Correspondence

Tavakol et al. [5] showed in the Iranian population that G allele was significantly higher in CSU patients at locus –238G/A and –308G/A of TNF-α gene and concluded that this polymorphism can affect susceptibility to this disorder. Our data did not confirm the observation of a potent link between TNF-α polymorphisms at –1031 T/C, –857C/T, and –308G/A and CSU in the Polish population. To the best of our knowledge, this is the first study considering the role of the above-mentioned polymorphisms in the pathogenesis of CSU. Further analyses should be conducted on large population stratified by ethnicity. Genetics seem to be a promising direction in further search for CSU pathogenesis.

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Conflicts of interest
There are no conflicts of interest.

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A Rare Case of Kimura Disease

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Sir,
A 32-year-old male presented with the complaints of multiple, gradually progressive, painless, dark-colored, symmetrical, retroauricular swellings for the past 10 years. Swelling initially appeared behind the left ear for which he underwent complete surgical excision, but there was gradual recurrence of similar swellings behind the left ear, left cheek, left side of the jaw, and also behind the right ear over the next 6 years. The patient complained of heaviness over the head, had difficulty in...
lying down sideways, and also had low self-esteem due to the facial disfigurement. There was no history of itchy rash over the body, grittiness or watering of eyes, nasal blockage, dyspnea, cough, chest pain, or wheeze.

On examination, there was significant lymphadenopathy in the form of multiple nontender, discrete, soft-to-firm, freely mobile lymph nodes (LNs) over submental, submandibular cervical, axillary and inguinal regions varying in size from 0.5 to 1.5 cm which were not fixed to underlying structures or overlying skin. Systemic examination was essentially normal.

Dermatological examination revealed multiple, skin-colored to hyperpigmented masses over the left parotid, left submandibular region, and bilateral retroauricular regions measuring 18 cm × 8 cm over the left side, and 12 cm × 8 cm and 2 cm × 2 cm on the right side which were discrete, soft-to-doughy in consistency, nontender, nonfluctuant, and nontransilluminant with normal local temperature [Figure 1a and b]. Swellings were adherent to overlying skin and fixed to underlying structures.

Investigations revealed eosinophilia of 41% on peripheral blood smear with absolute eosinophil count of 5230/mm³. Serum immunoglobulin E (IgE) was 3285 kU/L. Serum biochemistry and urine examination including 24-h urinary protein were within the normal range. Fine-needle aspiration cytology of the left cervical LN showed reactive lymphadenitis.

Biopsy from mass over the right ear revealed normal epidermis. Dermis showed numerous blood vessels lined by plump endothelial cells. A few lymphoid follicles with germinal centers were noted with mixed inflammatory infiltrate consisting of lymphocytes and eosinophils [Figure 2a and b]. On IHC, CD3-positive T-cells, CD20-positive B-cells, and CD34-positive blood vessels were highlighted [Figure 3a-c].

Chest X-ray suggested right paratracheal lymphadenopathy. Magnetic resonance imaging (MRI) of the head-and-neck region revealed heterogeneous intensity lesions on T2W1 in the subcutaneous tissue of both retroauricular regions (L > R) extending into the left parotid region but seen separately from the left parotid and muscles of mastication. Magnetic resonance angiography revealed the absence of vascular supply to the lesions. To rule out any underlying vascular malformations, a Doppler ultrasound was done that showed heterogeneous echogenicity lesions with anechoic vascular channels in both the retroauricular regions extending along the parotid region and the soft tissues of the neck. However, no flow was demonstrated in these anechoic vascular channels on Doppler study. Ultrasonography of the neck also showed multiple, enlarged cervical, and intraparotid LNs. Computed tomography (CT) of the head and neck confirmed the findings of retroauricular masses and highlighted the intraparotid and cervical LNs in the anterior and posterior triangles of the neck [Figure 4a-c]. Platelet-derived growth factor receptor alpha (PDGFRA) gene mutation study was negative.

Based on the clinical findings and investigations, he was managed as a case of Kimura’s disease (KD) with tapering doses of tablet methylprednisolone at the dose of 1 mg/kg body weight daily with the addition of cyclosporine as maintenance therapy.

The patient showed significant reduction in the size of all masses after 2 weeks of therapy [Figure 5]. Investigations done after 2 weeks showed resolution of the right paratracheal lymphadenopathy. Ultrasound of the neck showed significant reduction in vascularity of lesions and cervical lymphadenopathy.

He was not offered Imatinib mesylate as his PDGFRA gene mutation study was negative. At present, the patient is under regular follow-up.

Kimura disease (KD) is a rare, chronic inflammatory disease of unknown etiology causing subcutaneous swellings, and lymphadenopathy affecting commonly men of Asian origin in the second to third decades of life. It was first described in 1937 by Kim in China as “eosinophilic hyperplastic lymphogranuloma.”[1] It later came to be known as KD after Kimura et al. reported their findings in many Japanese men.[2] Peripheral blood eosinophilia and increase in serum IgE levels are commonly seen.[1,2]
The etiology of KD is unknown. The presence of eosinophilia and increased IgE, tumor necrosis factor-\(\alpha\), interleukin-4 (IL-4), IL-5, and IL-13, and mast cell levels both in peripheral blood and in lesional tissue denote an allergic reaction or an alteration of immune system.\(^3\) Autoimmune, infective, and neoplastic etiologies have also been proposed; however, exact cause is still elusive.\(^3\) Epstein–Barr virus, human herpesvirus-8, \textit{Candida albicans}, insect bites, and parasitic infection leading to persistent antigenic stimulus has been mentioned.\(^4\) KD in a hemodialysis patient has been reported in the literature.\(^5\) KD can affect the kidneys in approximately 20%–60% of cases presenting generally as nephrotic syndrome with albuminuria; however, it can manifest as all types of glomerulonephritis too.\(^4\)

The common sites for the nodules and subcutaneous masses are preauricular, submandibular, parotid, oral cavity, larynx, groin, epicranium, and popliteal regions. Other rare sites include the axilla, oral cavity, and nasal sinuses. Regional LNs and salivary glands are usually involved.\(^5\)

Definitive diagnosis is based on the histological picture of germinal center hyperplasia, intact nodal morphology, postcapillary venule proliferation, and eosinophilic infiltrates. Other frequent findings include multinucleated giant cells, sclerosis, eosinophilic microabscesses, necrosis, and vascular proliferation. Immunofluorescence shows germinal centers containing heavy IgE deposits.

KD is commonly confused with angiolymphoid hyperplasia with eosinophilia (ALHE). ALHE is an uncommon, vasoproliferative, idiopathic condition-related to inflammatory stimulation, affecting middle-aged, western women. Generally presents with a superficial well-circumscribed mass with histology showing proliferation of blood vessels with distinctive large endothelial cells. ALHE is now considered to be a type of histiocytoid hemangioma. Patients with ALHE have normal IgE levels and no albuminuria.\(^5\)

Among the imaging modalities, ultrasound generally reveals hypoechoic, solid, and round areas. Radiologically, since KD tends to mimic many chronic and malignant disorders such as tuberculosis and lymphoma, histopathological diagnosis becomes very important. CT and MRI are very useful in demonstrating the extent of gland and LN involvement like in our case.

There is no definitive treatment till date for KD. Treatment aims to preserve function and esthetics while preventing recurrences. In asymptomatic cases, conservative observation is adequate as lesions sometimes
undergo spontaneous resolution. Surgical excision is considered as first line of the treatment in symptomatic cases, though recurrence is common.[6] Topical, intralesional, and systemic steroids are frequently used, but the swellings may become refractory to the treatment.[9] Radiotherapy (20–45 Gy) is also effective, and cyclosporine (5 mg/kg/day) has shown good results in many studies.[8,9]

Imatinib mesylate is now being considered as an effective treatment for KD. As an inhibitor of the protein-tyrosine kinases (PTK), imatinib works by selectively blocking PTK, such as PDGFR and c-Kit.[10] Azathioprine, all-trans retinoic acid, leflunomide, pentoxifylline, pranlukast, and intravenous immunoglobulin have been tried with variable response.

However, the prognosis of KD is excellent, and the disease has no potential for malignancy. This case is hereby reported, because of its rarity and excellent response to therapy.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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