Kimura disease with a history of Budd-Chiari syndrome: a case report

Tao Wang, Yong-Jun Mei, Zhi-Jun Li

Department of Rheumatology, The First Affiliated Hospital of Bengbu Medical College, Bengbu, Anhui 233004, China.

To the Editor: A 25-year-old Chinese man complained of a swelling nodule over his right neck for 3 months, without pain, pruritus, or dermatitis. The patient had suffered from Budd-Chiari syndrome (BCS) since 2016, which was well controlled after receiving interventional treatment (angioplasty with stenting) in 2017 and appropriate management later. The patient had no history of hypertension or diabetes. The patient exhibited an oval-shaped subcutaneous swelling over his right neck region. Physical examination found that the border of the mass was clearly distinguished, without adhesions to the adjacent tissue, and measured 2.5 cm in diameter. Blood pressure and heart rate were 128/84 mmHg and 76 beats/min, respectively.

A full blood count at the first visit (May 15, 2019) showed white blood cell count of 7.22×10^9/L (normal range: 3.50–9.50 $\times$ 10^9/L); hemoglobin 148 g/L (normal range: 130–175 g/L); and eosinophil 2.19 $\times$ 10^9/L (normal range: 0.02–0.52 $\times$ 10^9/L). Serum immunoglobulin E (IgE) level increased to 2530 IU/mL (normal range: <165 IU/mL). The results of other laboratory tests, including liver and kidney function tests, routine urinalysis, serum immunoglobulin G4, anti-nuclear antibody, anti-neutrophil cytoplasmic antibodies were all normal. There were no positive findings in chest radiography.

The patient underwent excision of the masses, which showed eosinophilic hyperplastic lymphoid granuloma and reactive hyperplastic lymph node [Figure 1]. Immunohistochemical staining was positive for cluster of differentiation (CD) 3, CD10, CD20, CD21, and Ki-67, but negative for CD68, S-100, CD138, CD30, and B-cell lymphoma 2 [Figure 1]. The patient received the T cell-spot test for tuberculosis infection, and the result was negative. Histopathology test also showed no evidence of tuberculosis or tumors. The diagnosis of Kimura disease (KD) was proposed.

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Based on clinical features and typical histopathological results, the patient was finally diagnosed with KD. Prednisone 65 mg daily (1 mg/kg body weight) was administered for a month, followed by a gradual reduction of 5 mg weekly. Follow-up was carried out for 7 months, and prednisone 15 mg daily was administered recently. No relapse of subcutaneous swelling was observed. Recent (October 11, 2019) full blood count showed white blood cell count of 4.90×10^9/L (normal range: 3.50–9.50 $\times$ 10^9/L); hemoglobin 149 g/L (normal range: 130–175 g/L); and eosinophil 1.28 $\times$ 10^9/L (normal range: 0.02–0.52 $\times$ 10^9/L). Serum IgE level was 1700 IU/mL (normal range: <165 IU/mL).

KD is a rare idiopathic condition of unknown cause and pathogenesis that presents as lymphadenopathy without pain, and subcutaneous masses in the neck and head. Most reported cases occurred in young Asian males and are characterized by elevated serum IgE level and eosinophilia. The definitive histological description of the disease was first reported by Kimura in 1948.[1] KD occurs mostly in Asian patients and has been considered to be limited to the Far East.

The exact etiology and pathogenesis of KD remain unknown, but it is considered an allergic or autoimmune disease invoked by an unclear antigenic stimulus. A study suggested that the proliferation of cytokines released by T-helper 2 and CD4+ T cells could be the cause of KD, such as the excessive releasing of interferon-γ, interleukin (IL)-4, IL-5, IL-13, granulocyte macrophage colony-stimulating factor, and tumor necrosis factor-α. These factors may increase IgE and eosinophil infiltration, leading to the disease development and recurrence. The immune disorder may also be associated with KD accompanied by allergic conditions such as rhinitis, chronic urticaria, asthma, and pruritus. Under microscope, KD is characterized by cellular (lymphocyte hyperplasia and eosinophil infiltration are present, and endothelial cells are flat and usually lack atypical cytology or vacuolization), fibrocollagenous and

Correspondence to: Dr. Tao Wang, Department of Rheumatology, The First Affiliated Hospital of Bengbu Medical College, Bengbu, Anhui 233004, China
E-Mail: wangtao@bbmc.edu.cn

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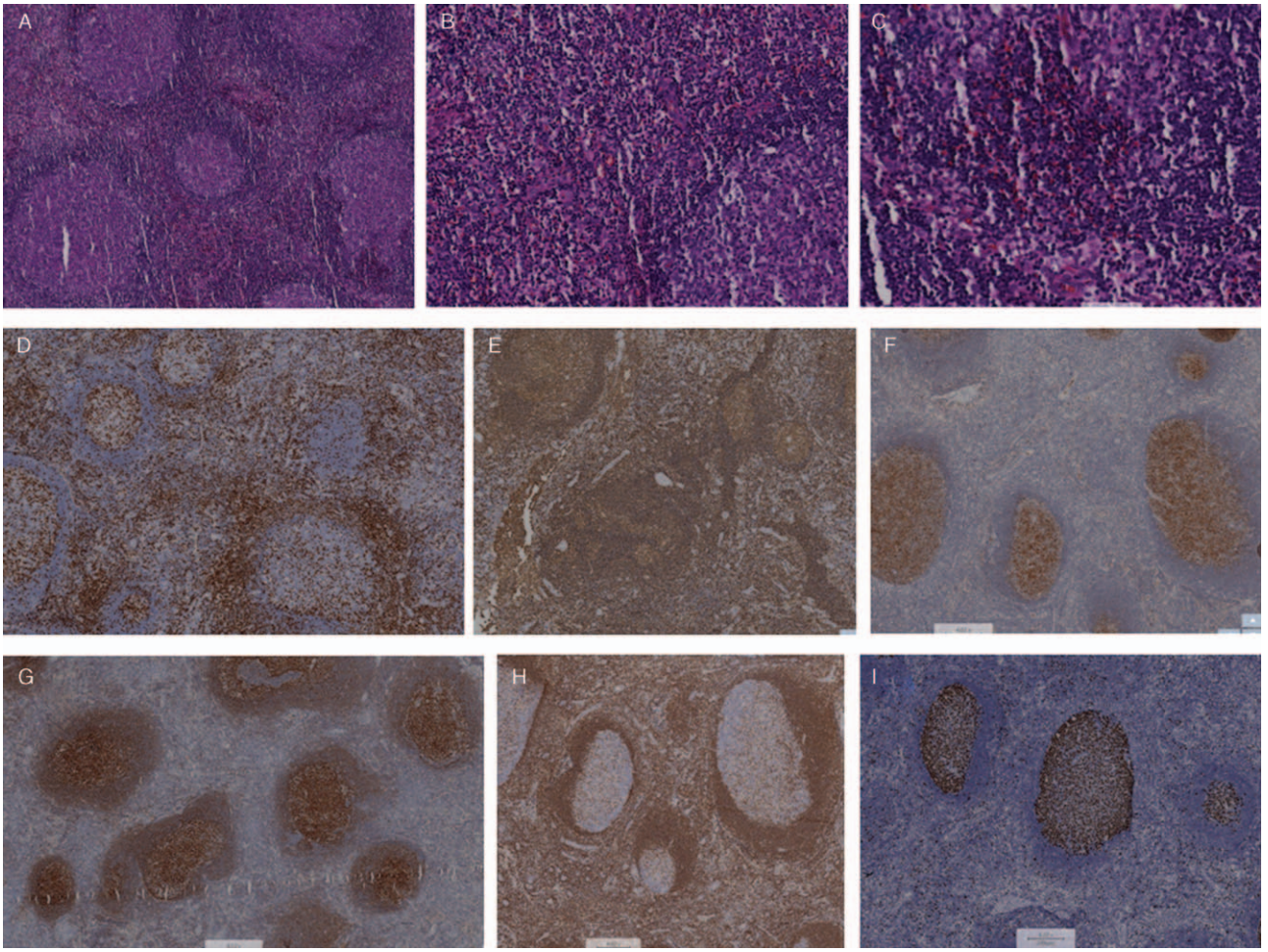

Figure 1: Histopathology of the case of Kimura disease with a history of Budd-Chiari syndrome. Lymph node specimen showed abundant eosinophils infiltration. A: H&E staining, original magnification ×80; B: H&E staining, original magnification ×200; C: H&E staining, original magnification ×400. Immunohistochemical staining (Elivision™ Plus immunohistochemical staining, original magnification ×40): paracortical area CD3+ (D), lymphoid follicular CD20+ (E), germinal center CD10+ (F), CD21+ (G), Bcl-2− (H), Ki-67+ 80% (I). Bcl-2: B-cell lymphoma 2; CD: Cluster of differentiation; H&E: Hematoxylin and eosin.

vascular features (proliferation of arborizing post-capillary venules is present).

There are no uniform diagnostic criteria for KD currently. The following manifestations should raise suspicion of KD: (1) young male, neck and/or head mass without pain; (2) enlarged retroauricular and subclavian lymph nodes; (3) other parts of body displaying multiple painless masses, accompanied by dermatitis and pruritus in the lesion area; (4) a long disease history; and (5) increased serum IgE level and blood eosinophil count. Computed tomography/ultrasonography/magnetic resonance imaging scans can help in delineating the extent and evaluating the progression of the disease. Primary diagnosis of KD could be made on the basis of clinical characteristics and auxiliary examination results. However, the final accurate diagnosis depends on pathological results.

Differential diagnosis of KD includes Hodgkin's lymphoma, angiolymphoid hyperplasia with eosinophilia (ALHE), Langerhans cell histiocytosis, angioimmunoblastic T-cell lymphoma, dermatopathic lymphadenopathy, Castleman disease, Kikuchi disease, Mikulicz disease, reactive lymphadenopathy, salivary gland tumor, and parasitic infections. It is reported that the most common disease that resembles KD is ALHE,[2] which mainly affects middle-aged females, with pathological characteristics of aberrant vascular proliferation, diffuse excessive eosinophil infiltration, and proliferative capillary endothelia with round to polygonal-shaped nuclei. However, KD often affects Asian young men, and laboratory examinations show increased blood eosinophils and serum IgE levels. Moreover, ALHE patients have normal IgE levels and rarely have kidney diseases.

The first-line treatment for KD is surgery, especially in the case of lymph node or parotid gland lesions, for which partial surgical resection is preferred. However, the high recurrence rate makes the disease difficult to be completely cured. The reported recurrence rate is about 62%, and the recurrence mainly occurs between 1 and 3 years after surgery. Reoperation or long-term maintenance of corticosteroid therapy can prevent recurrence. Glucocorticoids can also be prescribed for the patients with kidney diseases. Radiotherapy at a dose of 20 to 30 Gy can be considered in those with poor response to corticosteroids or in cases where corticosteroid therapy could not be accepted due to the adverse effects. Other therapeutic methods are low-

dose tacrolimus therapy[3] (0.05 mg/kg), cyclosporine or mycophenolate mofetil[4] therapy. Anti-IgE therapy was also reported in KD patients,[5] which reduced peripheral blood eosinophil count and the size of lesion.

Some factors influence the prognosis and recurrence of KD, such as the size of the lesion, single or multiple, boundary, onset time, eosinophil count and IgE level, resection range, and glucocorticoid dose used after surgery.

The patient in this study also had a history of BCS. Although the pathogenesis of these two diseases is not completely clear, vascular disease is their common feature, and immune disorders are involved. The release of free radicals and oxidative injury are complicated in both diseases. We speculate that there might be some correlation between the two diseases, but it needs to be further elucidated in future studies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has his consent for his image and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

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