

KIMURA'S DISEASE: Presenting as unilateral parotid mass

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Objectives: Kimura's disease (KD), or eosinophilic lymphogranuloma, is a rare chronic inflammatory condition with unclear etiology. We aim to present our experience with this condition and review the available literature. **Methods:** This report depicts a pathologically proven case of KD in a 44-year-old man with gradually increased swelling in his left parotid region for the past year, which was painless, and pruritus. **Results:** This report depicts a pathologically proven case of KD in a 44-year-old man with gradually increased swelling in his left parotid region for the past year, which was painless, and pruritus. **Conclusion:** This report depicts a pathologically proven case of KD in a 44-year-old man with gradually increased swelling in his left parotid region for the past year, which was painless, and pruritus.

Keywords: Parotid, Eosinophils, Eosinophilic lymphogranuloma, Parotidectomy

Introduction

Kimura's disease (KD), or eosinophilic lymphogranuloma, is a rare chronic inflammatory condition that presents with multiple painless subcutaneous nodules, especially in the head and neck, with coexisting lymphadenopathy, salivary gland hypertrophy, and peripheral eosinophilia [1,2]. Since its histopathological diagnosis, only 200 cases have been reported worldwide [3]. The disease is generally seen in young adults, with most patients aged 20 and 40 years; men are affected more commonly than women, with a 3:1 ratio [4,5]. The disease is endemic in Asians but occurs sporadically

in other racial groups [5]. The commonly involved sites are periauricular, groin, orbit, and eyelids. Peripheral blood eosinophilia and elevated serum immunoglobulin E (IgE) levels are constant features of KD [6]. Coexisting renal disease is expected, with an incidence ranging from 10% to 60% [5]. Diagnosing KD is often complex, and the biopsy or excision of the involved mass for a pathological study is necessary. In this article, we present the case of a 44-year-old male patient with KD on his left parotid area.

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Case report

A 44-year-old male herdsman presented to the Department of Surgery, Mongolia-Japan Hospital, Mongolian National University of Medical Sciences (MNUMS). He had complained of swelling in the parotid gland since last year, which was insidious in onset and gradually progressive. The swelling was painless and pruritus, with no history of fever, trauma, or discharge from the swelling due to severe itching in the left parotid area, with multiple red-pinkish bumps, scratches, and scars. Localized examination revealed a 3 cm × 2 cm non-tender, firm, partially mobile subcutaneous nodule in the left parotid region. Facial asymmetry was maintained with normal facial nerve functions. The rest of the ENT examination was also within normal limits. The patient has advised a contrast-enhanced computed tomography, which revealed multiple intra-parotid lymph nodes in the superficial lobe of the left parotid gland with an enlarged parotid gland but normal parotid parenchyma (Figure 1). Hematological examination revealed WBC 8.04 gm/dl, Hb 14.4

gm/dl, Neutrophils 31.1%, Lymphocytes 24.4%, Eosinophils 36.6%, Monocytes 7.2% and adequate platelets.

Pre-operative fine needle aspiration cytology (FNAC) was done, and it revealed a mixed population of large and small lymphocytes and some histiocytes. These findings were consistent with a negative for malignancy, a reactive process (Figure 2). The patient underwent superficial parotidectomy with intra-parotid lymph node excision. The surgical specimen consists of a lump of brown-tan hardish tissue measuring 5.2 x 3.5 x 2.5 cm (Figure 3A). It shows a white-gray homogenous appearance on multiple cut sections without defined mass formation. The histopathological examination revealed disruption of normal parotid gland structure by the proliferation of lymphoid follicles and fibrosis (Figure 3B). Many germinal centers of lymphoid follicles exhibited necrosis with protein debris, diffuse infiltration of eosinophils, and eosinophilic abscess formation (Figure 3C&D). Based on those histopathological findings, the diagnosis of Kimura's disease was confirmed.

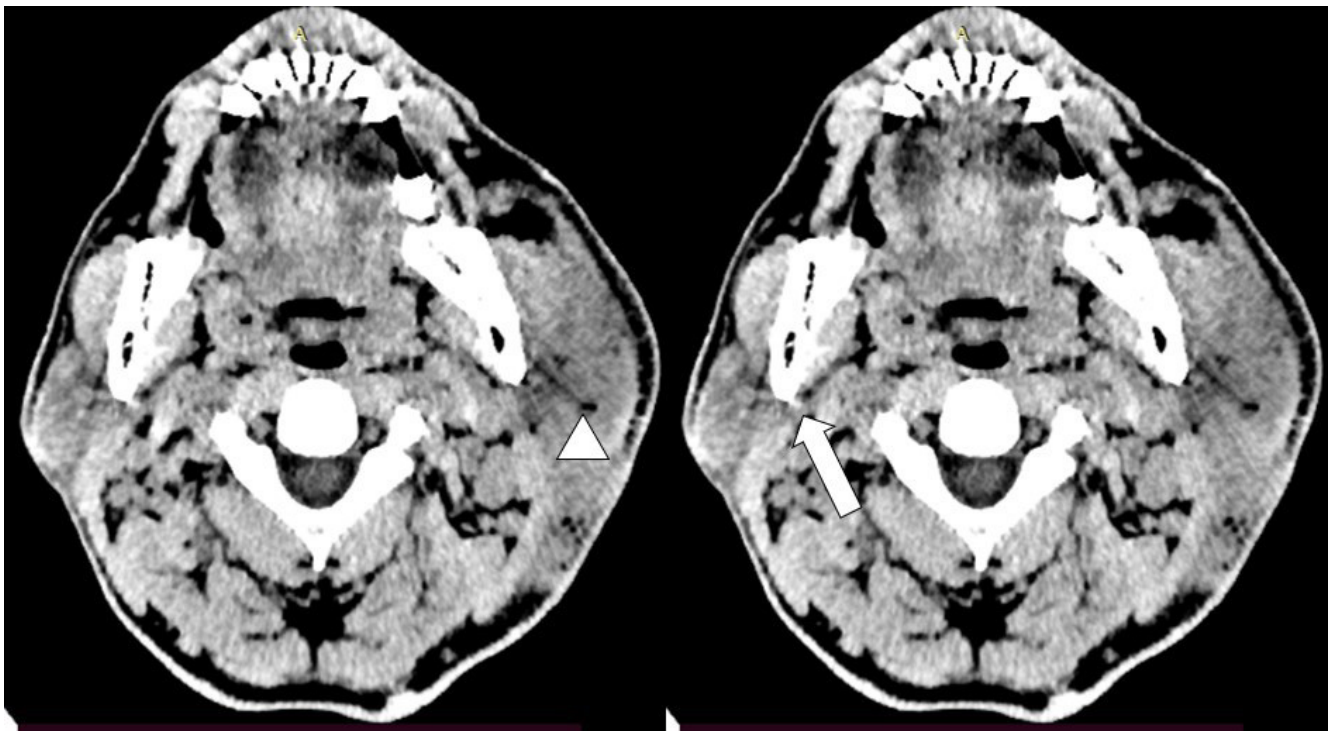


Figure 1. CECT shows an enlarged left parotid gland with a blurry margin, surrounding fat inflammation involving the parotid, masticular, and posterior cervical spaces (arrow), and intraparotid and superficial cervical lymph nodes enlargement llb space in the left side lymphadenopathy enlarged lymph nodes with homogenous enhancement (arrowhead).

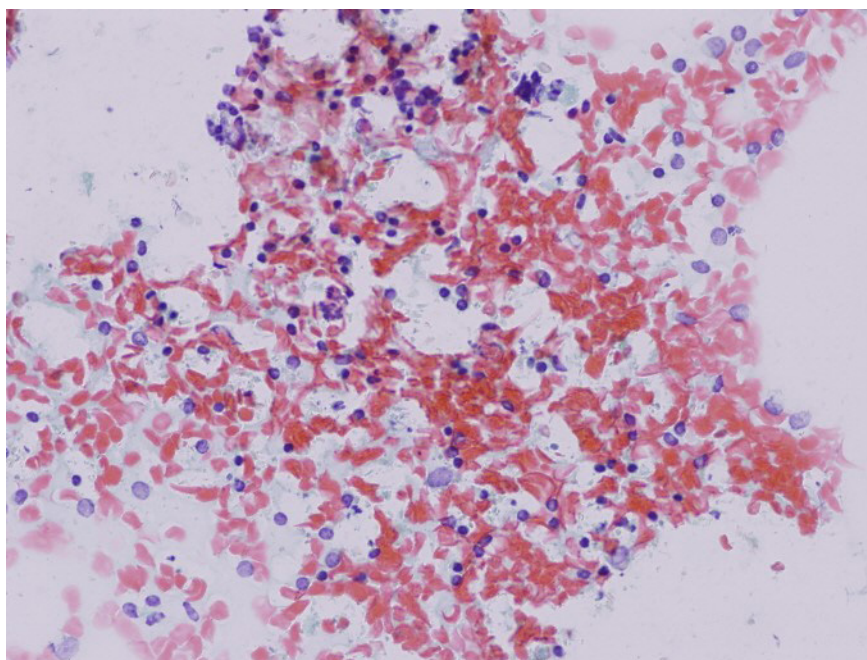


Figure 2. Fine needle aspiration cytology of the left parotid gland. A mixture of small and large lymphocytes and a few histiocytes are dispersed in a blood-rich background, consistent with reactive change (Pap stain x40).

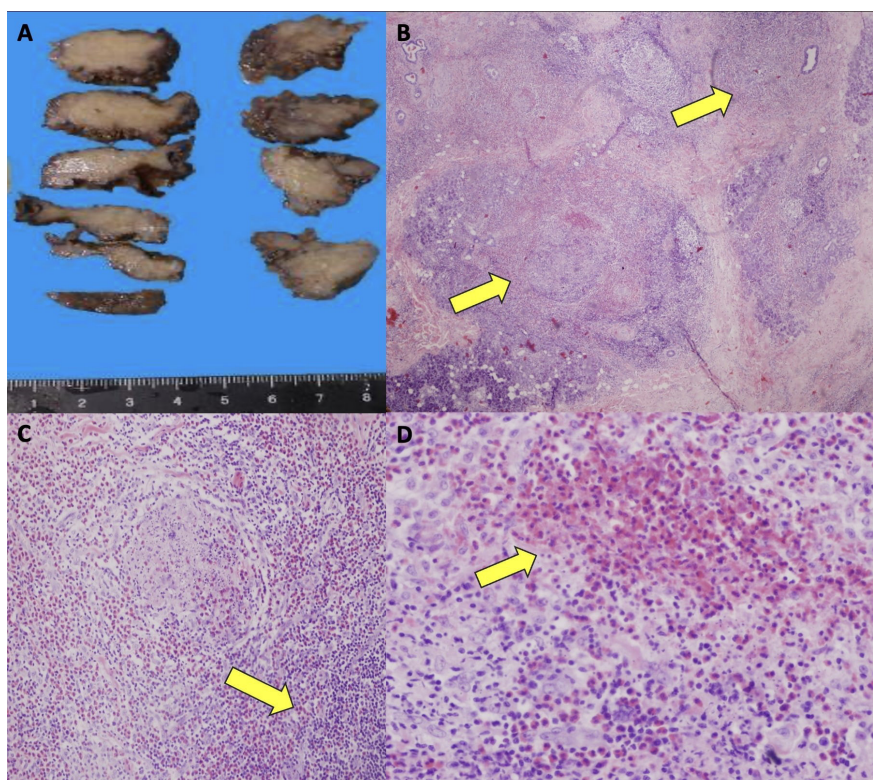


Figure 3. Pathological findings.(A) The gross specimen shows the homogenous grey-white cut surface of the parotid. (B) Histopathological picture showing germinal center hyperplasia (H&E, 4X). (C) Lymphoid follicle with prominent germinal center (arrow shows eosinophilic micro abscess) (H&E, 10X). (D) The germinal center is infiltrated by eosinophils and histiocytes (H&E, 40X).

Discussion

Kimm and Szeto first described Kimura's disease (KD) in 1937 in Chinese literature [1]. The histological description was given by Kimura et al. in 1948, thereby crediting the name of the disease. The condition is endemic in Oriental Asia and sporadic in the rest of the world [3,4]. It has a high male preponderance of a ratio of 3.5 to 7: 1 [3]. The peak age of onset is the third decade. KD presents with a usual triad of one or more subcutaneous indolent nodules, peripheral eosinophilia, and increased serum IgE levels [2]. The nodules are slowly progressing in size, located mainly in the head and neck, mostly painless, rarely painful, and pruritic [5]. Lymphadenopathies and increased volume of salivary glands may be accompanying entities. Renal involvement is seen in proteinuria and Nephrotic syndrome [4].

The pathophysiology of KD remains unknown. It has been hypothesized that an infection or toxin may trigger an autoimmune phenomenon or lead to a type I (IgE-mediated) hypersensitivity reaction. Some evidence has suggested a predominance of T_H 2 cells in patients with KD [7]. Additional studies have shown elevated granulocyte-macrophage stimulating factor (GM-CSF), tumor necrosis factor- α (TNF- α), soluble interleukin (IL)-2 receptor (sIL-2R), IL-4, IL-5, IL-10, and IL-13 [8,9]. Another study indicated that activating the IL-21/pERK1/2 pathway is a component of KD immunopathogenesis and that pERK1/2 could be a potential prognostic indicator of the disease [10]. These findings may help lay the groundwork for elucidating the underlying pathophysiology of KD.

The immune reaction believed to be the root of KD also predisposes the patient to allergic conditions like asthma, chronic urticaria, pruritus, and rhinitis [11]. Moreover, up to 60% of these patients exhibit renal involvement as extra membranous glomerulonephritis and nephrotic syndrome [12]. Although there is no specific diagnostic feature of KD, FNA is helpful in preoperatively diagnosing KD. Smears show significant numbers of eosinophils in the background of lymphoid cells with occasional fragments of collagenous tissue and Warthin-Finkeldey polykaryocytes [13].

Our FNAC smear case revealed a polymorphous population of lymphoid cells and histiocytes in the background of lymphohistiocytic and fibrous stroma. Regional lymphadenopathy, serum eosinophilia, and elevated IgE levels are rare [14]. KD can be mistaken for a parotid tumor or malignant disorder (acute

lymphocytic leukemia, T-cell lymphoma, Kaposi's sarcoma). Differentiating KD from angiolymphoid hyperplasia with eosinophilia (ALHE) has been a challenge for a long time [15-17].

Histologically, KD presents as preserved lymph node architecture with reactive and prominent germinal centers. Dense eosinophilic infiltration of the interfollicular zones, lysis of the follicles, and occasional microabscesses are seen. Some granuloma formations contain infiltrations of eosinophils, lymphocytes, plasma cells, and histiocytes. Tissue fibrosis, sclerosis, and vascular proliferation are also present. Immunofluorescent studies reveal germinal centers with heavy IgE deposits with variable amounts of IgG, IgM, and fibrinogen [15,16,18].

The diagnosis of KD is not easy, and the differential diagnosis includes ALHE, Hodgkin's disease, Kaposi sarcoma, eosinophilic granuloma, epithelioid hemangioma, Castleman's disease, tuberculosis, dermatopathic lymphadenopathy, lymphadenopathy of drug reactions, parasitic lymphadenitis, eosinophilic granuloma, epithelioid hemangioma and many more [7]. Histologically, KD has three components: cellular (inflammatory infiltrate including increased eosinophils and follicular hyperplasia), fibro collagenous, and vascular (arborizing vascular proliferation of the postcapillary venule, endothelial cells are usually flat and lack cytologic atypia or vacuolization). In contrast to KD, vascular proliferation is most significant in ALHE, forming aggregates or lobules comprising plump endothelial cells with epithelioid or histiocytoid changes demonstrating cytologic atypia and vacuolization [19,20]. In parasitic infection, histological features from KD are granuloma or eosinophilia. Detection of parasite remnants may lead to the diagnosis.

Ultrasound of the neck must be performed in case of lymphadenopathy; in KD, lymph nodes are hypoechoic, solid, round, or oval in parotid or submandibular areas with normal surrounding tissues [21]. On radiological examination, KD mimics other chronic or granulomatous diseases. Despite the similar radiological characteristics in the case of KD, it is impossible to exclude malignancy; thus, the diagnosis must not be based exclusively on imaging alone. Histological confirmation is necessary.

So far, there has yet to be a consensus regarding KD's management aspects. However, primary prophylactic surgery is performed as a therapeutic or diagnostic procedure.

Conservative treatment includes oral steroids, which are reported to be responsible for decreasing the size of enlarged lymph nodes [15,16]. Remissions reach 25% in groups of patients treated surgically. Surgery and subsequent steroid treatment are proposed as alternative treatments [16]. Radiation therapy is helpful to control lesions that relapse after surgery or are non-responsive to steroids. An effective dose of radiation is proven to be 20–30 Gy [22]. Besides traditional therapy, many other treatment methods have been studied. These methods include retinoids, immunosuppressants, monoclonal antibodies (imatinib) antiallergic like cetirizine, leukotriene receptor blockers (panlukast), and pentoxiphylline with variable effects [22].

Conclusion

Kimura's disease (KD) should be considered a differential diagnosis in patients presenting with head & neck mass and lymphadenopathy and investigated accordingly. KD has a high recurrence rate but a good prognosis. However, pathological examination is the gold standard for diagnosis of KD, which should be confirmed by surgical specimens.

Conflict of Interest

The authors state no conflict of interest.

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