Kikuchi's Disease (Histiocytic Necrotizing Lymphadenitis) Associated with Cutaneous Lupus Erythematosus

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Histiocytic necrotizing lymphadenopathy (Kikuchi’s disease) is a rarely observed clinical entity characterized by fever and solitary or multiple lymphadenopathy predominantly in the posterior cervical region. Kikuchi’s disease has been reported to precede, coexist with or follow the diagnosis of systemic lupus erythematosus. In only rare instances has its association with cutaneous lupus erythematosus without systemic involvement been reported. We report two cases who presented with characteristic manifestations of Kikuchi’s disease. One to two months later, they developed lesions of cutaneous lupus erythematosus. The American Rheumatism Association criteria for systemic lupus erythematosus were not fulfilled. The possible pathogenic relationships between the two processes are discussed. (Dermatol Sinica 23: 158-161, 2005)

Key words: Histiocytic necrotizing lymphadenopathy, Kikuchi’s Disease, Cutaneous lupus erythematosus

組織細胞壞死性淋巴病變合併皮膚紅斑性狼瘡

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組織細胞壞死性淋巴病變(Kikuchi’s disease，菊池氏病) 爲一種罕見的以發燒及主要侵犯後頸部單一性或多發性淋巴病變為特徵的臨床疾病。文獻曾報告過菊池氏病發生於系統性紅斑性狼瘡之前，或後者同時存在，或發生於系統性紅斑性狼瘡之後。只有在極少數的病例中，菊池氏病僅與皮膚紅斑性狼瘡合併存在但無任何系統性病灶。我們在此報告二例具有典型菊池氏病症狀的病例，患者於診斷菊池氏病後一至二個月出現皮膚紅斑性狼瘡的病灶。但患者並未符合美國風濕學會對系統性紅斑狼瘡的評分標準(American Rheumatism Association criteria for systemic lupus erythematosus)。我們於此對菊池氏病與皮膚紅斑性狼瘡二者間可能的致病關聯性作一探討。(中華皮誌 23: 158-161, 2005)
INTRODUCTION

Kikuchi’s disease (KD), or histiocytic necrotizing lymphadenitis, was first described in 1972 as a benign self-limiting disorder\(^1,2\) characterized by painless lymphadenopathies in the cervical region, mild leukopenia, and fever. This idiopathic disease mainly affects women with a mean age of 30 years. Usually, it resolves spontaneously within 1-4 months and no treatment is needed. The diagnosis of KD is established on the basis of characteristic pathological features in the lymph node, including areas of necrosis, nuclear debris, aggregates of histiocytes, medium-to-large transformed lymphocytes and plasmacytoid T cells, and absence of neutrophils and eosinophils.\(^1\)

Skin rashes have been noted in 16-40% of KD patients.\(^3,4\) The first case of KD with cutaneous involvement and histologic findings was reported in 1990.\(^5\) Most cutaneous lesions present as erythematous macules, papules, plaques, nodules, or ulcers on the upper part of the body (i.e., the trunk, upper extremities, and face).\(^6-10\)

In a few cases, the condition is associated with cutaneous lupus erythematosus.\(^11-13\)

CASE REPORTS

Case 1

An 8-year-old Taiwanese girl presented with intermittent high grade fever and cervical lymphadenopathy for 10 days. Examination of other systems was unremarkable. The laboratory data revealed leukopenia (white blood cell count 1600/mm\(^3\)), positive antinuclear antibody (ANA) (1:40; speckled pattern), and positive anti-double-stranded DNA antibody (1:10). Anti-SS-A/Ro, anti-SS-B/La, anti-RNP, anti-Sm, and anticardiolipin antibodies were all negative, and complement level was normal. Viral serology screening (including hepatitis B, cytomegalovirus, and Epstein-Barr virus) was negative. Cultures of blood and urine for microorganisms were repeatedly negative. Chest X-ray and abdominal ultrasonography were normal. A cervical lymph node biopsy showed a necrotizing lymphadenitis with diffuse infiltration by plasmacytoid monocytes and histiocytes with phagocytosis (Fig. 1). On the basis of these findings, a diagnosis of KD was established.

One month later, erythematous papules were noted perinasally and periorally and over the forehead and arms (Fig. 2). Under the impression of cutaneous LE, skin biopsy was performed. Histopathology revealed (1) minimal vacuolar alteration of the basal cells, (2) moderate perivascular lymphocytic infiltrate, and (3) predominantly periadnexal lymphocytic infiltrate. Abundant mucin deposits were present in the interstitium of dermis and subcutaneous tissue (Fig. 3). Direct immunofluorescence (DIF) was negative. This clinicopathological picture was diagnosed as cutaneous lupus erythematosus. The patient did not have other symptoms and signs, and the diagnosis did not fulfill American Rheumatism Association criteria for the diagnosis of systemic lupus erythematosus (SLE). No systemic involvement and cutaneous recurrence was detected at the one-year follow-up.
Case 2
A 47-year-old Taiwanese woman presented with intermittent fever and bilateral cervical lymphadenopathy for 2 weeks. Examination of other systems was unremarkable. The laboratory data revealed leukopenia (white blood cell count 1600/mm³) and a negative (1:40) ANA titer. Anti-double-stranded DNA antibody, anti-SS-A/Ro, anti-SS-B/La, anti-RNP, anti-Sm, and anti-cardiolipin antibodies were all negative, and complement levels were normal. DIF was also negative. A cervical lymph node biopsy showed a necrotizing lymphadenitis with diffuse infiltration by plasmacytoid monocytes and histiocytes with phagocytosis. On the basis of these findings, a diagnosis of KD was established.

Two months later, erythematous papules and plaques over face, V-neck, and arms were noted (Fig. 4). Under the impression of cutaneous LE, skin biopsy was performed. Histopathology revealed hyperkeratosis, thin epidermis with a smudged dermo-epidermal interface, a thickened basement membrane zone, and beneath this zone, sclerosis and melanophages in the upper part of the dermis (Fig. 5). Discoid lupus erythematosus was diagnosed. Topical application of an anti-inflammatory (Elomet) resulted in lesion improvement, which was noted during a 3-month follow-up at the OPD.

DISCUSSION
KD is considered to be the clinical expression of an inadequate immunological reaction to an antigenic infectious agent, which manifests as a self-limited hyperstimulation of the lymphoid tissue. The association of KD with SLE as well as the possible evolution from KD to SLE has been reported. In the latter, development of SLE usually occurs a few months after the onset of KD. Both clinical and histopathological manifestations of KD and SLE are similar, and may lead to problems in differentiating the two entities. Similar intracytoplasmic tubular structures have been observed by electron microscopy, both in stimulated lymphocytes and histiocytes from KD lesions and in endothelial cells and lymphocytes from patients with SLE. Spies et al. have observed vacuolar degeneration in the basal cell layer,
necrotic keratinocytes, and edema in the papillary dermis of KD patients presenting ‘nonspecific’ cutaneous lesions. These histological findings are similar to those observed in cutaneous lupus erythematosus (LE). For all of these reasons, several authors have suggested that KD may represent a forme fruste of SLE. The cutaneous lesions reported in patients with coexisting KD and SLE correspond to those in patients with acute cutaneous LE (mainly ‘butterfly malar rash’). The association of pure cutaneous LE and KD seems to be exceedingly rare. Lo'pez et al. reported the case of a woman who developed chronic cutaneous LE one year after developing KD. Toll et al. recently reported a case of cutaneous lesions of subacute cutaneous lupus erythematosus (SCLE) that developed several months after diagnosis of KD. Lecoules et al. reported recurrent KD in a patient with discoid LE. The possibility that our cases may represent a minor form of SLE presenting nodular inflammatory and acute cutaneous lesions, or KD involving the skin (with histopathological features similar to those observed in cutaneous LE) cannot be completely ruled out. The clinical and the laboratory findings in our case are consistent with the co-presentation of KD and cutaneous LE with dermal and subcutaneous mucinosis; however, they may also be interpreted as KD with nonspecific skin lesions or a minor form of SLE with lymphadenitis and cutaneous LE.

In conclusion, our report illustrates that cutaneous LE without systemic involvement may be observed in patients with prior histiocytic necrotizing lymphadenitis. This association expands the spectrum of connective tissue diseases associated with KD. Taking into account the well-recognized association of KD and SLE, and that a percentage of cutaneous LE evolves to SLE, continuous monitoring is recommended in patients showing such association.

REFERENCES