Kimura disease

No age or ethnicity limit

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ABSTRACT

داء كيمورا هو مرض التهابي مزمن يظهر أساساً لوجود تكتل في منطقة العنق. على الرغم من أن الفيزيولوجيا المرضية ليست واضحة حتى الآن، إلا أنه يمكن تحديد التشخيص على أساس الخصائص التشريحية المرضية المحددة. وقد وصفت الحالة الأولى لهذا المرض في الصين وكذلك معظم الحالات اللاحقة التي وصفت في بلدان الشرق الأقصى جعلت مرض كيمورا داء شائع لدى المرضى الآسيويين البالغين. ويصف هذا التقرير وقوع داء كيمورا في مرضى طب الأطفال غير الآسيويين مع عرض سريري إمراضي مماثل.

Kimura disease is a chronic inflammatory disease that mainly manifests as a lump in the cervical region. Although the underlying pathophysiology is not clear yet, the diagnosis can be established based on specific histopathological characteristics. The first case of this disease was described in China, as well as the majority of subsequent cases that were also described in the Far East countries made Kimura disease traditionally a disease of adult patients of Asian descent. This report describes the occurrence of Kimura disease in pediatric non-Asian patient with a similar clinicopathologic presentation.

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Although Kimura disease can be grouped under inflammatory disease of chronic nature, the underlying cause is still to be investigated. The disease usually present with enlarged, but painless cervical lymph node or subcutaneous masses in the cervical region.[1,2] Clinical and histological characteristics of Kimura disease (primary allergic reaction or an alteration of immune regulation) help to differentiate it from angiolymphoid hyperplasia with eosinophilia (an arteriovenous malformation with secondary inflammation mostly involving dermal or subcutaneousparts), which were previously thought to be the same disease.[1,2] Most cases have been reported in adult patients from the Far East of Asia.[1,2] Elevation of inflammatory mediators that are usually elevated in autoimmune disorders made hypersensitivity a possible underlying pathophysiological mechanism of this disease.[1,2] Patients usually present with non-tender mass in the cervical region with elevated eosinophils count and high levels of serum immunoglobulin type E (IgE).[2] Unfortunately, there are no specific radiological characteristics of that disease.[2] The only way to diagnose Kimura disease is through its histopathologic features, which necessitate a surgical biopsy.[1,2] Treatment usually start with medical therapy and if that fail or show no spontaneous resolution then surgical excision would be the choice at that point with radiotherapy reserved for selected cases.[1,2] The main objective of presenting this case report is to emphasize that Kimura disease can involve pediatric Saudi patients in contrast to what was historically described as a disease of adult Asian only. Secondary, it is to support what had been reported of occurrence of the disease in non-Asian patient with a similar clinicopathologic presentation of the Asian patients.[2,3]

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Case Report. We report a case of an 11-year-old Saudi boy, whose family were consented for reporting of his medical condition. He is not known to have any medical condition and presented to the clinic with a 5-year history of right-sided non-painful facial mass. The non-painful solitary progressively enlarging mass, tend to recur after multiple investigational and therapeutic interventions. He had history of recurrence after a trail of excision prior to presentation. Also, there was a temporary improvement upon receiving intravenous (IV) steroids, but the swelling recurred one-year later. Embolization of right internal maxillary artery also has failed to show any resolution of the mass. There were no orbital or oral complaints in relation to that mass. Family history is unremarkable for tumors or hematological diseases, and there was no history of trauma or tattooing of the face.

On examination, there was a 2 ×3 cm soft, mobile and non tender mass over the region of right zygomatic prominence and the overlying skin was darker than the surrounding normal skin (**Figure 1**). The rest of the head and neck exam including the ears, nose, and throat were within normal limits. There were no palpable cervical, axillary or inguinal lymph nodes. Ophthalmological and dental evaluations were within normal limits. Early differential diagnosis included arterovenous malformations hemangioma, lymphangioma, soft tissue sarcoma, tuberculosis, or actinomycosis infections. Laboratory investigations including complete blood count (CBC), urea and electrolytes and coagulation profile were within normal. Immunoglobulin E levels were elevated at 8977 (normal level <200). Computed tomography scan was performed (**Figure 2**) and showed a large 2.6 x 7 x 8 cm soft tissue mass at the right buccal

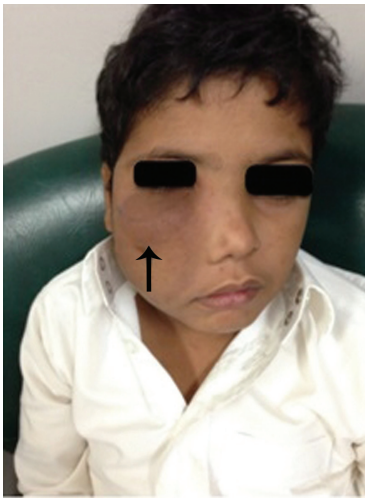

Figure 1 - The patient on presentation, with right side facial mass (arrow).

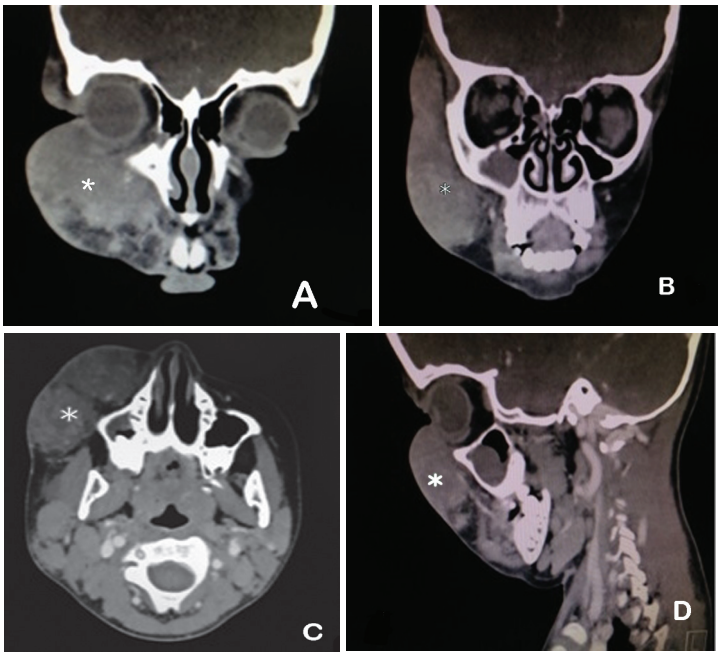

Figure 2 - Computed tomography scan of facial bones and neck showing hypo- to iso-intense soft tissue mass at the right buccal region (asterisk): **A, B)** coronal view, **C)** axial view, and **D)** sagital view.

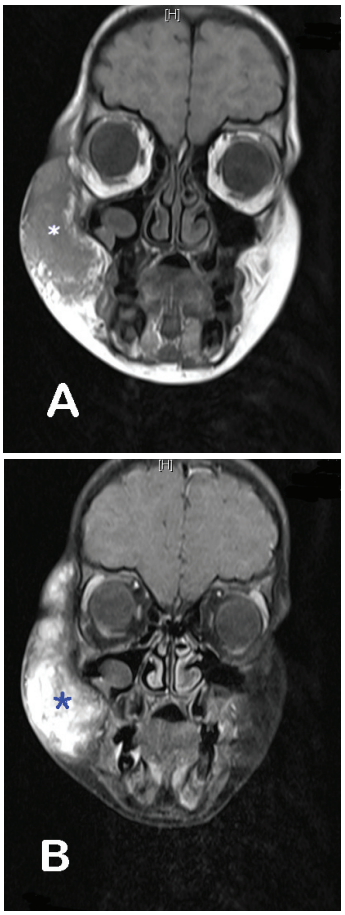

Figure 3 - Magnetic resonance image of facial bones and neck: **A**)T1 prior to gadolinium administration. **B**)T2 after gadolinium administration with fat suppression. Mass is indicate (asterisk)

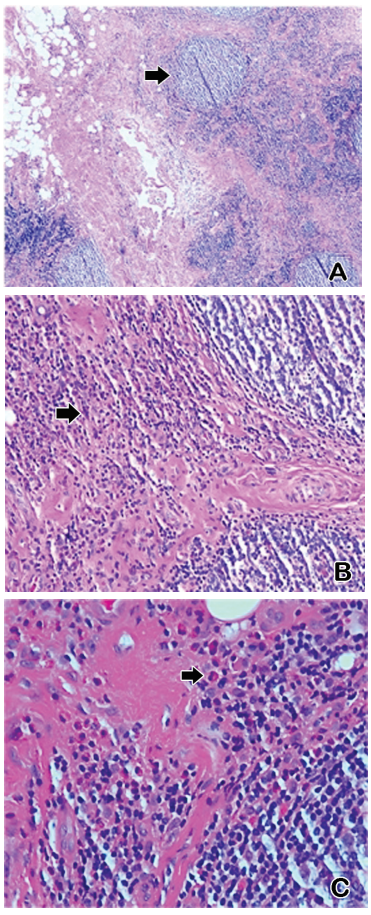

Figure 4 - Histopathological slides stained with hematoxylin and eosin stain (H&E) under microscope: **A**) reactive germinal centers (arrow). Note adjacent adipose tissue, areas of fibrosis, and the infiltrates in between the reactive germinal centers (x50, H&E). **B**) severe mixed inflammation (arrow): eosinophils, lymphocytes, histiocytes, and plasma cells (x200, H&E), and C) bilobed nuclei with granular red cytoplasm (arrow) of infiltrating eosinophils (x400, H&E).

region inferior to right orbit that is hypo to iso-dense to muscles with no evidence of bone or skin involvement.

To better evaluate the mass, an MRI was performed (**Figure 3**) to delineate the nature of this mass. It demonstrated the mass with heterogeneous high signal intensity on T2 and heterogeneously enhancing mass post contrast administration on T1 with no intraorbital extension. The patient underwent a transoral biopsy through sublabial approach. The histopathological results showed portions of vascularized fibroadipose tissue with infiltration by inflammatory cells. The inflammatory cells were arranged in germinal centers and scattered dense mixed inflammatory cells. The germinal centers showed a polymorphous population of lymphocytes and scattered tangible-body macrophages. In the inter-follicular areas, the inflammatory infiltrate was composed of mostly eosinophils, mast cells, lymphocytes, histocytes, and plasma cells. Amongst the intra-folicullar area, an increased number of blood vessels lined by endothelial cells was seen and showed moderate cytoplasm, but no hobnail or prominence of the endothelial cells. The stroma showed increased fibrocollagenous stroma associated with the areas of inflammation (**Figure 4**).The diagnosis of Kimura disease was made according to its histopathological features. He was followed through out-patient department for 15 months with the mass disappeared initially after the use of oral loratidine (5 mg once a day for 30 days [Spimaco, AlQassim Pharmaceutical Plant Saudi Pharmaceutical Industries and Medical Appliances Corporation, Saudi Arabia) and oral prednisone (5 mg 3 times a day for 3 months, 2.5 mg in the morning and 5 mg in evening time for 4 months, 2.5 mg 2 times a day for 2 weeks, 5 mg once a day for 7 months (CP Pharmaceuticals

Ltd, Ash Road North, Wrexham, United Kingdom). The mass appeared again (**Figure 5**) when the oral prednisone was stopped. This issue of recurrence along with the known side effect of prednisone guided us to consider the use of IV immunoglobulin in combination with oral prednisone or radiotherapy after consulting to the concerned specialties.

Discussion. Kimura disease was described in China in 1937 and the description of definitive histological criteria was reported by Kimura et al in 1948.[4,5] Most of the cases were from Asian descent with marked adult male predominance. Some other sporadic cases were also reported from patients of other descents. In another study,[2] carried out in a multi-racial country: Caucasians (n=7), Blacks (n=6), Asians (n=6), Hispanic (n=1), and Arab (n=1) were included, and it was found that Kimura disease does occur in non-Asians with a similar clinicopathologic presentation.[3] Occurrence of the disease in the pediatric age group also has been reported. PubMed search was made for searching Kimura disease, pediatric, and case report. It revealed that Kimura disease was reported in patients of different ethnicity. The youngest patient was a 15-month old African American boy who had a fever, neck and head subcutaneous masses, asthma, eczema, and nephrotic syndrome.[1,2] Another search was conducted and was limited to Kimura disease and Saudi, which yield in 6 cases in relation to Saudi Arabia, but only one was a Saudi patient of pediatric age group (16-year-old) who had been reported to have Kimura disease.[6]

Regarding Kimura disease, certain findings such as predominant TH 2 cells and elevated granulocyte macrophage-stimulating factor (GM-CSF), tumor necrosis factor-α (TNF-α), soluble interleukin-2 receptor (sIL-2R), IL-4, IL-5, IL-10, and IL-13 lead to the hypothesis that an infection or toxin may trigger an autoimmune phenomenon or lead to a type I hypersensitivity reaction IgE mediated reaction.[2]

Patients typically complain of painless lump or mass in the cervical region, associated with pruritus. Renal diseases, especially nephrotic syndrome, and hypercoagulable state was found to be associated with the disease. Typical findings on exam are non-tender subcutaneous nodules and masses in the cervical region. Sites that are more frequently involved include the parotid and submandibular regions while less frequent ones are the orbit (including the eyelids, conjunctiva, and lacrimal glands), paranasal sinuses, epiglottis, tympanic membrane, and parapharyngealspace. Extra-cervical sites such as the extremities, inguinal lymph nodes, or pulmonary hilar mass were reported.[2]

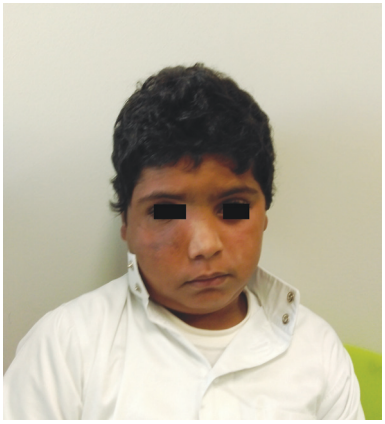

Figure 5 - The patient 15 months after diagnosis and trial of oral loratidine and steroid.

Laboratory studies usually show peripheral eosinophilia and high levels of serum IgE.[2] Renal profile including urine protein must be carried out to rule out renal involvement (especially nephrotic syndrome).[1] Appearance on radiological findings by different modality such as CT or MRI are variable and not well defined (due to variable degrees of vascular proliferation and fibrosis), but heighten lesions surround the parotid gland, with lymph node enlargement is a distinctive feature.[2] Diagnoses of Kimura disease is based on identifying its histopathologic features, so an incisional biopsy is usually required.[1,2] Persistent findings are conserved lymph node architecture, florid germinal centers, eosinophilic infiltration, and high amount of postcapillary venules. The variable finding include hardening or thinking (sclerosis), an increased number of immature red blood cells (RBCs) in both the germinal centers and the paracortex, vascularity of the germinal centers, protein deposits in germinal centers, necrosis of germinal centers, eosinophilic abscesses, and atrophy in the small veins in sclerotic areas.[2]

Treatment of Kimura disease is variable.[1,2] Surgical excisions have been considered as the gold standard treatment for Kimura disease, but recurrence is possible.[2] Different medications have been used in treatment of Kimura disease with the response ranging from mild improvement to a complete remission or even cure of the disease. However, the use of those medications was based on their known anti-allergic or anti-inflammatory effects which have been reported to be effective in other case reports. Moreover, a

maintenance dose was often required to prevent disease relapse. Those medications include corticosteroids, cyclosporine, cyclophosphamide, and loratidine.[1,2,7] The longest disease free period reported was after the use of intravenous immunoglobulin in combination with prednisone, which resulted in disease free period of more than 6 years.[8] Radiotherapy is used to treat recurrent or persistent lesions with better rates for local control, but the side effects of radiotherapy along with benign nature of the disease limited its use as primary modality.[2,9]

In conclusion, Kimura disease should be considered as a part of the differential diagnosis of head and neck masses in general and not only in adult Asian male patients as it was historically thought to be. There is no clinical, laboratory or imaging diagnostic criteria have been developed yet. The diagnosis of this disease can be only established by histopathological features. The response to prednisolone and loratidine is in support to what was described in earlier studies and emphasize on reporting and documenting any similar case in the future to increase our awareness of this disease. This is in order provide patients suffering from Kimura disease with a better care.

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