



## CASE REPORT

### KIMURA'S DISEASE: A DIAGNOSTIC CHALLENGE

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#### SUMMARY

Kimura's disease is a rare, chronic, benign disorder primarily seen in male Orientals during second and third decades of life. Many clinicians don't have enough knowledge about clinical presentation of this entity. Disease presents itself as a tumor like lesion with a predilection for the head and neck region often with parotid gland involvement and usually associate with lymphadenopathy, peripheral eosinophilia and markedly elevated serum IgE levels. The diagnosis of Kimura's disease is frequently based on the biopsy or excision of the involved node. Resection of the tumor mass, systemic and intralesional corticosteroids local irradiation are the three major therapeutic options. A 43 years old Turkish male who had been misdiagnosed was referred to our clinic for treatment of recurrent neck mass. In addition to pathological reevaluation of patients histologic speciemens, various blood work was done. Kimura's disease was discussed with treatment options.

*Keywords: Kimura's disease, neck mass, peripheral easinophilia*

#### KİMURA HASTALIĞI: TANISI ZOR BİR PATOLOJİ

##### ÖZET

Kimura hastalığı, özellikle sarı ırkta hayatın iki ve üçüncü on yılında rastlanan nadir, benign, kronik bir hastalıktır. Bir çok klinisyen bu hastalığın klinik seyri hakkında yeterli bilgiye sahip değildir. Hastalık kendini baş boyun bölgesinde, çoğunlukla parotis bezini de içeren, tümör benzeri lezyonlar ve eşlik eden lenfadenopati, periferik eosinofili ve belirgin olarak artmış serum IgE seviyesi ile belli eder. Kimura Hastalığının teşhisi tutulan lenf nodlarının biopsisi veya çıkartılması ile konulur. Tümörün çıkartılması, sistemik ve lezyon içi steroid uygulanması ve lokal radyoterapi üç ana tedavi seçeneğidir. Bu makalede tekrarlayan boyun kitlesi ile kliniğimize başvuran, daha önce değişik tanılar konulmuş 43 yaşında erkek bir hasta sunulmuştur. Hastanın patolojik olarak tekrar değerlendirilmesine ek olarak çeşitli kan testleri de yapılmıştır. Kimura Hastalığı tedavi seçenekleri ile tartışılmıştır.

*Anahtar Sözcükler: Kimura hastalığı, Boyun kitlesi, Periferik eosinofili*

#### INTRODUCTION

Kimura's disease is a chronic benign disorder primarily seen in male Orientals during second and third decades of life.<sup>1</sup> Disease presents itself as a tumor like lesion with a predilection for the head and neck region often with parotid gland involvement and usually associate with lymphadenopathy, peripheral eosinophilia and markedly elevated serum IgE levels. After the first described as 'eosinophilic lymphogranuloma' by Kung et al.<sup>1</sup> in 1937, then disease was made known as Kimura's disease by Kimura et al.<sup>1</sup> in 1948. Disease usually affects the Orientals but there are isolated case reports from other parts of the world affecting other races<sup>2,3,4</sup>. Recognition of the clinical picture may allow clinicians to reduce the concern about the possibility of malignant disease and limit the number of laboratory tests.

We report a case of Kimura's disease to draw attention to this disease as its presentation could easily confused with malignancy.

#### CASE PRESENTATION

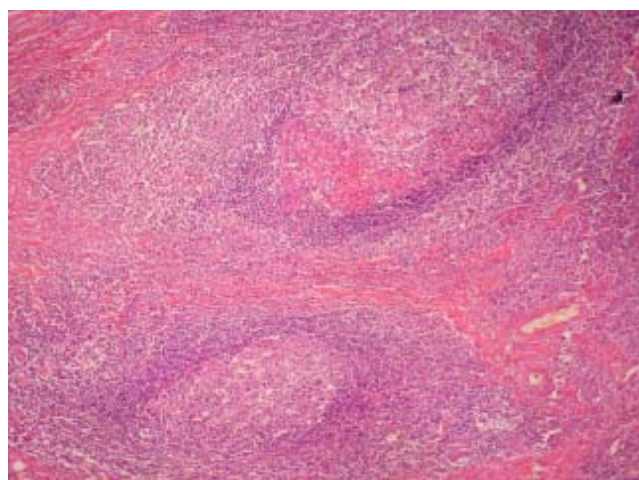
A 43 year old Turkish male was first seen, in 2000, with a painless diffuse superficial swelling in the left postauricular area. The swelling had grown gradually to the size of 3x2 cm since it had been first noted 1 year earlier. Ultrasonography showed solid round mass in postauricular region. Fine needle aspiration cytology (FNAC) was performed. The aspirate showed mature and transformed lymphocytes, hystiocytes, leucocytes, atypical cells with hyperchromatic nucleus. Then for accurate diagnosis, excisional biopsy performed and histologic diagnosis made as sialoadenitis chronica. One month after the operation swelling recurred firstly on the insicion scar and rapidly growing tumor again developed at the left postauricular area. At this time tumor was enucleated by direct approach, the histologic diagnosis was at this time pseudolymphoma. Two years after last procedure, tumor recurred again. This time physical examination revealed 3x2 cm endured mass overlying parotid

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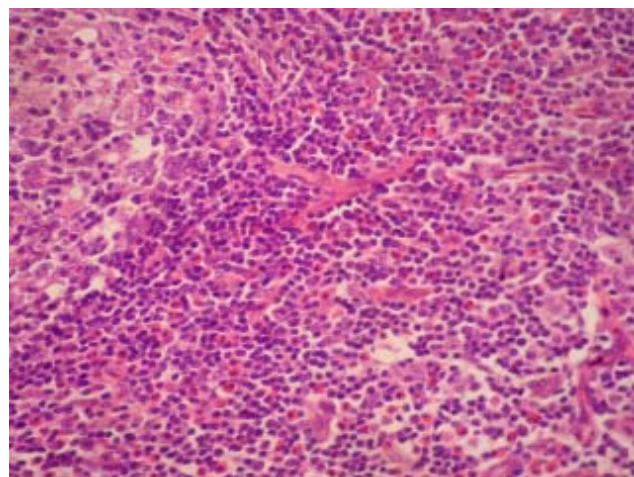
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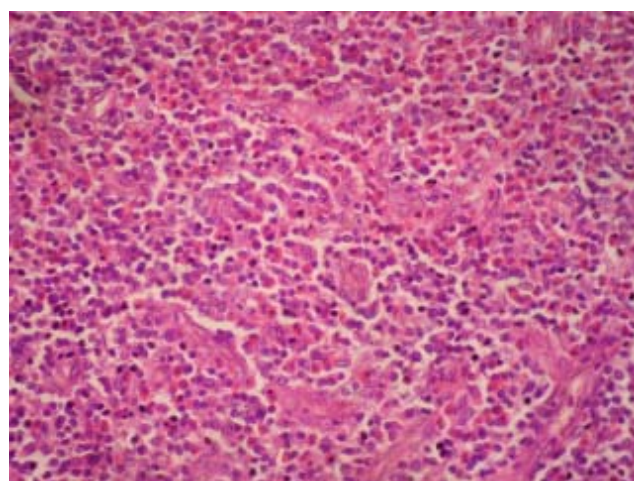
gland and postauricular area in association with multiple lymph nodes measuring less than 1 cm that were palpable anterior to the left sternocleidomastoid muscle. Facial nerve functions were intact. Ultrasonography and computed tomography showed solid mass with diffuse margins in left superficial parotid gland and periauricular area. FNAC was inconclusive, complete tumor removal with left superficial parotidectomy was performed. At the time of surgery, dissection was difficult. Parotid tissue was noted as firm but without palpable tumor. Tumor was adherent to the skin and closely related to the facial nerve. The histology again showed sialoadenitis chronica and pseudolymphoma. The patient was consulted by our clinic, because of the discrepancy between the aggressive clinical course and previous benign diagnosis. We advised to reevaluate the last specimens. The specimens were reevaluated by a different pathology department. The diagnosis of Kimura's disease was made at last. This was based on picture of inflammatory cellular infiltrate in the interfollicular area consisting of lymphocytes, plasma cells, eosinophils and the lymphoid follicles with prominent germinal centers that surrounded by a fibrous tissue without impairment of follicular structure (Fig.1,2,3). Laboratory studies revealed peripheral eosinophilia of 28 per cent, and increased blood IgE concentration. The urinary protein was checked, there was no proteinuria. Patient was treated with 30 mg of prednisolon for 12 days then put on 8 mg prednisolone. He has been followed up in our clinic regularly. When the medication had been decreased, tumor recurred, dosage increased to 8 mg again, tumor resolved. At present patient show no recurrence (Fig. 4), the blood eosinophils and serum IgE are in normal levels .



**Figure 1.** Interstitial fibrosis and lymphoid follicles which has prominent germinal centers (H+E×10).



**Figure 2.** Perinodal eosinophil and plasma cell infiltration (H+E×100).



**Figure 3.** Eosinophil and plasma cell infiltration, capillary proliferation (H+E×100).



**Figure 4-5.** No recurrence 18 months after last surgery with continuous low dose steroid therapy.

## DISCUSSION

Kimura's disease is a rare, benign chronic inflammatory disease which commonly occurs among the Oriental population. But there are isolated case reports from other parts of the world affecting other races<sup>2,3,4</sup>. The patients are usually in the second





or third decade of life (reported mean age 27 to 40) with a male predominance (M:F=5/1).

The typical physical manifestation of this disorder is slowly enlarging swelling with diffuse margins in the head and neck area, predominately in the preauricular or submandibular area. Rare cases have been reported to include tympanic membrane<sup>2</sup> and eye lids<sup>3</sup>. Lesions can occur in parts of the body other than in the head and neck (axilla, groin, limb and trunk etc.). Visceral involvement is rare, in some cases there may be associated proteinuria with or without nephrotic syndrome, so urinary protein level should be checked in every patient. Renal involvement is the only frequent systemic manifestation, nephrotic syndrome has been reported in up to 60% of patients<sup>5</sup>. The onset is insidious, often long duration. Peripheral eosinophilia and elevated serum IgE levels almost always present<sup>5</sup>.

Kimura's disease can be confused clinically and histologically with angiolymphoid hyperplasia with eosinophilia (ALHE). Kimura's disease and ALHE was thought to be same disease<sup>1</sup> but recent literature describes these as two distinct clinical entity<sup>3</sup>.

The diagnosis of Kimura's disease is often difficult. FNAC is a safe procedure, but has only limited value<sup>2</sup>. Pathologic diagnosis is frequently based on the biopsy or excision of the involved node. The characteristic histological features include preserved nodal architecture, florid follicular hyperplasia with reactive germinal centers, protein and IgE deposits in germinal centers, germinal center necrosis, eosinophilic infiltrates, proliferation of postcapillary venules, sclerosis, polykaryocytes of the Whartin-Finkeldey type, eosinophilic folliculolysis, and prominent eosinophilic microabscesses<sup>5,6</sup>.

The clinical differential diagnoses of Kimura's disease should include ALHE, reactive lymphadenopathy secondary to drug reaction and parasitic infections, lymphoma, parotid tumor with nodal metastasis, and Mikulicz disease<sup>5</sup>. A healing abscess can be differentiated by its content of large number of polymorphs and histiocytes. Appropriate cultures, histochemical stains, and immunophenotyping studies will help separate these unique and distinct lesions.

The pathophysiology of Kimura's disease is not understood at this time, may be related to a disturbance of an interaction between type 1 and 2 T helper cells (Th1 and Th2). Patients with Kimura's disease have been shown to have high levels of circulating eosinophilic cationic protein (ECP) and major basic protein (MBP) with heavy concentrations

of IgE in their tissue<sup>6</sup>. Atopic reaction to a continuous antigenic stimulus (specially candida albicans)<sup>7</sup>, parasitic infection, neoplasm have been actively thought in the etiology for Kimura's disease but not defined. Perhaps continuous antigenic stimulus causing IgE deposits along the glomerular capillary membrane causes epitheloid damage to renal glomeruli, results renal disease in Kimura's disease<sup>8</sup>. No evidence of antigenic stimulus was found in our case.

Three major management options exist for Kimura's disease. Resection of the tumor mass may be effective but lesions tends to recur<sup>5,7</sup>. At the time of surgery the affected tissue are described as poorly circumscribed, matted together, fibrous and vascular<sup>5</sup>. Systemic and intralesional corticosteroids have been shown to reduce the size of lesion, but the tumor tends to recur when these drugs are discontinued as experienced in our case<sup>8</sup>. Long term steroid treatment may side affects that limit its use. Finally local irradiation has also been shown to be effective but generally not advocated in younger patients<sup>8</sup>. Indications for radiotherapy include patients who have failed with medical management. Sometimes, even with aggressive treatment plan, complete remission is not possible.

These lesions are benign, malignant degeneration has never been observed<sup>4</sup>. It may be advisable to take a conservative approach, treating only if the mass continues to grow or causes significant deformity<sup>4</sup>. Patients should be followed up for recurrence, proteinuria and for side effects of steroid treatment regularly.

## CONCLUSION

In a view of presentation in the head and neck region with a mass or nodular lesion Kimura's disease should be in the differential diagnosis. A routine protocol for treating recurrent and systemic Kimura's disease has not been accepted yet. Kimura's disease usually affects the Orientals and thus many clinicians and pathologists in the other parts of the world are unaware of this entity; it could easily misdiagnosed. Recognition of the clinical picture may allow practitioners to reduce the concern about the possibility of malignant disease and limit the number of laboratory tests.

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