Case Report

Kikuchi's Disease Accompanied by Lupus-like Butterfly Rash

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ABSTRACT. Kikuchi's disease (KD) is a benign and self-limiting lymphadenitis, particularly affecting young women. KD is often associated with fever, arthralgia, and leukopenia, features also found in systemic lupus erythematosus (SLE). Lymphadenitis associated with SLE is indistinguishable from that in KD, and the association of KD and SLE has been previously reported. We describe a case of KD who developed a typical butterfly rash, reminiscent of SLE. However, histological and laboratory findings excluded the diagnosis of SLE. This case emphasizes that careful differential diagnosis between KD and SLE is required. (J Rheumatol 2003;30:857–9)

Key Indexing Terms:
KIKUCHI'S DISEASE
SYSTEMIC LUPUS ERYTHEMATOSUS
BUTTERFLY RASH
HISTIOCYTIC NECROTIZING LYMPHADENITIS

Kikuchi's disease (KD) is a clinicopathological entity first described by Kikuchi in 1972[1]. It is a rare, benign, and self-limiting lymphadenitis affecting particularly young women and characterized by tender lymphadenopathy, which is usually cervical but can also be generalized. Malaise and swinging fever are common features and can last from 1 to 24 months. In 30% of cases, a skin eruption has been reported, which is not diagnostic of this condition and can mimic drug eruption, erythema mulitiforme, or subacute lupus erythematosus[2-5]. Diagnosis of the KD is usually based on lymph node histology, which shows a patchy necrotizing process affecting the paracortical areas of the lymph node with eosinophilic fibrinoid material and the presence of atypical mononuclear cells. Foamy histiocytes are also present around foci of necrosis[6]. A viral etiology has been suspected in view of the association with viral infections such as Epstein-Barr virus (EBV) and human herpes virus 6 (HHV6)[6].

Although KD has rarely been associated with systemic lupus erythematosus (SLE), KD should be ruled out given its different prognosis and management[7-9]. We describe a case of KD with butterfly rash reminiscent of SLE.

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Submitted February 4, 2002; revision accepted September 19, 2002.

CASE REPORT

A 15-year-old Japanese girl was admitted to our hospital because of butterfly rash and cervical lymphadenopathy. Family and medical history were unremarkable. She first noted an enlarged and painful lymph node in her left cervical area in late February 2001, with no prior symptoms of upper respiratory infections. Three weeks later, she had fever over 38°C, a raised butterfly malar rash sparing the nasolabial folds (Figure 1), oral ulcers, and mild arthralgia of wrists and knees. Laboratory investigations showed a mild leukopenia with a white blood cell (WBC) count of 2800/µl. She was referred to our hospital with a presumptive diagnosis of SLE.

On admission, she displayed cervical lymphadenopathy involving multiple lymph nodes, oral ulcer, and mild arthralgia at both wrists. Skin manifestations included a butterfly rash, suggestive of SLE, as well as a few small papular erythematous lesions on her dorsal fingers. She was not febrile during hospitalization. Laboratory tests revealed normal blood cell counts except for leukopenia (WBC 2800/µl, neutrophils 36%, lymphocytes 56%), C-reactive protein 0.4 mg/dl, erythrocyte sedimentation rate 74 mm/h, aspartate aminotransferase 33 IU/l, alanine aminotransferase 27 IU/l, lactate dehydrogenase 1073 IU/l. Electrolytes and kidney function tests were normal. Serum antinuclear antigens (ANA) and anti-DNA antibodies were negative, and serum C3 and C4 were within normal ranges. Blood culture and urinalysis were negative. Serologic tests were negative for hepatitis B and C viruses, HHV6, parvovirus, mycoplasma, rubella virus, cytomegalovirus, and human T cell leukemia virus (HTLV-1). EBV serology was consistent with a chronic EBV infection. Magnetic resonance imaging of wrists revealed mild synovitis. Cervical lymph node biopsy showed massive necrosis with thrombosis and proliferation of transformed lymphocytes including immunoblasts, histiocytes (both with and without phagocytosis), necrotic cells, and abundant nuclear debris (Figure 2). Neutrophils and hematoxylin bodies were absent. Diagnosis of KD was made based on these findings as well as on the negative test for ANA. Pathological findings of the skin biopsy from the facial erythema revealed mononuclear cell infiltration around small vessels (Figure 3). Degeneration of the basal layer in epidermis and immune complex deposition by immunofluorescence (features associated with SLE) were not observed. These serological and histological findings were against a diagnosis of SLE. Without treatment, the patient's temperature returned to normal within a week, and malar rash, cervical lymphadenopathy, and leukopenia disappeared within 3 weeks.

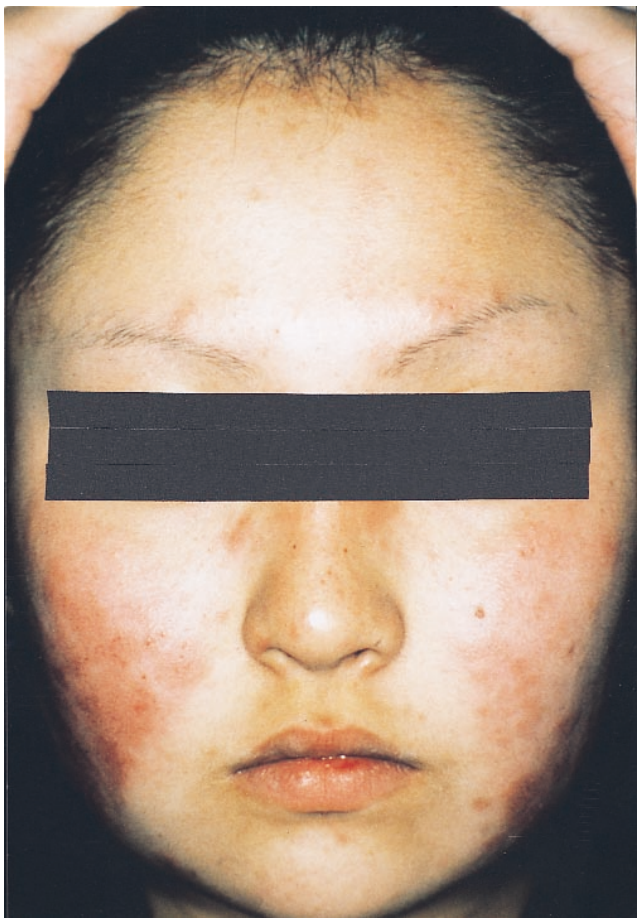
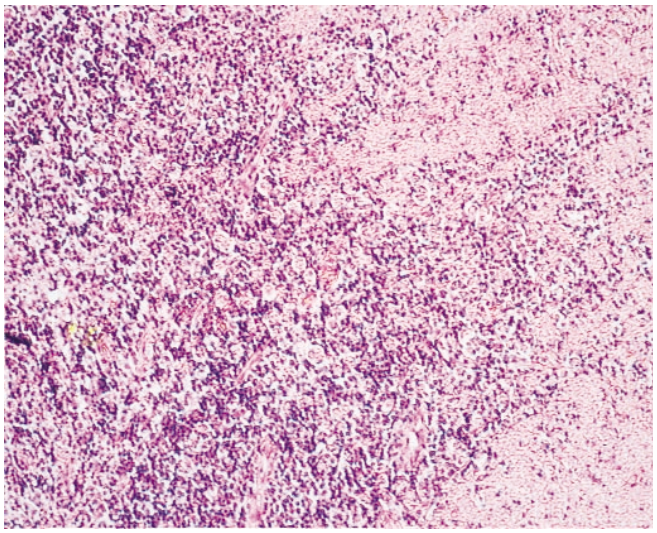


Figure 1. A raised butterfly malar rash sparing the nasolabial folds.



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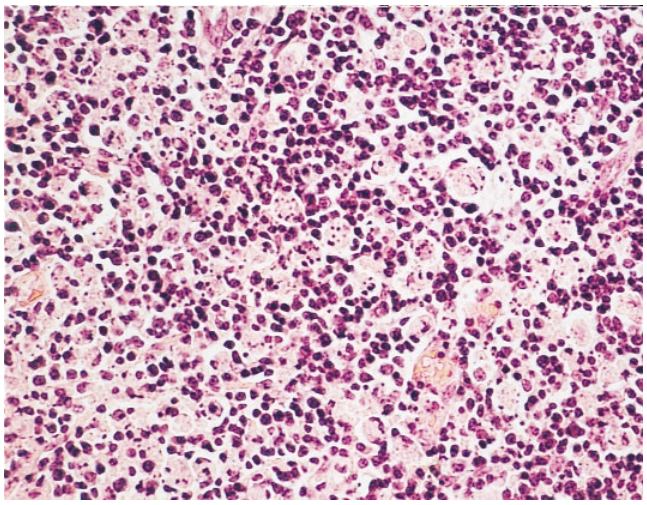

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Figure 2. (A) Lymph node sections showing histiocytic necrotizing lymphadenitis with extensive necrosis (hematoxylin-eosin, original magnification ×25). (B) High magnification to show the karyorrhexis and numerous histiocytes containing phagocytosed nuclear fragment (H&E, original magnification ×100).

DISCUSSION

We describe a case of KD with butterfly rash suggestive of SLE. In this disease, about 30% of patients have a skin eruption, but cutaneous manifestations have not been reported in detail[2-5]. In most cases the eruption has been described as drug eruption-like, rubella-like, urticarial, maculopapular, or disseminated erythema. No characteristic skin lesions have been reported. Facial involvement has been reported only in a few cases. In a patient described by Kuo, an erythematous plaque developed on the face[4]. Facial erythema was present in a patient reported by Sumiyoshi, *et al*[2]. Bataille, *et al* described a case of HTLV-1 associated KD where the skin eruption was macular erythema with mild scaling on the face, suggestive of subacute lupus erythematosus[5]. To our knowledge, this is the first case of KD with a typical raised butterfly rash sparing the nasolabial folds. A skin biopsy in our case showed a mild dermal mononuclear cell infiltrate. Basal cell degeneration and immune complex deposition by immunofluorescence, diagnostic features of SLE, were not observed. Thus, the pathogenic process of a malar rash in our case may be different from that in SLE.

KD primarily affects young women and is often associated with fever, arthralgia, and leukopenia, features common in SLE. SLE also can be associated with necrotizing lymphadenitis, known as lupus lymphadenitis. Lupus lymphadenitis is often indistinguishable from that in KD by histology, although the presence of hematoxylin bodies and the prominent plasma cell component are reported to be diagnostic of lupus[10]. Our case emphasizes that careful differential diagnosis between KD and SLE is required.

The association of KD with SLE has been reported in more than 17 cases[7-9]. In such cases, KD usually precedes

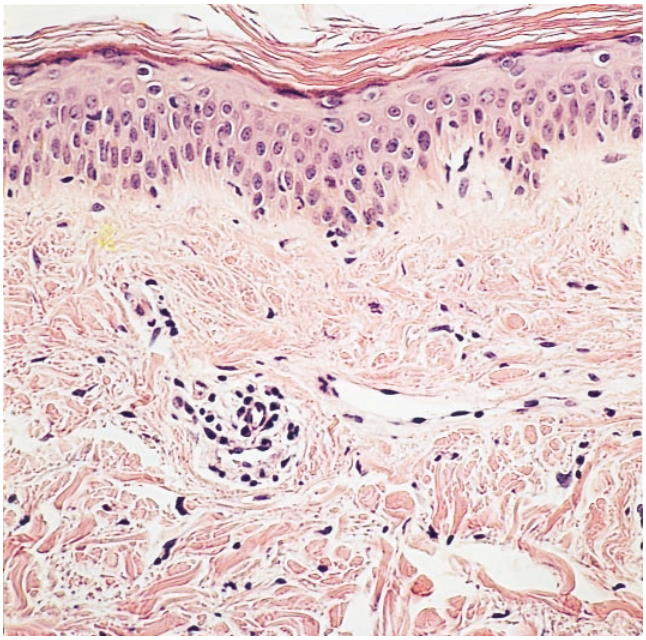

Figure 3. Skin biopsy shows mononuclear cell infiltration in the dermis (H&E, original magnification ×100).

the onset of SLE, but also can follow or occur simultaneously. Indeed, our patient fulfilled the revised criteria for classification of SLE at hospitalization, as she had butterfly rash, oral ulcer, arthralgia, and leukopenia[11]. However, we excluded the coexistence of SLE in this case because of the absence of ANA and the benign self-limiting clinical course. Longterm followup is required, however, to rule out the possibility that her condition may evolve to SLE.

The pathogenic process of lymphadenitis in KD is not clear, although viral infection is thought to be important as a trigger. One study has suggested that subsequent autoimmune responses induced by viral infection play a critical role in this disease[12]. Thus, CD8 positive cells activated by viral infection may induce apoptosis of CD4 positive cells. Apoptotic cells are engulfed by macrophages, resulting in the presentation of typical necrotizing lymphadenitis. Autoantigens in SLE are enriched in apoptotic blebs, and increased apoptosis and/or impaired clearance of apoptotic cells are thought to be important in the initiation of SLE[13-15]. In this context, KD and SLE may share initial pathological processes, such as common viral infection and subsequent autoimmune response.

ACKNOWLEDGMENT

We thank Dr. K. Ohnishi, Department of Dermatology, Gunma University School of Medicine, for the critical comments on the skin biopsy.

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