DOI: http://dx.doi.org/10.3315/jdcr.2012.1108

Journal of Dermatological Case Reports

Kikuchi disease with skin lesions mimicking lupus erythematosus

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Key words:

fever, hydrochloroquine, lupus, lymphadenopathy, necrotizing lymphadenitis, prednisone

Abstract

Background: Kikuchi disease (Kikuchi-Fujimoto disease, histiocytic necrotizing lymphadenitis) is a systemic illness of unkown etiology. It is characterized by cervical lymphadenopathy and fever. The skin is the most frequently affected extranodal organ. Cutaneous Kikuchi-Fujimoto disease can mimic both clinically and histologically skin lesions in lupus erythematosus, a disorder with which it seems to be closely related. A close follow up is required as systemic lupus erythematosus development has been reported.

Main observation: We report a case of a 23-year-old woman, who was admitted to our department with high fever, skin lesions and arthralgia. Scaly and erythematous plaques were noted on both cheeks and earlobes. In pads of feet and hands and periungual area, multiple purple papules with a perilesional erythematous halo were evident. A thoracoabdominal computed tomography scan revealed lateral cervical, mediastinal, paratracheal, subcarinal and submandibular lymphadenopathy. Excisional node biopsy was consisten with Kikuchi disease with skin involvement.

Conclusion: It has to be kept in mind that Kikuchi disease is a differential diagnosis in case of fever, lymphadenopathy and lupus-like skin lesions. Skin lesions in this disease and may resemble clinically and histologically to those of subacute lupus erythematosus or systemic erythematosus lupus. (*J Dermatol Case Rep*. 2012; 6(3): 82-85)

Introduction

Kikuchi-Fujimoto disease (KFD) know also as Kikuch disease or histiocytic necrotizing lymphadenitis is an entity of unkown etiology. It is characterized by cervical lymphadenopathy and fever. The skin is the most frequently affected extranodal organ. Cutaneous Kikuchi-Fujimoto disease can mimick both clinically and histologically skin lesions in lupus erythematosus. A close follow up is required as systemic lupus erythematosus (SLE) development has been reported.[1]

Case Report

A 23-year-old woman with no relevant past medical history was admitted to our department of Dermatology with symptoms of high fever, skin lesions and arthralgia. Despite 2 weeks of previous broad-spectrum antibiotic therapy, the patient had had no clinical response.

The patient was in a relatively fair clinical condition. Physical examination revealed palpable cervical lymphadenopathy. Scaly and erythematous plaques were noted on both cheeks and earlobes (Fig. 1A). In pads of feet and hands and periungual area, multiple purple papules with a perilesional erythematous halo were evident (Fig. 1B). Semi mucosa lip involvement with mild mucositis and small aphthous ulcers were also present. There were no signs of arthritis.

Laboratory studies showed: haemoglobin (Hb) 9.7 g/dL; lactate dehydrogenase (LDH) 742 U/L, C reactive protein (CRP)108.2 mg/L: erythrocyte sedimentation rate (ESR) 57; total Immunoglobulin E 1925 UI/mL; antinuclear antibodies (ANA) titer 1/320 with speckled pattern and peripheral antineutrophil cytoplasmic antibodies (p-ANCA) 39 U/mL, and positive Coombs test (++/++++). Viral and bacterial serology tested negative except for Epstein Barr Virus (EBV) Ac VCA IgG +, Ig M+, Ac EBNA +. Further laboratory findings were not relevant.

Two skin biopsies, performed from a periungual lesion and a facial papule, showed interface dermatitis with basal vacuolar degeneration, colloid bodies and isolated necrotic keratinocytes (Fig. 2). Papillary dermis showed edema and a linfohistiocytic perivascular and periadnexal infiltrate, with accumulations of histiocytes and karyorrhexis. Indirect immunoflourescence was negative. No images of vasculitis were seen.

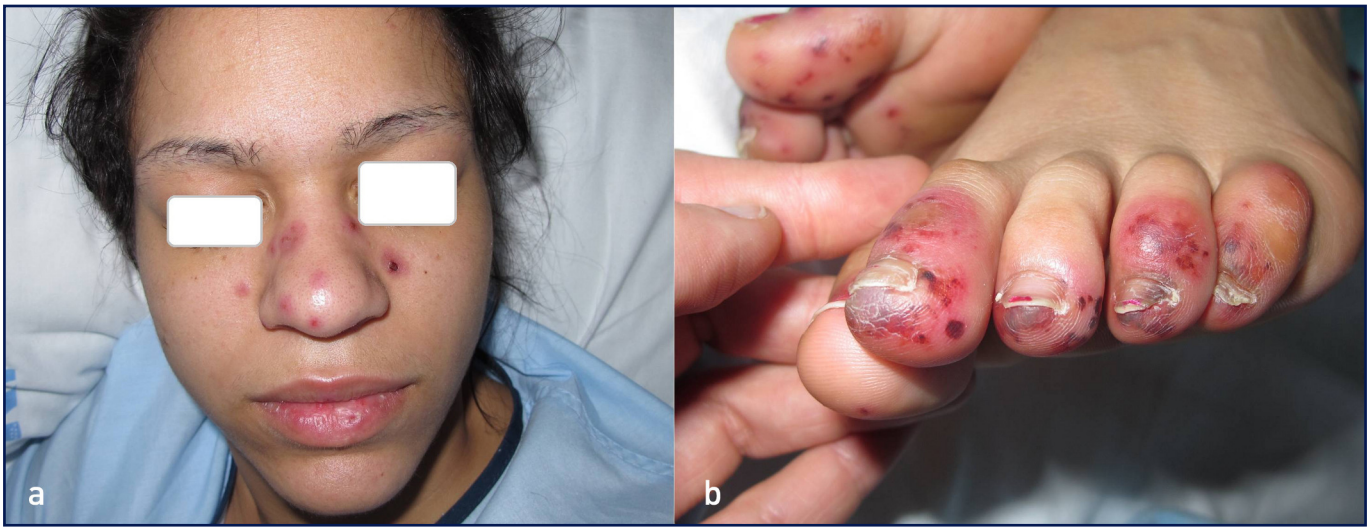

Figure 1

(a) Scaly and erythematous plaques on both cheeks and nose.
(b) Numerous purple papules with an erythematous halo are present in toes' pads.

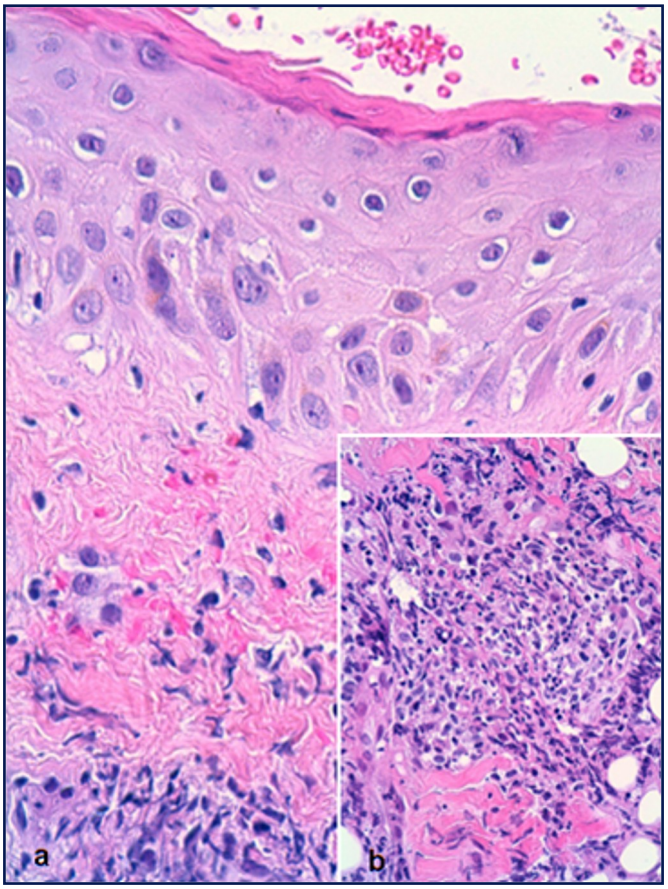

Figure 2

Skin biopsy. (a) Interface dermatitis. Vacuolar layer degeneration and colloid bodies. (b) Lymphohistiocytic aggregates with kariorrhexis.

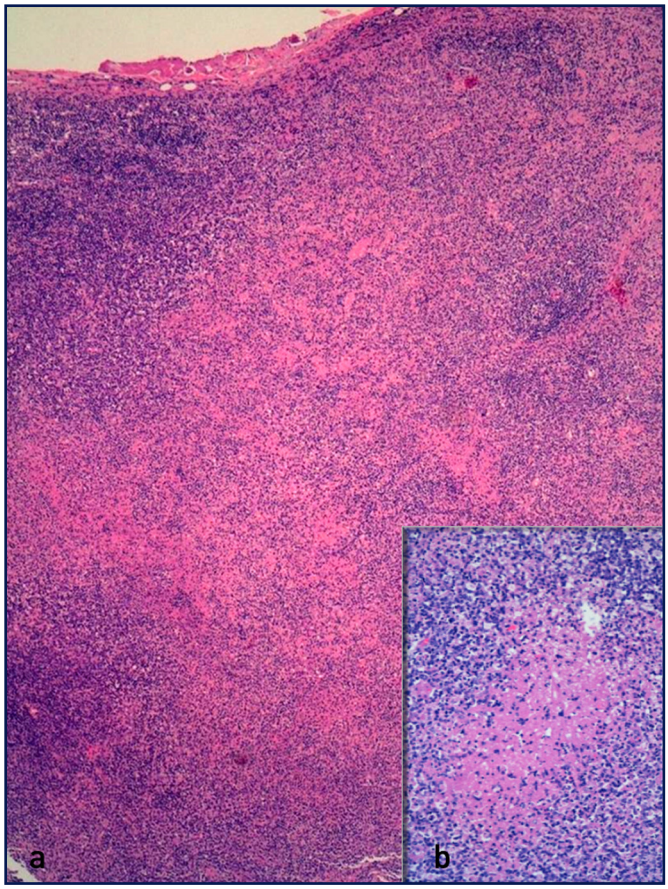

Figure 3

Lymph node biopsy. (a) Paracortical necrotic foci. (b) Necrosis and kariorrhexis.

On the echocardiography a slight pericardial effusion was detected. A thoracoabdominal computed tomography scan revealed lateral cervical, mediastinal, paratracheal, subcarinal and submandibular lymphadenopathy up to 1.7 cm of diameter.

Despite the fact that clinical and laboratory findings suggested a diagnosis of systemic lupus erythematosus, the extensive lymph node involvement forced us to rule out a lymphoma and tuberculosis, even though the skin histology was not consistent.

Excisional lymph node biopsy confirmed the histological diagnosis. Paracortical patchy necrotic areas with abundant cellular debris and profuse peripheral hystiocitic cells were seen (Fig. 3). AFB staining was negative.

A diagnosis of Kikuchi-Fujimoto Disease with skin involvement was made. Treatment was initiated with oral prednisone at a dose of 30 mg/day and hydrochloroquine at a dose of 200 mg/day. A clinical and analytical improvement was seen within the following weeks although arthralgia persisted for 6 months. The patient did not develop more skin lesions and the ANA titer lowered and remained low for 6 months.

Discussion

KFD or necrotizing lymphadenitis is a rare disease of unknown cause and pathogenesis, usually characterized by cervical lymphadenopathy and fever. Initially described in young women in Asia, there are now cases reported in all races. Some reports raised the hypothesis that previous infection is probably responsible for the massive CD4 T cells apoptosis mediated by CD8 that occurs.[1] EBV RNA has been detected in the lymph nodes of some patients. This finding favors the pathogenic role of certain types of viruses, especially EBV, which could also be a fact in our patient.

Even though high fever and cervical lymphadenopathy are the most common clinical manifestations, neck and mediastinal nodal areas can also be affected. In addition, involvement of other organs is not uncommon so clinical findings include autoimmune hepatitis, aseptic meningitis, neuritis, panuveitis and pancytopenia. Atypical lymphocytes without outliers are observed in 25% of patients. ANA test is positive in 7% of the cases.

Skin involvement occurs in 40% of cases of KFD, being the most frequently affected extranodal organ. A non-specific rash is usually found but other skin manifestations such as acral leucocytoclastic vasculitis, malar erythema, oral aphthous ulcers, diffuse alopecia, pruritus, photosensitivity, pustules and lupus-like papules and plaques can also be seen. Lupus-like lesions of KFD are more similar to the skin lesions of subacute lupus erythematosus than to those of systemic lupus erythematosus. Small observational studies have described a more intense skin involvement accordingly to more severe cases,[2] as well as more heterogeneous skin lesions correlated with an increased apoptotic activity.[3]

Specific KFD's skin histological features have not been fully described, but the most common patterns are: dermal lymphohistiocytic infiltrate, epidermal changes with occasional necrotic keratinocytes, karyorrhexis, vacuolar layer degeneration and dermal papillae edema.[4] These patterns are also frequent findings in SLE except for the last one. Dermal infiltrate is similar to that found in the lymph node with CD68+ histiocytes and plasmacytoid monocytes.

Diagnosis is based on the excisional lymph node biopsy. The histological features correspond to three evolving phases: early or proliferative, necrotizing and xanthomatous phase. The most characteristic finding is the appearance of multiple foci of patchy paracortical necrosis with a peripheral CD68+ cell and CD123+ plasmacytoid dendritic cell infiltrate. In early stages, large lymphocytes with immunoblast morphology may be increased which gives a picture resembling high-grade lymphoma. Plasma cells are scarce and neutrophils and eosinophils are characteristically absent. SLE lymphadenitis is considered as the most challenging differential diagnosis but it can be distinguished from KFD by the presence of abundant plasma cells, a more diffuse involvement, vasculitis and typical uncommon aggregates of nuclear debris or so-called hematoxylin bodies.[5]

The most common laboratory findings are leukopenia and elevated values of ESR, C-reactive protein (CRP) and LDH.[6]

KFD is a self-limited condition with a 20% recurrence rate. However, systemic steroids may improve its evolution. A well designed prospective study found that predictive values of recurrence are fever, fatigue, extranodal involvement and long symptomatic duration.[7] Some cases of fatal evolution have been reported.

KFD has been related to Cobalamin deficiency, Hemophagocytic Lymphohistiocytosis, Drug-induced hypersensivity syndrome, and several autoimmune diseases. A progression to SLE is a well-known fact, although its association with exclusively cutaneous lupus is rare.

Current knowledge of KFD is scarce and based on small case series so doubt remains on whether the disease should be considered as an independent entity of SLE.[8] Both conditions share common features as skin involvement, fever and lymphadenitis. Additionally, the histologic appearance of lymph nodes in patients with Kikuchi disease is similar to that of lymph nodes in patients with SLE lymphadenitis. Moreover, lymphadenitis is present in 50% of SLE cases and some authors recommend its inclusion in the SLE criteria.

Based on this data, KFD could be a "forme frustre" or an early stage of SLE. However, some other authors suggest that KFD is only an inadequate apoptotic response to a previous infection. Based on retrospective observational studies, basal layer vacuolar degeneration in skin samples and elevated ANA have been proposed as markers of transformation into SLE.[9] A close follow-up with periodically ANA determination is mandatory in these patients. Our opinion is that KFD and SLE may share a common pathogenic pathway and could be closely related.

Conclusion

In conclusion, we present a new case of KFD with skin involvement resembling clinical and histological skin lesions of Lupus Erythematosus. Our patient's high ANA titer makes us believe that she could develop SLE in the future. KFD is

a major differential diagnosis in case of fever, lymphadenopathy and lupus-like skin lesions especially when the patient is an Asian woman. Lymphoma and tuberculosis should be considered as alternative diagnoses. Skin lesions are not uncommon in KFD and may resemble clinically and histologically to those of Subacute Lupus Erythematosus or Systemic Erythematosus Lupus. Diagnosis is based on excisional lymph node biopsy, showing multiple foci of patchy paracortical necrosis. A close follow up of these patients is necessary, especially when a high ANA titer is present, in order to discard a progression to SLE.

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