiopian case report

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ABSTRACT

Introduction: Kimura disease is a chronic inflammatory disorder predominantly affecting the head and neck region. The etiology of Kimura disease remains unclear. The disease mainly affects young adult males of Asian descent, with a higher prevalence in East Asian countries.
Clinical presentation: a 48-year-old Ethiopian woman presented with swelling in both her lower extremities, which gradually progressed to include her abdomen and the rest of her body. Additionally, she had pain in multiple joints in her upper and lower extremities, high-grade fever, loss of appetite, night sweats, and unexplained weight loss over the same duration. Physical examination revealed swelling around the eyes (periorbital puffiness), enlarged nodes in the axillary, and inguinal areas on both sides of the body, and pitting edema. Investigations showed pneumonia, elevated renal function tests and kimura disease. Unfortunately, the patient signed medical advice before completing her management.
Conclusion: despite its rarity in Ethiopia, it is imperative to consider Kimura disease as a potential diagnosis when evaluating lymphadenopathy and renal derangement.

1. Introduction

Kim and Szeto originally described Kimura disease as "eosinophilic hyperplastic lymphograuloma" in Chinese literature in 1937 [1]. It was subsequently described in a 1948 publication by Kimura et al. under the heading "On the unusual granulation combined with hyperplastic changes of lymphatic tissue." [2]. Kimura disease is an uncommon benign chronic inflammatory illness that often affects the head and neck region's lymph nodes and deep subcutaneous tissue, sometimes accompanied by recurrent regional lymphadenopathy or an enlargement of the salivary glands. There have also been reports of involvement in the oral cavity, axilla, groin, limbs, and trunk. It is uncommon to have systemic signs including weight loss, sweats at night, and fever. Middle-aged Asian males are most commonly affected by this condition. It is rare in non-Asian populations and endemic in Asia (China and Japan). The third decade is the highest age of onset. Peripheral blood eosinophilia and elevated serum immunoglobulin E (IgE) levels are also often observed [3].

What causes Kimura illness or its pathophysiology is unknown. The disease is categorized as a reactive process that is benign. It has been proposed that autoimmune responses with an abnormal immune response, infections, and allergic reactions can have a role [4].

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Increased mast cells, eosinophils, interleukin 5, and IgE levels indicate aberrant T-cell activation leading to a hypersensitivity-type reaction [5]. Kimura disease has a chronic history, indicating that lesions often stay or recur even after therapy. Because Kimura disease tends to affect the head and neck, deformity may result from untreated lesions growing larger [6]. Here we report a case of Kimura disease in a 48-year-old female patient.

2. Case presentation

She is a 48-year-old Ethiopian woman who was relatively healthy four months ago at which time she began to experience swelling in both her lower extremities, which gradually progressed to include her abdomen and the rest of her body. Additionally, she had a history of experiencing pain in multiple joints in both her upper and lower extremities. Alongside these symptoms, she also suffered from high-grade fever, loss of appetite, night sweats, and unexplained weight loss over the same duration. She had been producing whitish sputum and coughing for three months. Furthermore, she reported feeling easily fatigued, experiencing difficulty breathing when lying flat, and having nocturnal breathing difficulties in certain positions. It is important to note that she has no prior history of tuberculosis treatment, asthma, cardiac illness, or hypertension. Additionally, there is no family history of similar illnesses. Furthermore, she has never smoked, consumed alcohol, or taken any drugs.

Upon examination, the patient appeared to be acutely ill, displaying symptoms such as a rapid pulse rate of 120 beats per minute (tachycardia), a respiratory rate of 28 breaths per minute (tachypnea), and an oxygen saturation level of 96 % on room air. Her blood pressure was within the normal range (130/80 mmHg), and she had a temperature of 37.8 °C. Physical examination revealed swelling around the eyes (periorbital puffiness), pink conjunctiva, and non-icteric sclera. Examination of the lymph nodes revealed multiple enlarged nodes in the neck, axillary, and inguinal areas on both sides of the body. These lymph nodes were firm, non-tender. During the abdominal examination, fluid accumulation was observed, and the patient had grade 2 bilateral pitting edema in her legs.

Upon investigation, the complete blood count revealed a white blood cell count of 6820, with a neutrophil count of 4890/mcl and a hemoglobin level of 8.3 g/dl. Additionally, the erythrocyte sedimentation rate (ESR) was found to be 108 mm/hr. The thyroid-stimulating hormone (TSH) level was normal, and the patient tested non-reactive to antinuclear antibodies (ANA). An abdominal ultrasound indicated the presence of ascites and left-sided pleural effusion, although the organs appeared to be grossly normal. Analysis of the pleural fluid showed an abundance of lymphocytes and only a few macrophages against a proteinaceous background. Renal function tests revealed a creatinine level of 2.11 and a blood urea nitrogen level of 88, while liver function tests and serum electrolyte levels were within the normal range.

Posteroanterior chest x-ray (Fig. 1) showed multifocal consolidation with a diagnosis of pneumonia to rule out tuberculosis. Given these findings, the differential diagnoses considered include pulmonary tuberculosis, bacterial or viral pneumonia, kimura disease with pulmonary involvement, eosinophilic pneumonia, and non-infectious causes (autoimmune/inflammatory disorders: conditions like sarcoidosis, granulomatosis with polyangiitis). Subsequently, fine-needle aspiration cytology (FNAC) and lymph node biopsy samples were sent for further examination. FNAC revealed a diverse population consisting of significantly elevated eosinophils, along with a mixture of inflammatory cells such as lymphocytes, plasma cells, and occasionally histiocytes (Figs. 2 and 3). Subsequent incisional biopsy showed hyperplastic lymphoid follicles with reactive germinal centers and prominent mantle zone (Fig. 4) and increased eosinophils mixed with lymphocytes and occasional histiocytes (Fig. 5).

Hence, following a diagnosis of disseminated tuberculosis (considering her age, local epidemiology, and the chest x-ray finding) with severe community-acquired pneumonia, the patient was initiated on ceftriaxone 1g IV twice a day and azithromycin 500 mg po



Fig. 1. posteroanterior chest x-ray showing multifocal consolidation suggestive of multifocal pneumonia to rule out tuberculosis.

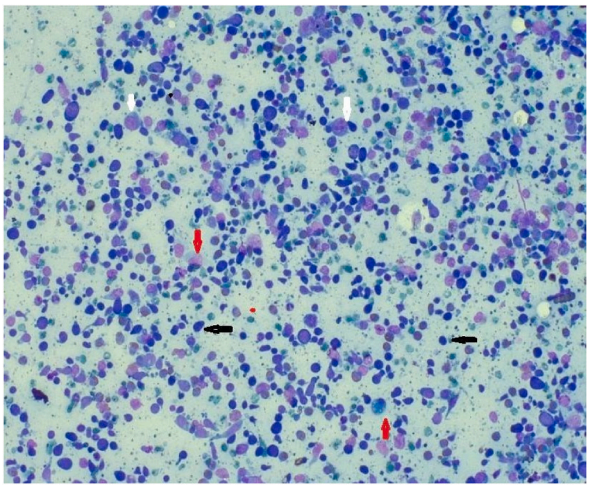


Fig. 2. FNAC (20x) showing polymorphous population comprised of markedly increased eosinophils admixed with inflammatory cells (mature lymphocytes (black arrow), plasma cells and occasionally histiocytes(red arrow)). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

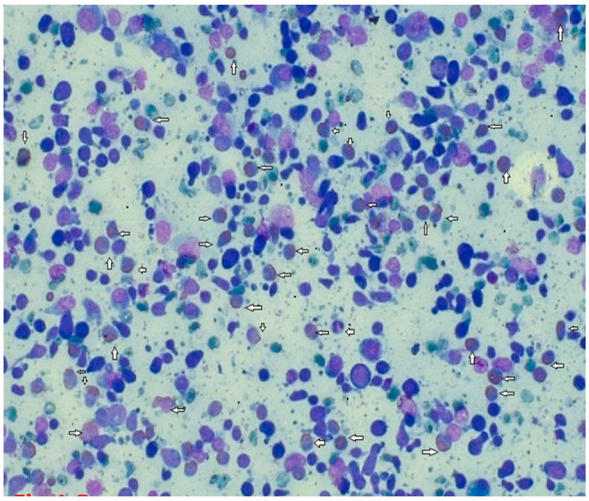


Fig. 3. FNAC (40x) showing polymorphous population comprised of markedly increased eosinophils (white arrow) admixed with inflammatory cells (lymphocytes, plasma cells and occasionally histiocytes).

daily and antituberculous drugs (rifampicin, isoniazid, pyrazinamide, and ethambutol), alongside other necessary supportive measures. Subsequently, her creatinine levels decreased from 2.2 to 1.2, and her vital signs exhibited signs of normalization. Regrettably, the patient chose to depart from the hospital without awaiting the biopsy results and before the diagnosis was settled, against the medical advice provided. However, the patient was advised and was given the antituberculous drugs to be continued at home and local health center.

3. Discussion

An allergic or autoimmune mechanism is suggested by the recurring discovery of peripheral blood eosinophilia and elevated IgE levels, as well as the sporadic correlation between KD and immunologically caused renal illness. Raised levels of IgE may be related to renal illness in KD, according to morphologic and immunologic investigations of renal disease linked to nephrotic syndrome and the presence of IgE in the renal glomeruli [12–14]. Increased levels of soluble interleukin (IL)-2 receptor (sIL-2R), tumor necrosis factor-α (TNF-α), granulocyte-macrophage stimulating factor (GM-CSF), IL-4, IL-5, IL-10, and IL-13 have all been reported in other research [15].

According to other studies, the immunopathogenesis of KD includes the activation of the IL-21/pERK1/2 pathway, and pERK1/2 may be a possible prognostic marker for the illness [16]. Two investigations that support a reactive nature involve molecular

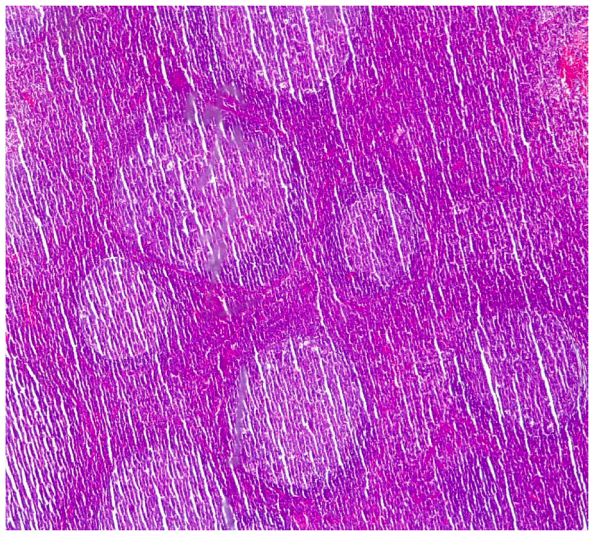


Fig. 4. incisional biopsy of the lymphnode showing hyperplastic lymphoid follicles with reactive germinal centers and prominent mantle zone (10x).

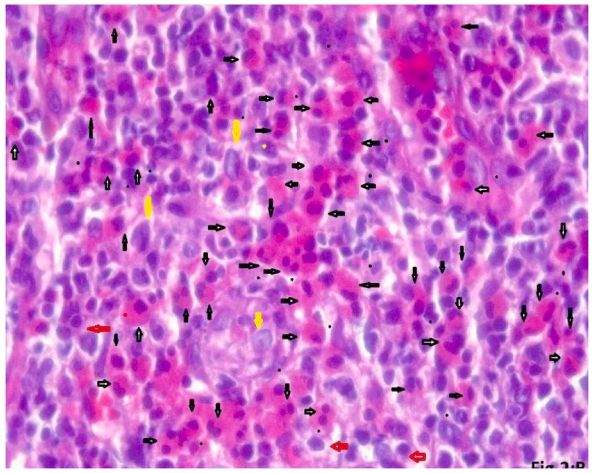


Fig. 5. incisional biopsy of the lymph node showing increased eosinophils (dark-white arrow) mixed with mature lymphocytes (white arrows) and occasional histiocytes (yellow arrow) (40x). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

diagnostics for immunoglobulin heavy chain and T-cell receptor gene rearrangement [17]. Interestingly, a recent single-case report reports that an old man with Kimura syndrome had a polymerase chain reaction-based clonal T-cell receptor gamma gene rearrangement. The full sequencing of the VDJ rearrangement verified the clonal T-cell rearrangement as well. Previously biopsied specimens exhibited the same polymerase chain reaction rearrangement [18,19].

Either a large, deeply seated soft-tissue swelling or several bilateral nodules make up the often slow-growing KD lesion; neither one significantly alters the skin on top. Given that the lesion typically presents with no symptoms, some patients may choose to disregard it. Sites less often affected include the groin (15 %), extremities (12 %), and trunk (3 %); rare sites of involvement include the kidneys [20], orbits [21], ears (external) [22], and spermatic cord [23]. Our patient presented with bilateral cervical, axillary, and inguinal matted lymphadenopathy. Although we did not have renal biopsy to confirm the diagnosis of kimura disease, our patients' elevated creatinine and blood urea nitrogen (BUN) can be explained by the disease's involvement of the kidneys.

A number of conditions are included in the differential diagnosis: florid follicular hyperplasia, dermatopathic lymphadenopathy, allergic granulomatosis of Churg and Strauss, drug reaction, angiolymphoid hyperplasia with eosinophilia (ALHE), Hodgkin lymphoma, angioimmunoblastic T-cell lymphoma, Langerhans cell histiocytosis, parasitic lymphadenitis, and tuberculosis. In endemic areas, differentiating pulmonary tuberculosis from Kimura disease with pulmonary involvement on chest X-rays can be challenging. Certain radiographic signs may assist in distinguishing between these conditions (Table 1). In earlier research, KD and ALHE were

frequently treated as interchangeable terms. However, KD is a chronic inflammatory condition, while ALHE is a blood vessel neoplasm. Individuals diagnosed with ALHE often have a subcutaneous lump in the head and neck area. Large muscle arteries are often involved in the formation of plump cuboidal or hobnail endothelial cells that line the aggregation and lobules that the vascular endothelium forms under the microscope. Serum eosinophilia, increased IgE levels, and regional lymphadenopathy are infrequent in ALHE [24].

Treatments for KD that have not been successful well include surgical resection, radiation, systemic steroid therapy, and conservative care. Up to 25 % of individuals experience a recurrence of the KD lesion following surgical excision and varying follow-up times [18]. Additionally, given the necessity for future face reconstruction and the risk of neurologic deficiency, full surgical excision of a head or neck lesion may be challenging; in these situations, radiation treatment coupled with the use of an immunosuppressive medication may be more successful [4]. Radiotherapy is not used as monotherapy for KD; instead, it is utilized with residual and recurrent KD lesions in postsurgical instances, where it provided local control in 74 % of treated lesions and the recurrence rate following radiotherapy was 11 % [25]. Our patient signed against medical advice and did not show up for follow-up visit as well.

Kimura disease has a chronic history, meaning that lesions frequently persist or recur even after therapy. Because untreated lesions tend to grow, Kimura disease can cause deformity, especially as the condition mostly affects the head and neck. Recurrence following therapy is also thoroughly explained. Poor prognosis of the illness has also been linked to smoking behaviors and a history of systemic disease [6]. Our patient had a systemic illness.

4. Conclusion

In conclusion, Kimura disease presents itself as a captivating and complex condition, posing a significant challenge for both researchers and clinicians. Its intricate nature continues to captivate the interest of experts in the field. However, further studies are imperative to fully comprehend the precise mechanisms that drive its pathogenesis. By unraveling these mechanisms, we can pave the way for the development of targeted therapies, ultimately leading to improved outcomes for those affected by this disease. Moreover, fostering collaborative efforts across international borders will greatly contribute to enhancing our understanding of the disease's epidemiology and aiding in the identification of potential genetic predispositions.

CRediT authorship contribution statement

Yohannis Derbew Molla: Writing – review & editing, Writing – original draft, Conceptualization. **Hirut Tesfahun Alemu:** Writing – original draft, Conceptualization. **Kassa Berie Zegeye:** Writing – original draft, Conceptualization. **Tiruzer Bekele:** Writing – review & editing, Conceptualization. **Amanuel Kassa Tadesse:** Writing – review & editing. **Isak Omer Answar:** Writing – review & editing.

Ethical clearance

The case report has been submitted for Ethical Board Review and approved as ethically sound report.

Consent

Written informed consent was taken from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review for the editor-in-chief of this journal on request.

Availability of data and materials

The authors of this manuscript are willing to provide any additional information regarding the case report.

Table 1
the table shows the possible x-ray differences of pulmonary TB and Kimura disease with Pulmonary involvement (The upper lobe preference, cavitation, and fibrotic changes are more characteristic of TB, while non-cavitary nodules, lack of lobe preference, and eosinophilic infiltrates are suggestive of Kimura disease).

Kimura Disease with pulmonary involvement	Pulmonary Tuberculosis (PTB)
Nodular Lesions: Kimura disease often presents with multiple nodular lesions in the lungs without a specific lobe preference [7].	Cavitation: PTB frequently shows cavitary lesion, especially in the upper lobes of the lungs [8].
Lymphadenopathy: Enlarged lymph nodes, particularly in the mediastinum and hilar regions, are common and are usually non-calcified [9].	Consolidations: areas of consolidations are common, often with lobar or segmental distribution. lymphadenopathy is less common (except primary TB) [10].
Diffuse or Patchy Infiltrates: Less common but possible, particularly if there is associated eosinophilic infiltrate [7].	Miliary pattern: in disseminated TB, a miliary pattern with numerous small nodules throughout the lungs can be observed [8].
Soft Tissue Masses: Soft tissue masses may be seen, which are typically associated with subcutaneous tissues rather than the lung parenchyma. They are usually homogenous and non-calcified [11].	Fibrosis and Scarring: chronic TB can lead to fibrosis and scarring [10].
Eosinophilia: Kimura disease is often associated with peripheral blood eosinophilia, which may be a clue if seen with pulmonary infiltrates [7].	Eosinophilia is very uncommon

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39651.

References

[1] K. HT, Eosinophilic hyperplastic lymphogranuloma, comparison with Mikulicz's disease, Chin Med J. 23 (1937), 699–670.
[2] T. Kimura, On the unusual granulations combined with hyperplastic changes of lymphatic tissue, Trans. Soc. Pathol. Jpn. 37 (1948) 179–180.
[3] M. Abuel-Haija, M.T. Hurford, Kimura disease, Arch. Pathol. Lab Med. 131 (4) (2007) 650–651.
[4] M. Mitsui, S. Ogino, K. Ochi, T. Ohashi, Three cases of eosinophilic lymphfolliculoid granuloma of the soft tissue originating from the parotid gland, Acta Oto-Laryngol. Suppl. 522 (1996) 130–132.
[5] D.K. Rajpoot, M. Pahl, J. Clark, Nephrotic syndrome associated with Kimura disease, Pediatr. Nephrol. 14 (6) (2000 May 22) 486–488.
[6] Q.L. Chen, S. Dwa, Z.C. Gong, K. Abasi, B. Ling, H. Liu, et al., Kimura's disease: risk factors of recurrence and prognosis, Int. J. Clin. Exp. Med. 8 (11) (2015) 21414.
[7] P. Javadi, Rare case of eosinophilic pneumonia in patient with kimura's disease, Pediatr Oncall 10 (2013 May 1).
[8] M.T.A. Wetscherek, T.J. Sadler, J.Y.J. Lee, S. Karia, J.L. Babar, Active pulmonary tuberculosis: something old, something new, something borrowed, something blue, Insights Imaging 13 (1) (2022 Jan 9) 3.
[9] R. Paneru, M. Pokhrel, S. Lamichhane, S. Basnet, S. Poudel, S. Gautam, et al., Kimura disease masquerading tuberculosis: a rare case presentation, Ann Med Surg. 85 (6) (2023 Jun) 3079.
[10] Pulmonary tuberculosis disease in adults: Clinical manifestations and complications - UpToDate [Internet]. [cited 2024 Oct 14]. Available from: https://www.uptodate.com/contents/pulmonary-tuberculosis-disease-in-adults-clinical-manifestations-and-complications/print.
[11] J. Jung, J.H. Han, S.Y. Park, Kimura's disease as a solitary intrapulmonary lymphadenopathy, Eur. J. Cardio. Thorac. Surg. 50 (1) (2016 Jul) 183–184.
[12] N. Ohta, S. Fukase, Y. Suzuki, T. Ito, H. Yoshitake, M. Aoyagi, Increase of Th2 and Tc1 cells in patients with Kimura's disease, Auris Nasus Larynx 38 (1) (2011) 77–82.
[13] A. Yamada, K. Mitsuhashi, Y. Miyakawa, K. Kosaka, K. Takehara, M. Iijima, et al., Membranous glomerulonephritis associated with eosinophilic lymphfolliculosis of the skin (Kimura's disease): report of a case and review of the literature, Clin. Nephrol. 18 (4) (1982) 211–215.
[14] P.B. Googe, N.L. Harris, M.C. Mihm, Kimura's disease and angiolymphoid hyperplasia with eosinophilia: two distinct histopathological entities, J. Cutan. Pathol. 14 (5) (1987 Oct) 263–271.
[15] K. Katagiri, S. Itami, Y. Hatano, T. Yamaguchi, S. Takayasu, In vivo expression of IL-4, IL-5, IL-13 and IFN-γ mRNAs in peripheral blood mononuclear cells and effect of cyclosporin A in a patient with Kimura's disease, Br. J. Dermatol. 137 (6) (1997) 972–977.
[16] Q li Chen, Li C. xi, B. Shao, Z cheng Gong, H. Liu, B. Ling, et al., Expression of the interleukin-21 and phosphorylated extracellular signal regulated kinase 1/2 in Kimura disease, J Clin Pathol [Internet] 70 (8) (2017) 684–689 [cited 2024 Jan 24]; Available from: https://jcp.bmj.com/content/early/2017/01/20/jclinpath-2016-204096?versioned=true.
[17] C.S. Chim, W.H. Shek, R. Liang, Y.L. Kwong, Kimura's disease: no evidence of clonality, Br. J. Ophthalmol. 83 (7) (1999), 878–878.
[18] I.T.M. Kung, J.B. Gibson, P.M. Bannatyne, Kimura's disease: a clinico-pathological study of 21 cases and its distinction from angiolymphoid hyperplasia with eosinophilia, Pathology 16 (1) (1984) 39–44.
[19] C.S. Chim, A. Fung, T.W.H. Shek, R. Liang, W.K. Ho, Y.L. Kwong, Analysis of clonality in Kimura's disease, Am. J. Surg. Pathol. 26 (8) (2002) 1083–1086.
[20] O. Matsuda, K. Makiguchi, K. Ishibashi, Y. Chida, T. Ida, K. Matsuda, et al., Long-term effects of steroid treatment on nephrotic syndrome associated with Kimura's disease and a review of the literature, Clin. Nephrol. 37 (3) (1992) 119–123.
[21] I.C. Francis, M.B. Kappagoda, J. Smith, K. Kneale, Kimura's disease of the orbit, Ophthal Plast Reconstr Surg 4 (4) (1988) 235–240.
[22] N. Baba, T. Nagatani, H. Nakajima, Kimura's disease–immunohistochemistry using monoclonal and polyclonal antibodies, Nihon Hifuka Gakkai Zasshi Jpn J Dermatol. 99 (11) (1989) 1183–1189.
[23] T.M. Van Gulik, J.W. Jansen, C.W. Taat, Kimura's disease in the spermatic cord, an unusual site of a rare tumor, Neth. J. Surg. 38 (3) (1986) 93–95.
[24] D.M. Don, A. Ishiyama, A.K. Johnstone, Y shi Fu, E. Abemayor, Angiolymphoid hyperplasia with eosinophilia and vascular tumors of the head and neck, Am. J. Otolaryngol. 17 (4) (1996) 240–245.
[25] G.E. Kim, W.C. Kim, W.I. Yang, S.K. Kim, W.Y. Oh, H.S. Suh, et al., Radiation treatment in patients with recurrent Kimura's disease, Int. J. Radiat. Oncol. Biol. Phys. 38 (3) (1997) 607–612.