Kimura's disease in a young Balkan male

Bolest Kimura kod dečaka sa Balkana

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Abstract

Introduction. Kimura’s disease is a rare, chronic inflammatory condition of unknown cause. It was initially described in Chinese literature and it became known as KD after its publication by Kimura et al. of similar cases in Japan. It mainly affects young Asian men, although it occurs sporadically in other areas and ethnic groups. To our knowledge it has not been reported previously in persons from the Balkan countries. Case report. We presented a 15-year-old male with Kimura’s disease manifested as chronic left neck mass. The diagnosis was based on the histopathological findings of the excised lesion. Peripheral blood eosinophilia and raised serum Immunoglobulin E (IgE) level supported the diagnosis. Conclusion. The presented patient confirmed the fact that Kimura’s disease could occur in different ethnic groups. Histopathological examination, should be performed prior to making the definitive diagnosis.

Key words: lymph nodes; neck; diagnosis; biopsy; immunohistochemistry; eosinophilia; diagnosis, differential; angiolymphoid hyperplasia with eosinophilia; adult.

Introduction

Kimura’s disease (KD) is a rare, chronic inflammatory condition of unknown cause. It was initially described in Chinese literature and it became known as KD after its publication by Kimura et al. of similar cases in Japan. It mainly affects young Asian men, although it occurs sporadically in other areas and ethnic groups. To our knowledge it has not been reported previously in persons from Balkan countries. Kimura’s disease occurs predominantly as a unilateral manifestation in the head and neck and it is frequently associated with regional lymphadenopathy with or without involvement of salivary glands. Other unusual sites of involvement include the auricle, scalp and orbit. We report a case of KD in a young Serbian male. We present this unusual case to increase awareness of KD in different ethnic groups and to elucidate the pitfalls in its diagnosis.

Case report

A 15-year-old male was presented to the University Clinical Center in Niš for evaluation of a left neck palpable mass (4.5 × 3.5 × 3 cm) of 6-month duration. The patient was treated with antibiotics, but the tumor persisted. There was no history of pain, fever, or weight loss and he seemed well. No redness was noted on the overlying skin. Neither axillary or inguinal lymphadenopathy nor hepatosplenomegaly was noted. Laboratory findings revealed an eosinophilia in the peripheral blood and elevated serum Immunoglobulin E (IgE) level. Clinically, the differential diagnosis included infectious lymph node enlargement (tuberculosis, toxoplasmosis), although neoplastic conditions (Hodgkin’s disease and non-Hodgkin’s lymphoma) were the first diagnoses considered and an open biopsy was recommended. Stains and cultures for bacteria, fungi and mycobacteria were negative.
In March 2007, the patient underwent an open biopsy of the left neck mass with excision of cervical lymph nodes and salivary gland. The obtained tissue was fixed, embedded in paraffin and stained with hematoxylin-eosin (H&E). Immunohistochemical analysis was performed on paraffin sections with the alkaline phosphatase anti-alkaline phosphatase (APAAP) technique, using antibodies against CD20, CD3, CD45, CD15, CD34, S100 protein and alpha-smooth muscle actin (DAKO, Copenhagen, Denmark).

The sections stained with H&E showed diffuse, dense, lymphoid and eosinophilic infiltrates forming eosinophilic microabscesses (Figure 1). The inflammatory infiltrates involved the salivary gland and perinodal adipose tissue. Histopathology of the lymph nodes revealed a follicular lymphoid hyperplasia with focal eosinophilic infiltration within the paracortex and interfollicular region. Mitoses were confined to the reactive germinal centers. The lesion was markedly of vascular type; the thin-walled blood vessels were numerous with plump endothelial cells. There was no evidence of atypia. Large caliber arteries were rarely seen. Although plasma cells and histiocytes were present, no epithelioid cells and multinucleated giant cells were seen.

Immunohistochemical findings: CD20 highlighted the follicle center B-cells; CD3 and CD45 demonstrated numerous interfollicular T-cells; stains for CD15 and S100 protein were negative. There was a strongly positive reaction to CD34 on the endothelial lining cells of proliferating blood vessels. The majority of the vessels showed prominent perithelial cells, which were distinctly demonstrable by alpha-smooth muscle actin antibody (Figure 2). The diagnosis of KD was made based on histopathological findings after surgical excision. Peripheral eosinophilia and elevated serum IgE level further supported the diagnosis.

**Discussion**

The etiology and pathogenesis of KD is unclear, although it might be a self-limited allergic or autoimmune response triggered by an unknown stimulus. A viral or parasitic trigger may alter T-cell immunoregulation or induce an IgE-mediated type 1 hypersensitivity resulting in the release of eosinophilic cytokines. Activated CD4 cells of the Th2 phenotype can release cytokines such as interleukin (IL)-4, IL-5 and IL-13, which in turn would act in B-cells favoring the production of antigen-specific IgE. T helper 2 (Th) cell proliferation and the overexpression of cytokines would play an essential role in the development of KD. The prognosis of KD is excellent, and the disease has no potential for malignancy. Prior to biopsy, we did not consider the diagnosis of KD in our patient because of its rarity in this region. Patients with KD are often extensively evaluated for other disorders, such as Mikulicz’s disease, eosinophilic granuloma, salivary gland tumors and lymphoma. Although the intense eosinophilia are suggestive of a parasitic infection, no parasites have been identified. The morphological and immunohistochemical features excluded Hodgkin’s disease and non-Hodgkin’s lymphoma. The thin-walled blood vessels were prominent, but there was no true vasculitis, so that systemic vascular disease was unlikely. Kimura’s disease can also be confused with angiolymphoid hyperplasia with eosinophilia (ALHE). In the past, KD and ALHE were often considered to be the same disease. Although subtle clinical and histological similarities, KD and ALHE now are considered to be separate entities. Angiolymphoid hyperplasia with eosinophilia is a vascular malformation resulting from an arteriovenous shunt, typically presenting in women during early to mid-adult life. Lymphadenopathy and salivary gland involvement are uncommon in ALHE; eosinophilia in the peripheral blood is frequently absent, as well as the levels of IgE which are normal. Angiolymphoid hyperplasia with eosinophilia is characterized by dilated blood vessels which have irregular shapes, in addition to enlarged epithelioid-appearing endothelial cells with prominent vacuoles in the cytoplasm. These vacuoles are not present in KD. Additional morphologic features present in our case and characteristic of KD include the noncircumscribed inflamma-
tory infiltrates within extranodal tissues associated with re-
active germinal center formation and eosinophilic microab-
scesses (Figure 1). The immunohistochemistry of the lesion
demonstrated prominent perithelial cells by alpha-smooth
muscle actin antibody in the majority of the blood vessels
(Figure 2). A previous study suggested the table of differ-
etial histopathological features between ALHE and KD in
which the absence of smooth muscles in blood vessel wall
is a characteristic feature of KD. Nevertheless, in our
opinion the alpha-smooth muscle actin could be very useful
diagnostic marker of KD.

Conclusion

Clinicians and pathologists may be unfamiliar with the
clinical presentation and histopathology of this rare disease.
Early diagnosis of KD may spare a patient from potentially
harmful and unnecessary invasive diagnostic procedures. A
definitive diagnosis can be made only by histopathological
examination of the excised lesion, demonstrating the role of
the surgical pathologist in the detection of this uncommon
chronic inflammatory disorder.

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