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CASE REPORT

Kimura's Disease Finding on Ocular Adnexal Mass

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Abstract

Introduction: Kimura's disease is an unknown chronic lymphoproliferative inflammatory disease affecting the skin, soft tissues, and lymph nodes. Until September 2020, only 200 cases of Kimura's disease were reported worldwide, however, their exact incidence is unknown. Here, we are interested in reporting a patient with Kimura's disease of the ocular adnexa due to its rarity and to enhance the knowledge of ophthalmologists about confirming the diagnosis of Kimura's disease. **Case Presentation:** A 40-year-old female presented with a chief complaint of a mass on her left nasal orbit for the last year. The mass gradually increased for six months, and it was painless. The systemic laboratory workup revealed eosinophilia and increased serum IgE. Contrast CT-Scan revealed a benign tumor, suspect dermoid cyst. She underwent surgery, and the histopathologic showed Kimura's disease. The patient was followed up on a scheduled basis, and there was no recurrence during four months of monitoring. **Conclusions:** A clinical, systemic laboratory, and histopathological examination is required to confirm the diagnosis of Kimura's ocular adnexa disease and determine the best therapy for the patient due to the high recurrence rate. Combining surgical excision with postoperative radiation is recommended as the most effective treatment in terms of controlling the residual lesion and minimizing the recurrence rate while causing the fewest side effects. Eosinophil screening regularly is advised to evaluate the recurrence rate.

Keywords: Kimura's disease; ocular adnexal mass; eosinophilia

Introduction

Kimura's disease is an unknown chronic lymphoproliferative inflammatory disease[1] affecting skin, soft tissues, and lymph nodes.[2] Reactive lymphoid proliferation may be triggered by an autoimmune process or parasitic manifestation.[3] This disease was first introduced in China in 1938 by Kim and Szeto, however, its name was given in 1948 by Kimura in Japan.[4] Until September 2020, only 200 cases of Kimura's disease were reported worldwide, however, their exact incidence is unknown.[5] The majority of cases are observed in young Asian men under the age of 30; however, women and all other ethnicities can be affected.[1]

Kimura's disease typically manifests as subcutaneous edema and localized lymphadenopathy.[1] The most seriously affected regions were the head and neck, the parotid glands, and the local lymph nodes.[6] In 42–100% of cases, there has been a report of associated lymphadenopathy[7], and it has been reported in the submandibular, retro auricular, cervical regions, and mastoid, as well as less frequently in the orbit, arm, axilla, and groin.[8] Despite its benign, indolent history, its clinical appearance can be mistaken for other more aggressive diseases.[8]

Systemic symptoms are usually absent, however, an association with nephrotic syndrome has been reported. The kidney is the most severely impacted visceral organ, and nephrotic syndrome is the most common presentation.[9] Characteristic findings in the systemic laboratory include eosinophilia and increased serum IgE.[7] The pathological feature of Kimura's disease is hyperplastic follicles with germinal centers that are extensively infiltrated with eosinophils.[7] Here, we are interested in reporting a patient with Kimura's disease of the ocular adnexa due to its rarity and to enhance the knowledge of ophthalmologists about confirming the diagnosis of Kimura's disease.

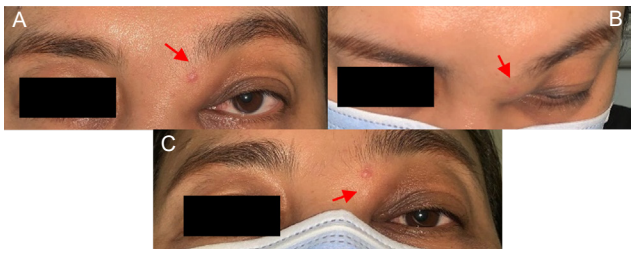

Figure 1. Clinical features of patient showing a 3 cm x 5 cm solid non-tender mass on left nassal orbita (red arrow).

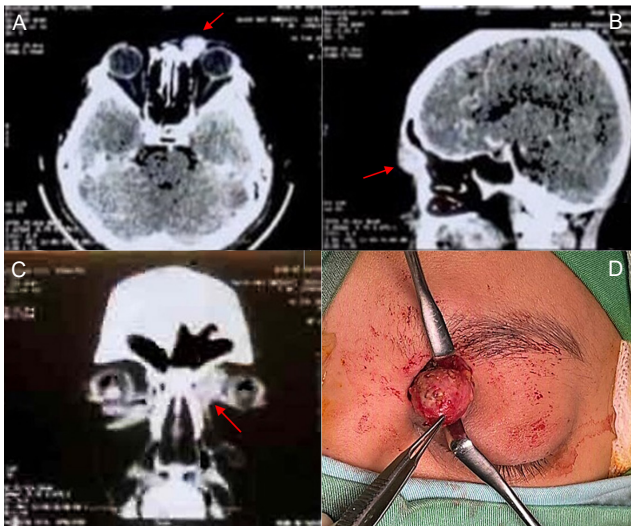

Figure 2. (A-C) Contrast CT-Scan of the head revealed a solid mass, size +/- 1.7 x 1.7 x 2.1 cm on the left medial pre-septal side suggesting a benign tumour suspect dermoid cyst (red arrow); (D) Complete removal of the mass.

Case presentation

A 40-year-old female presented with a chief complaint of a mass on her left nasal orbit for the last year. The mass gradually increased for six months, and it was painless. There was no previous history of trauma or other systemic disease.

The visual acuity of the left eye was 6/9, and the right eye was 6/9. The intra-ocular pressure of both eyes was normal palpation. Hertel measurements are normal. Inspection of the anterior segment showed edema on the left nasal orbital, and palpation examination found a 3 cm x 5 cm solid non-tender mass on the left nasal orbital. The mass was non-pulsatile, nonreducible, nonvascular, and painless. The skin over the mass had no hyperpigmentation, and the mass adhered to the underneath structures (Figure 1). The posterior segment was within normal limits. There was no lymphadenopathy. She had no additional systemic or other ocular abnormalities.

Systemic laboratory works revealed a leucocyte count of 8.430/cu mm with eosinophilia (6.4%), serum urea, and creatinine normal. Chest X-ray was normal and contrast computed tomography (CT)–a head scan revealed no contrast enhancement of solid mass, size +/- 1.7 x 1.7 x 2.1 cm on the left medial pre-septal side, suggesting a benign tumor suspect dermoid cyst (Figure 2A-C).

The patient underwent surgery under general anesthetic, and the mass was obliterated (Figure 2D). The postoperative time was uneventful, and she received her discharge two days later. The histopathological findings revealed follicular hyperplasia with a reactive germinal center; an extensive eosinophil secretion was seen in the interfollicular area, accompanied by partial disruption of the follicle by eosinophils (follicular lysis). The proliferation of blood vessels was also seen, with some of the blood vessel walls appearing thickened with fibrosis, and no malignancy was seen. The biopsy revealed a benign lymphoproliferative lesion, leading to Kimura's disease (Figure 3). Systemic laboratory follow-up revealed leucocyte count 13.040/cu mm with eosinophilia (8.5%), serum total IgE 1797.5 IU/mL (normal 1–190 IU/Ml), serum urea and creatinine normal.

After surgery, the patient was treated with oral antibiotics, oral steroids, oral analgetic, and eye ointment antibiotics. The patient was followed up on a scheduled basis, and there was no recurrence during four months of monitoring.

Discussion and conclusions

Kimura disease is an unknown chronic lymphoproliferative inflammatory disease[1] that affects the skin, soft tissues, and lymph nodes.[2] Kimm, Szeto, and others originally called it "eosinophilic hyperplastic lymphogranuloma" in Chinese literature in 1937.[10] Kimura et al.[11] published the histological description in 1948, and as a result, the disease bears his name. Subcutaneous angiolymphoid hyperplasia with eosinophilia (ALHE) was the name given to the disease by Wells and Whimster in 1969.[12] They claimed the two diseases were the same, with subcutaneous ALHE signifying any earlier stage that eventually developed into Kimura's disease.[12] Later research[13], however, based on histopathological results, separated the disorders into two distinct categories. Kimura's disease is currently assumed to be an uncommon chronic inflammatory or allergic condition, and ALHE is considered a benign vascular neoplasm.[13] Although several studies have been done, the etiology and pathophysiology of Kimura's

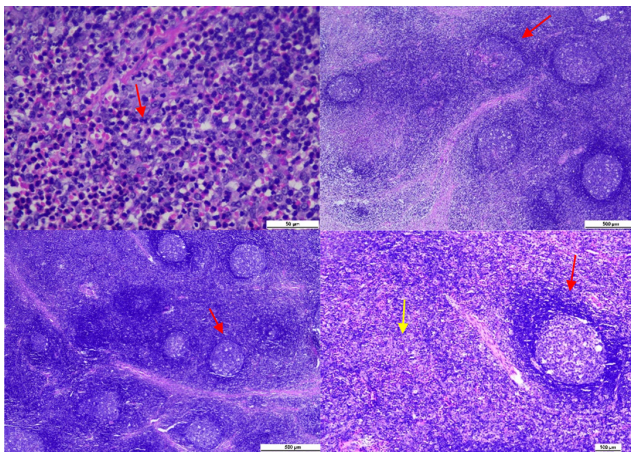

Figure 3. (A) An extensive eosinophil secretion was seen in the interfollicular area (red arrow); (B-D) Follicular hyperplasia with a reactive germinal center (red arrow) and an extensive eosinophil secretion (yellow arrow).

disease are still unknown. No particular antigens have been discovered despite higher levels of IgE, interleukin [IL]-4, IL-5, IL-13, tumor necrosis factor alpha, and mast cells found in peripheral blood and those with the lesions in most patients. Infections, allergic reactions, neoplasms, and autoimmune reactions with an abnormal immune response are all possible etiologies.[14]

In this case, the patient was a 40-year-old female with the chief complaint of a mass on her left nasal orbit without lymphadenopathy and systemic symptoms. The prevalence of Kimura's disease is reported to be around 200 cases worldwide. The disease is endemic in Asia (mainly Japan and Southeast Asia), and the incidence rate is high in the first and third decades of life.[15] The prevalence generally affects young adult men in the third decade compared to women, with a ratio of 3:1.[16]

The patient came with a chief complaint of a mass on her left nasal orbit without lymphadenopathy and systemic symptoms. Kimura's disease typically manifests as subcutaneous edema and localized lymphadenopathy.[1] Most of Kimura's disease lesions involve the deep subcutaneous tissues of the head and neck region, appearing as one or more deeper masses.[14] In some rare cases, pigment deposition and pruritus are noted along with the masses, which are otherwise non-tender and poorly defined.[14] In 42–100% of cases, there has been a report of associated lymphadenopathy[7], and it has been reported in the submandibular, retro auricular, cervical regions, and mastoid, as well as less frequently in the orbit, arm, axilla, and groin.[8] The ocular system is rarely affected by Kimura's disease, with the first incidence of orbital involvement reported in 1966.[17] Systemic symptoms are usually absent, but an association with nephrotic syndrome has been reported.[9]

The patient's blood analysis showed eosinophilia (8.5%) and increased serum IgE 1797.5 IU/mL, which led to Kimura's disease. Contrast CT–a head scan revealed no contrast enhancement of solid mass on the left medial pre-septal side. Based on the literature, characteristic findings in systemic laboratory work include eosinophilia and increased serum IgE.[7] Findings from CT with contrast enhancement usually show homogeneously enhancing non-specific lesions.[13] Based on literature studies[14], because there is no single specific diagnostic test for Kimura's disease, a biopsy or excision of the affected mass or lymph node is commonly required for a pathological diagnosis. The histopathological findings of Kimura's disease are hyperplastic follicles with germinal centers that are extensively infiltrated with eosinophils.[7] This patient's histopathological findings revealed there was follicular hyperplasia with a reactive germinal center and an extensive eosinophil secretion was seen in the interfollicular area accompanied by partial disruption of the follicle by eosinophils (follicular lysis). The biopsy revealed a benign lymphoproliferative lesion, leading to Kimura's disease.

Based on clinical presentation, histopathology, blood eosinophil, and IgE levels, we diagnosed the patient with Kimura's disease of the ocular adnexa. With its benign, indolent clinical course, Kimura's disease might be mistaken for other diseases, such as ALHE.[14] Kimura's disease is currently assumed to be an uncommon chronic inflammatory or allergic condition, and ALHE is considered a benign vascular neoplasm.[13] Several clinical characteristics and histopathological results can conceptually distinguish Kimura's disease from ALHE. Kimura's disease clinical presentation includes deep subcutaneous mass, mainly in the head and neck, also involvement of the main salivary glands, and lymphadenopathy. ALHE patients present superficial subcutaneous papules or nodules, mainly in the head and neck, usually accompanied by erythematous skin without eosinophilia, elevated IgE levels, and regional lymphadenopathy. ALHE patients' histological findings are similar to Kimura's disease but with more pronounced vascular proliferation and plump endothelial cells ranging from cuboidal to dome-shaped.[1],[7],[14],[16]

In this case, the patient underwent surgical excision under general anesthetic, and the mass was obliterated. The patient was followed up on a scheduled basis, and there was no recurrence during four months of monitoring, but due to the possibility of recurrence, long-term follow-up will be ensured by clinical examination initially every six months. Systemic laboratory follow-up post excision revealed leucocyte count 13.040/cu mm with eosinophilia (8.5%), serum Total IgE 1797.5 IU/mL (normal 1–190 IU/mL), serum urea and creatinine normal. According to earlier studies[18], elevated blood IgE levels persisted despite corticosteroid therapy, showing that IgE-secreting B cells in Kimura's disease patients may be long-lived. The eosinophil count was associated with therapeutic response in Kimura's disease patients, implying that it might be utilized as a prognosis marker for Kimura's disease.[17] In earlier literature[18], the measurement of eosinophils was also used as a Kimura's disease recurrence marker. There is currently no clear explanation about the risk factors that cause recurrence due to the rarity of Kimura's disease, however, in a few pieces of literature, it is stated that smoking and other systemic diseases act as risk factors for recurrence.[6]

Several therapeutic techniques, including observation, steroid medication, surgical excision, and radiation, have been introduced in the literature. However, no treatment has been identified as the optimum therapy because the therapeutic regimen for Kimura's disease is challenging to evaluate in the literature since most data is published

in case reports or short series. Previous research has shown[14] that steroids are beneficial in treating local lesions, lymphadenopathy, and nephrotic syndrome; however, relapses have been documented when the steroid dose was reduced. Local recurrence was common with steroid dose reduction or drug withdrawal, and long-term steroid use was associated with stomach ulcers, osteoporosis, and type 2 diabetes.[14],[19] Surgery may provide the most accurate diagnostic results and has long been the treatment of choice. Excision surgery can be performed for both diagnostic and therapeutic objectives; however, the pathology of Kimura's disease lesions often remains unknown. As a result, achieving incision-free margins during surgery is complex, and recurrence has been reported in approximately 25% of cases.[20] Based on the study by Chen et al.[6], 10 out of 32 patients with Kimura's disease were given only surgical therapy, two were cured, and eight had recurrence, however, there is no clear explanation about the type of mass of each patient.

Radiotherapy, despite being controversial due to its slow and non-malignant change, low-dose radiation is effective and safe both in the short and long term.[6] Hareyama et al.[21] found that radiating with 26-30 Gy resulted in a 90% local control rate and that the radiation field should be confined to the lesion and regional lymph node. Chang et al. also report that 63% of local control of Kimura disease was treated with radiation doses ranging from 20 to 45 Gy over a median follow-up of 65 months. [18] In other studies[19], combining surgical excision with postoperative radiotherapy resulted in a much lower local recurrence rate than surgery or radiotherapy alone. As a result, postoperative radiation may effectively control the residual lesion and lower the recurrence rate with minimum adverse effects. Based on the study by Chen et al.[6], 17 patients with Kimura's disease were given surgery and radiotherapy, ten were cured, and seven had recurrence. Eventhough, existing treatment options still have a chance of recurrence, Kimura's disease has a good prognosis and no chance of progressing to malignancy.[14]

In conclusion, a clinical, systemic laboratory, and histopathological examination are required to confirm the diagnosis of Kimura's ocular adnexa disease and determine the best therapy for the patient due to the high recurrence rate. Although Kimura's disease in the ocular system is rare, it can still be considered a differential diagnosis when there is an ocular mass. Combining surgical excision with postoperative radiation is recommended as the most effective treatment in terms of controlling the residual lesion and minimizing the recurrence rate while causing the fewest side effects. Eosinophil screening regularly is advised to evaluate the recurrence rate.

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