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Case report

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Kikuchi Fujimoto Disease: The First Reported Case in Mongolia

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Objectives: Kikuchi-Fujimoto Disease (KFD) is a rare, benign condition of necrotising histiocytic lymphadenitis, typically presenting in young women. This report is on the first diagnosed case of KFD in Mongolia. **Methods:** The patient was a 24-year-old female, who presented with fever, night sweats, rash, and cervical lymphadenopathy. Based on clinical features, histopathology, and immunohistochemistry findings, the diagnosis of KFD was confirmed. **Results:** Full recovery was achieved using symptomatic treatment. **Conclusion:** To minimize diagnostic confusion and potentially harmful and unnecessary treatments, we emphasize that clinicians should be aware of this condition.

Keywords: Histiocytic Necrotizing Lymphadenitis, Kikuchi Disease, Kikuchi Necrotizing Lymphadenitis, Kikuchi-Fujimoto's Disease.

Introduction

Kikuchi–Fujimoto disease (KFD) is a rare, self-limiting illness, described mostly in young women and frequently reported in Asia [1, 2]. This disease, characterized by cervical lymphadenopathy and fever, is often mistaken as a more serious conditions [3]. Though it is an uncommon cause for cervical lymphadenopathy, the clinician should be aware of this condition as a potential differential diagnosis for cervical lymph node enlargement. An accurate diagnosis avoids expensive and potentially harmful investigations and treatments.

To the best of our knowledge, this is the first publication on KFD in Mongolia. The aim of this case report is to introduce a KFD patient from our clinical practice in Ulaanbaatar, Mongolia.

Case Report

On November 8, 2016, a 24-year-old female was admitted to the University General Hospital of Mongolian National University of Medical Sciences (MNUMS), with a number of symptoms, including high fever, fatigue, night sweats, anorexia, and painful, swollen cervical lymph nodes. Cervical lymph node swelling had been present for three months and was associated with fever, persistent night sweats, and weight loss. She had been treated with 500 mg of Amoxiclav twice per day for five days with no clinical improvement. The patient exhibited swelling and pain in both sides of the neck 10 days prior to admission. She had no personal or family history that was relevant to her symptoms.

Physical examination revealed enlarged, tender lymph nodes, cervical, and left inguinal regions. She showed erythematous rashes on her face, neck, upper chest, and upper limbs, but they were not associated with organomegaly (Figure 1A-C). Her temperature was 38.9^{0}C, and her weight was 51 kg. Her laboratory data showed mild leukopenia (WBC 3,200/μL; neutrophils 49%) on complete blood count (CBC), elevated C-reactive protein (CRP) (11.3mg/l), and lactate dehydrogenase (452.7 U/L). Serologic tests for common viral infections, including HIV, EBV, and Hepatitis A, B, C, were

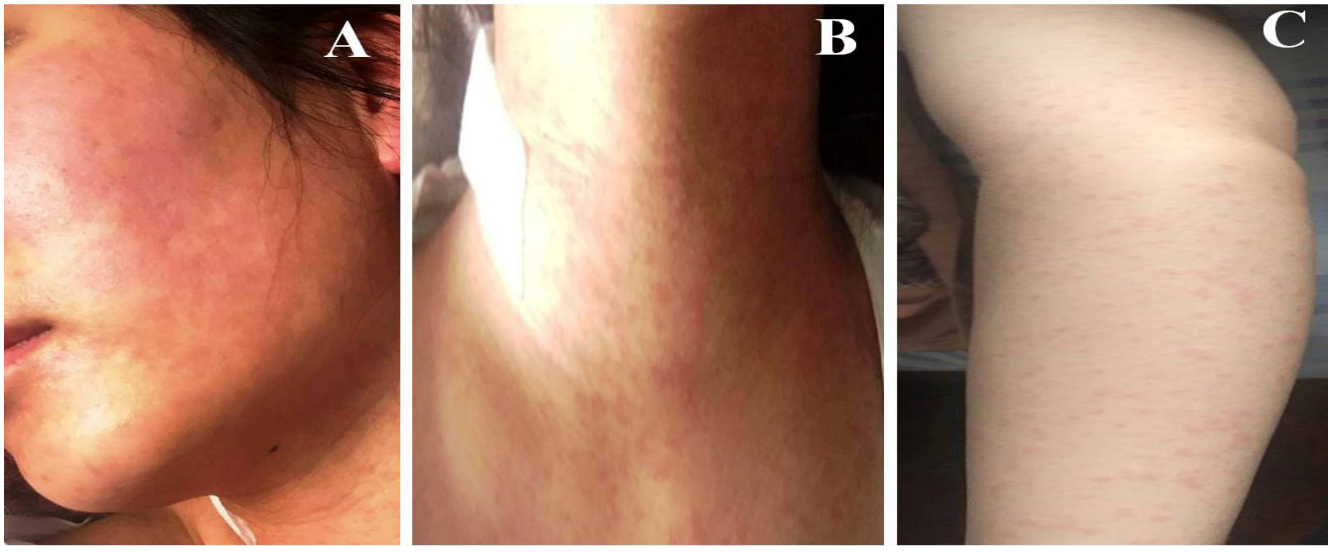

Figure 1. Erythematous rashes and multiple, generalized rubella like eruptions, reddish plaques, papules and macules on (A) face, (B) neck and upper chest, and (C) limbs at the time of diagnosis.

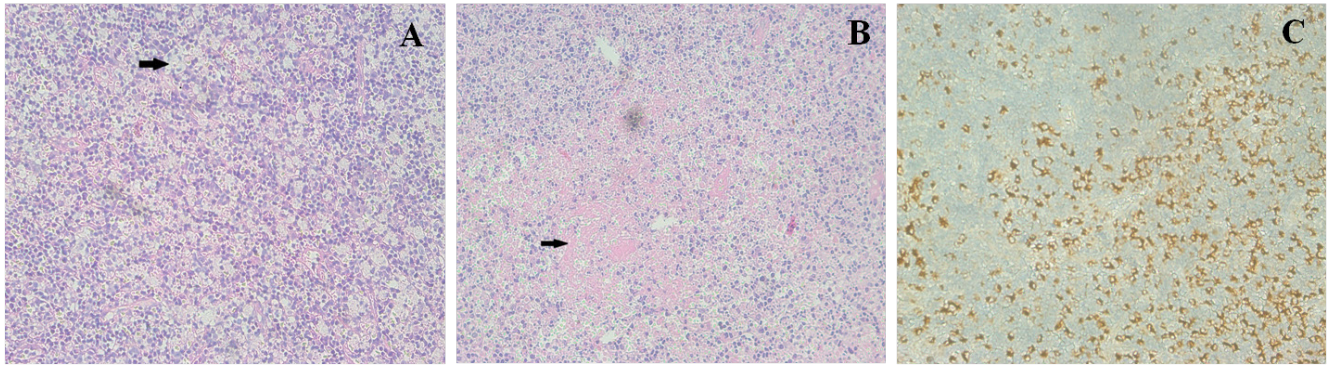

Figure 2. (A) Low magnification /HE, X10/ view showing necrotizing histiocytic inflammation. (B) Proliferation of phagocytic foamy histiocytes and infiltration of plasmacytoid monocytes /HE, X10/ (C) The histiocytes in the karyorrhectic foci are positive for the CD68 antigen /CD68 immunostaining, X20/.

negative, except for an elevated cytomegalovirus (CMV) IgG level. Antinuclear antibodies (ANA) and rheumatoid factor (RF) levels were normal. CT scans of the abdomen and pelvis with intravenous contrast revealed enlarged, bilateral, inguinal lymph nodes, measuring up to 1.5 cm. Furthermore, bone marrow aspiration did not reveal any abnormalities and any traces of hematological malignancies.

She subsequently underwent an excision biopsy of the right cervical lymph node mass and an immunohistochemical stain of histiocytes expressing CD68 (Ultra-View Universal DAB Detection Kit, Ventana Medical Systems, Inc. Arizona, USA). This revealed a cellular picture with focal areas of necrosis containing karyorrhectic nuclear debris, scattered fibrin deposits, and large collections of CD68 positive plasmacytoid monocytes and phagocytic histiocytes containing 'crescenteric' nuclei (Figure 2A-C). Based on clinical features, histopathology, and immunohistochemistry results, the diagnosis of KFD was confirmed. She was given 50 mg of oral Methylprednisolone (MP) daily. Her rash started to disappear and her lymph nodes returned to normal within two weeks. MP was tapered and stopped after 2 months. Upon further review at three months, it was confirmed that the patient achieved full recovery.

Discussion

KFD is a rare, self-limiting lymphadenitis, predominantly occurring in young women and typically presenting with fever, cervical lymphadenopathy, and flu-like symptoms. It was first reported in 1972 by Kikuchi and Fujimoto, independently [2, 3]. Following the initial descriptions of KFD in 1972, approximately 740 cases have been reported in the literature [4]. Of those cases, 593 (81%) were adult patients, and male to female ratio was 1:2 in adults, but young boys were more commonly affected than girls (1.4:1) [4, 5]. During the 1990's, researchers noted that women were affected four times more than men by this disease, and this female predominance attracted attention from the science community, however, recent reports from Eastern countries have suggested that the actual ratio is closer to 1:1 [1, 6-8].

The etiopathogenesis of KFD has not been fully elucidated, but the literature suggests viral and bacterial infections, including toxoplasma, human herpes virus 6 and 8, Epstein-Barr virus, parvovirus B-19, HIV, human T-cell lymphotropic virus, cytomegalovirus, Yersinia enterocolitica, Bartonella and Brucella; or possibly autoimmune components to play a role [9, 10]. Since 2010, researchers have performed many molecular genetic experiments to elucidate the pathogenesis of this disorder. In 2013, Ishimura M et al. investigated the high expression level of interferon-induced genes from patients with KFD, and they concluded that an analysis of the gene expression profile may provide a rapid non-invasive diagnosis of this disease [11]. In 2002 and 2004 Ohshima K et al. investigated apoptosis and cell-cycle associated gene expression and cytokine pathways in lymph node samples. The results of these studies were that apoptosis-associated genes, especially caspases, upregulated, but apoptosis inhibitory gene bcl-2 were down regulated. From these results, they confirmed that both apoptosis and proliferation are simultaneously present in affected lesions of lymph node, and additionally, the cytokine and chemokine pathways of interferon γ, interleukin 18, and interferon γ–induced protein 10 play an important role in the pathogenesis of apoptosis associated with KFD [12, 13].

The classical clinical manifestation includes unilateral cervical lymphadenopathy involving predominantly the posterior triangle. Typically, the patient has associated fever, night sweats, and weight loss [14]. Extranodal involvement of this disease, including skin, eye and bone marrow localisations, has rarely been described. The cutaneous manifestations can present as morbilliform and rubella-like eruptions, reddish plaques which resemble lymphoma, erythematous, and acneiform eruptions on face. Facial or malar "butterfly rash" may also be present. Skin involvement tends to occur in patients who have more severe and protracted course [14, 15].

Laboratory studies may reveal leukopenia, anemia, elevated erythrocyte sedimentation rate, and elevated CRP. Atypical lymphocytes may also be present in the peripheral blood [4, 14]. The diagnosis of KFD is usually based on lymph node histology, which shows a patchy, necrotizing process affecting the paracortical areas of the lymph node, with various types of histiocytes and plasmacytoid monocytes, particularly foamy histiocytes, are predominantly present around foci of necrosis [4, 7].

Up to 30% of patients with KFD are initially misdiagnosed as having lymphoma and are treated with chemotherapy, thus, an excisional biopsy of affected lymph node should be the requested diagnostic method used for patients with

suspected KFD [4, 14, 16]. The diagnosis of KFD is confirmed by immunohistochemical staining of CD68 positive plasmacytoid monocytes and histiocytes [17, 18]. Differential diagnosis for KFD include lymphoma, tuberculous adenitis and SLE [4].

No specific treatment is available for KFD. High dose glucocorticoids with intravenous immunoglobulin have been shown to have some benefit in severe symptoms. In supportive treatment, non-steroid anti-inflammatory drugs may be used to alleviate lymph node tenderness and fever [1, 19, 20]. Kuo T., et al. reported that, although KFD is essentially a self-limiting illness, there is a 3% risk of recurrence [8]. Fatal cases have been reported but are rare [21, 22].

In our clinical practice, we successfully diagnosed and treated KFD for the first time. Certain skin features, such as the erythematous facial lesions, acneiform eruptions, facial or malar "butterfly rash", as evidenced in our patient, should be considered possible, severe extranodal cutaneous manifestations of KFD. Awareness of this condition amongst physicians leads to an accurate diagnosis without the need for expensive and often potentially harmful investigations. KFD is a self-limiting, benign condition that responds well to symptomatic treatment.

Conflict of Interest

The authors state no conflict of interest.

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