Kimura's disease: two case reports with review of the literature

Kimura hastalığı: İki olgu sunumu ve literatürün gözden geçirilmesi

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Kimura’s disease is an uncommon, chronic inflammatory disorder of unknown etiology. The disease usually presents as a massive subcutaneous swelling with predilection for head and neck region of young men. Morphologically, the lesions are characterized with lymphoid follicles, intensive aggregations of eosinophils, vascular proliferation and fibrosis. Laboratory analyses detect hypereosinophilia and elevated total IgE in the blood. We present two cases of Kimura’s disease in which lymphadenopathy and cutaneous nodules were main findings. We reviewed the literature on Kimura’s disease.

Key Words: Kimura’s disease.

Kimura hastalığı nadir, etyolojisi bilinmeyen kronik enflamatuvar bir hastalıktır. Sıklıkla genç erkeklerde baş boyun bölgesinde belirgin subkutan şişlik şeklinde ortaya çıkar. Lezyon histolojik olarak; lenfoid follikiller, yoğun eosinofil agregatları, vasküler proliferasyon ve fibrozis ile karekterizedir. Laboratuvar incelmesinde; hipereozinofili ve yüksek total IgE kan değerleri söz konusudur. Lsentadenopati ve kutanöz nodül ana bulgusu olan iki olgu literatür eşliğinde sunuldu.

Anahtar Sözcükler: Kimura hastalığı.

Kimura’s disease is an idiopathic, chronic allergic-inflammatory condition usually involving young to middle-aged subjects and shows a striking male predominance. It is more prevalent but not exclusive among Orientals.¹⁻³ The disorder received its name in 1948 when Kimura et al.¹ described an “unusual granulation combined with hyperplastic changes in lymphoid tissue”. The patients usually have slowly enlarging mass in head and neck region, with involvement of the subcutaneous and soft tissues, major salivary glands, and lymph nodes.¹⁻⁴ The pathophysiology of Kimura’s disease is unknown. The presence of eosinophils in the inflammatory infiltrate and in the peripheral blood suggests Kimura’s disease is a hypersensitivity reaction.⁵ Although recurrences are common following surgical excision, the disease has a benign course.⁶⁻⁸

CASE REPORTS

Case 1 – A 42-year-old woman presented with a right cervical mass enlarging in size gradually over two years period. Besides to this mass, she had an right upper eyebrow swelling, with two months...
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history. She had neither pain nor discharge from the mass. She received no medical treatment and had no history of allergic symptoms. Otolaryngologic examination revealed a mass on the right side of neck. The mass was mobile, nontender and approximately 8x7 cm in diameter. In addition to this mass, another nontender, soft tissue mass was palpable subcutaneously in the right upper eyebrow region. A CT scan of patient revealed a multidense, round, well delineated mass occupying middle jugular area. The serum IgE level was 1051.0 U/ml (Normal range: 10-100 U/ml). The other laboratory findings were in normal ranges. There was no proteinuri. Lesions were surgically removed and clinical course following surgery was favorable. Cross-section of lesions were reddish-yellow and mottled. The histopathological investigation of the subcutaneous masses confirmed lymph node like tissue with markedly reactive follicular hyperplasia, intervening dense eosinophilic infiltration and fibrosis. Cross-sections also had marked vascular proliferation consisting of blood vessels with variable sizes lined by plump endothelial cells, and eosinophilic proteinaceous material in germinal centers (Fig. 1a). IgE strongly reacted in germinal centers (Fig. 1b). The histopathologic findings were specific for Kimura’s disease.

Fig. 1- (a) Case 1 Histology of lesion. Marked vascular proliferation consisting of blood vessels with lined by plump endothelial cells, and eosinophilic proteinaceous material in germinal centers. (b) IgE positive cells were stained reticular diffusely in the center of lymphoid follicle (H-E x 100).
**Case 2**—A 32-year-old male patient presented with an enlarging mass in right submandibular area. He had pain with accelerated growth of the lesion over the last 3 months. The mass was firm 4x4 cm in size. Multiple lymph nodes measuring less than 2 cm were palpable anterior to left sternocleidomastoid muscle. The IgE level was reported to be “somewhat elevated”. Preoperative CT scan revealed involvement of right submandibular and parotid gland, and cervical lymph nodes. Moreover, CT scan showed a contrast intensity in the parotid gland and ipsilateral lymph nodes (Fig. 2a). Two fine needle aspirations were performed. The two aspirate showed reactive lymhoid tissue. Incomplete surgical excision could be performed due to the attachment of lesion surrounding tissue and major vascular element. Microscopic examination revealed a similar essential histologic pattern in salivary gland, and lymph nodes. Main pathologic changes in the lymph nodes include vascularization of the germinal centers, folliculolysis, eosinophilic microabcesses within follicles, increased postcapillary venules in paracortex, eosinophilic infiltration and fibrosis. Subcutaneous lesion showed irregular areas of inflammation, formation of lymphoid follicles with germinal centers and varying degrees of glandular destruction. Glandular lobules were replaced by fibrous tissue and were densely infiltrated by eosinophils, lymphocytes, and plasma cells, resulting in atrophy and loss of acini. Periductal fibrosis was commonly noted (Fig. 3a, b). With anti-immunoglobulin E, there was reticular deposition in the follicle centers. The clinical and laboratory findings were correlated with Kimura’s disease.

**DISCUSSION**

Controversy exists in the literature regarding whether KD (Kimura Disease) and ALHE (Angiolymphoid Hyperplasia with Eosinophilia) are the same entity or not. Some authors believe KD represents a deep chronic form of ALHE; however, most recent papers tend to separate these two on the basis of the clinical and histopathologic characteristics. ALHE will no longer be confused with Kimura’s disease. Kimura’s disease is commonly seen among Whites, involves the superficial skin forming cluster of papules. In contrast, ALHE is common among asians and seated deep in subcutaneous tissues. More importantly, the lymphadenopathy is an essential part of Kimura’s disease which is rare in ALHE. Males are affected more commonly than females in KD, whereas a female predominance is noted in ALHE. KD is usually encountered in young adults, and occasionally associated with renal disease. However, ALHE has rarely been associated with renal disease. Distinct histological differences also can be noted between KD and ALHE. Histiocytoid vessels with particular endothelial cells, which are noted in ALHE, have very rarely been found in KD. Germinal centers of KD can become so heavily infiltrated with eosinophils that progressive destructions ensues, causing lysis of the follicles never been seen in ALHE. In KD, laboratory analyses detect hypereosinophilia and elevated total IgE in the blood. Serum IgE is usually normal in ALHE. The other difference is that immunohistochemical stains have

![Fig. 2](image-url)  
*Fig. 2—Case 2 CT image (a) preoperatively, (b) postoperatively (postradiotherapy).*
shown IgE in the germinal centers of KD but not in ALHE. In our cases, all features were favoring the diagnosis of Kimura’s disease over ALHE.

Treatment of Kimura’s disease is not codified. Surgical excision of the lesions is the first-line therapy, but recurrences are frequent. Systemic corticosteroid therapy with prednisone is prescribed for relapsing forms, and has been shown to have good efficacy, but with a risk of relapse in case treatment is withdrawn. Local radiation therapy (25-30Gy) is applied to lesions refractory to corticosteroid therapy or in cases where surgery is not feasible. In our Case 1, only surgical excision of lesions was performed. After a follow-up period of 8 months, the patient revealed no evidence of recurrence. In our Case 2, surgical excision was the main therapy. But we started with preliminary medication of 1 mg/kg prednisone daily one week postoperatively due to incomplete removal of mass. During operation, the margins of the lesion was hard to define and surgery was further complicated by parotid gland and lymph node involvement which was associated with matting together of the affected surroundings tissues. It was the previous inability to identify clearly preoperatively which contributed most heavily to the failure to eradicate the lesion completely.

Fig. 3- Case 2. Involved submandibular gland show marked infiltration of lymphocytes, plasma cells, and eosinophils that resulted in atrophy and loss of acini. (a) (H-E x 20), (b) (H-E x 200).
After surgical excision and corticotherapy the cervical mass was reduced in size. But, due to referral of patient one month following surgery with an area of recurrence, patient also received radiation therapy to the cervical region (4400 cGy in 22 fractions) from March 26, 2002 to April 24, 2002. The area has remained well healed with no further recurrence for 3 months (Fig. 2b).

In conclusion; it is important for otolaryngologists and pathologists to recognize the lymph node changes in KD to differentiate it from other disorders requiring more aggressive therapy.

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