□ Case Report □

A case of Kikuchi's disease with skin involvement

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Histiocytic necrotizing lymphadenitis, which is also commonly referred to as Kikuchi's disease (KD), is a self-limiting disease of unknown etiology. It affects individuals of all ages, although it is usually seen in young women. However, only a few descriptions of this disease are available in the pediatric literature. KD is clinically characterized by cervical lymphadenopathy, high fever, myalgia, neutropenia and, rarely, cutaneous eruptions. Cutaneous manifestations have been reported in 16-40 percent of KD cases. The specific skin changes occurring in cases of KD have yet to be completely characterized. In most of the reported cases thus far, the lesions have been located on the face and upper extremities. In this report, we describe a case of pediatric Kikuchi's disease, occurring in a 9-year-old boy. The boy exhibited transient erythematous maculopapular skin lesions over the entirety of his body, including his lower extremities. **(Korean J Pediatr 2006;49:103-106)**

Key Words : Histiocytic necrotizing lymphadenitis, Kikuchi's disease, Erythematous maculopapular skin lesion

Introduction

Kikuchi's disease (KD), also known as histiocytic necrotizing lymphadenitis, was initially described by both Kikuchi[1] and Fujimoto et al.[2] independently, in 1972. KD is normally a benign, self-limiting disease, of unknown etiology. KD has been reported to occur preferentially (3-4 : 1 ratio) in young women under the age of 30, and is seldom reported to occur in children[3]. KD is clinically characterized by an acute onset, which involves fever and cervical lymphadenopathy[4]. Less frequently, patients exhibit generalized lymphadenopathy, weight loss, night sweats, nausea, vomiting, diarrhea, and skin rashes[3, 5]. Cutaneous involvement, which was first reported by Kuo[5] in 1990, has been reported in 16-40% of KD cases. This cutaneous involvement is, however, of a nonspecific nature. Most cutaneous lesions tend to manifest as erythematous macules, papules, plaques, nodules, or ulcers, occurring on the upper part of the body, in locations including the trunk, the upper extremities, and the face[5-10]. Here, we present a case of pediatric Kikuchi's disease, with erythematous maculopapular skin lesions occurring over the entirety of the patient's body, including the lower extremities.

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Case Report

Patient : ○○ Kim, M/9 years

Chief complaint : Fever for 2 weeks, neck masses over the right posterior cervical area.

Present illness : A 9-year-old boy had been treated at another hospital, initially complaining of fever and cough. The boy was diagnosed with an upper respiratory infection and was treated with oral medications, which did not result in symptomatic relief. The fever persisted for 11 days. 3 days prior to the patient's first visit to our hospital, he developed neck masses over the right posterior cervical area. He was then referred to our institution.

Past and family history : The patient was born fullterm via transvaginal delivery, with a birth weight of 3.3 kg. He had no previous history of illness or hospitalization. There was no related family history.

Physical examination : On physical examination, the patient was febrile (38.5℃) and pale, with a blood pressure

of 100/60 mmHg, a pulse rate of 98/min, and a respiratory rate of 20/min. The patient weighed 27.7 kg ($25-50^{th}$ percentile). Posterior cervical lymph nodes, ranging in diameter from 1 cm to 3.5 cm, were palpable on the right side of the patient's neck. The lymph nodes were firm, tender, and discrete, with normal overlying skin. No lymphadenopathy in other locations was detected, nor was any hepatosplenomegaly. A systemic examination revealed no other abnormalities.

Laboratory data : Laboratory investigations revealed a hemoglobin (Hb) count of 11.5 g/dL, a total leukocyte count of 2.3×10^9/L, and the patient's platelet count was 204×10^9/L. The patient's erythrocyte sedimentation rate (ESR) was higher than normal (20 mm/h), and his C-reactive protein levels were also slightly elevated (13.1 mg/dL). Liver and renal function tests revealed no abnormalities, nor did urine analysis. Serum titers for Epstein-Barr virus and cytomegalovirus were both negative. Serum complement (C3, C4) levels were also normal. Serology for VDRL, RA factor,antinuclear antibody, and anti-double-stranded DNA antibodies were all negative.

Radiologic findings : Chest radiography revealed no abnormalities. On cervical computed tomography (CT), we noted multiple variably-sized and homogeneously-enhanced lymph node enlargements in the posterior cervical triangle.

Histopathologic findings : A cervical lymph node biopsy specimen revealed necrotic foci surrounded by a heterogenous mixture of activated lymphoid cells, histiocytes, and small lymphocytes, intermingled with abundant karyorrhectic debris (Fig. 1).

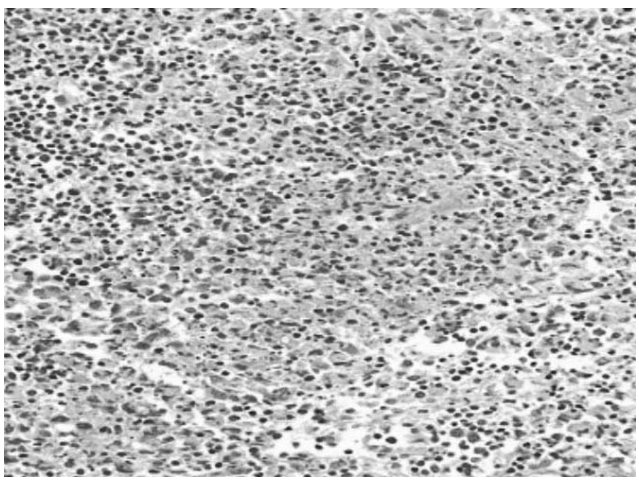

Fig. 1. The necrotic area evidences a heterogenous mixture of activated lymphoid cells, histiocytes, and small lymphocytes intermingled with abundant karyorrhectic debris (H&E, ×200).

Progress and treatment : After admission to our hospital, the patient received intravenous antibiotic therapy for 7 days. This, however, did not result in symptomatic relief. On the 9th day of admission, the patient's fever subsided. On the 15th day of admission, he manifested an erythematous maculopapular rash on his face, trunk, and upper and lower extremities (Fig. 2A, 2B). This rash was reminiscent of that observed in association with drug eruptions or rubella. However, the patient had no drug history, and the antibody titers against rubella were negative. After 4 weeks of conservative treatment, the patient's skin lesions

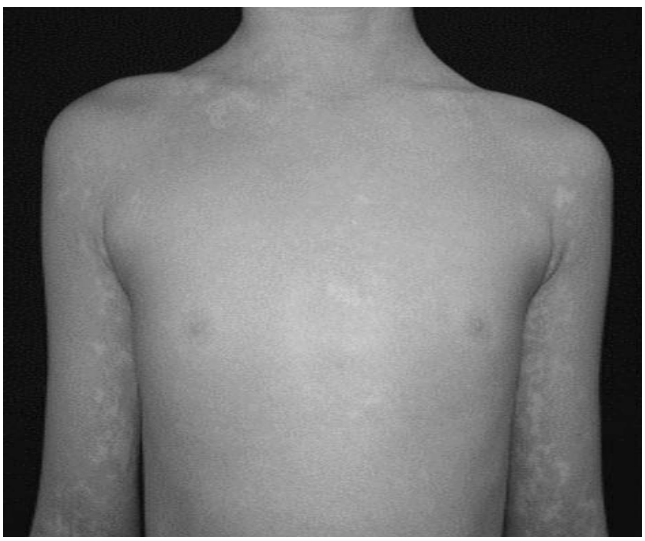

Fig. 2A. Multiple, variably-sized erythematous maculopapular lesions on the trunk & upper extremities.

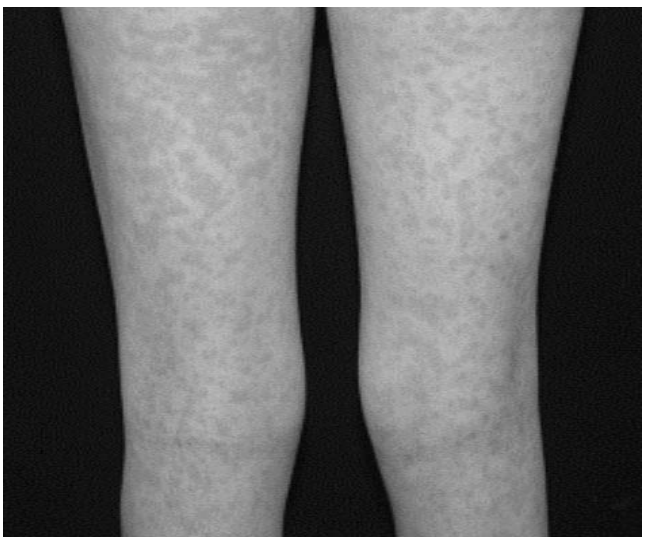

Fig. 2B. Numerous erythematous macules and papules on the lower extremities.

disappeared, and the cervical lymph nodes decreased in size.

Discussion

Kikuchi's disease (KD), also commonly referred to as histiocytic necrotizing lymphadenitis, was independently described by two researchers in 1972 : Kikuchi[1] and Fujimoto et al.[2], both of whom were from Japan. Kikuchi[1] and Fujimoto et al.[2] also both correctly described KD as a benign, self-limiting disease. KD appears to occur preferentially in Asians, particularly in Far East nations, including Korea[11]. In Korea, Koh et al.[6] reported 24 cases of KD in 1983, and Song et al.[12] reported the first case of a pediatric KD patient in 1990.

The cause of KD is unknown. Several infectious agents have been suggested, but none have been confirmed. The histologic and immunologic findings together with the typical clinical presentation suggest a hyperimmune reaction of immune cells to unidentified agents[11].

KD is clinically characterized by cervical lymphadenopathy and high fever. Less frequently, patients exhibit generalized lymphadenopathy, weight loss, nausea, vomiting, hepatosplenomegaly, night sweats, and neurological symptoms[1, 13]. Extranodal involvement occurs only rarely in KD, but includes skin lesions, arthritis, aseptic meningitis, and sometimes, unexpected death[11]. Cutaneous manifestations have been reported in 16.6-40% of KD patients[5]. These cutaneous manifestations are, however, non-specific and rather heterogeneous. They include facial erythema, eyelid edema, multiple erythematous papules and plaques on the scalp, face, chest, back, and upper extremities, leukocytoclastic vasculitis, and rashes, which may be urticarial, mobiliform, rubella-like, or polymorphic light eruption-like [5-10, 14]. In most of the reported cases, these lesions have been located on the face and the upper extremities. The skin eruptions manifested by our patient were different than those in other reported cases, as they were located not only on the face and upper extremities, but also on the lower extremities and trunk. Kuo[8] observed, however, that patients exhibiting skin lesions, particularly males, tend to simultaneously exhibit more severe clinical signs, including high fever and liver dysfunction, than do the patients who do not manifest skin lesions. It has been suggested that this disease is sometimes so active that apoptotic reactions occur not only in the lymph nodes, but also in the skin[14]. The heterogeneous nature of these skin lesions may correlate with the rate at which apoptotic activity is occurring in different cases of KD[16].

Currently, no specific laboratory tests are available for the diagnosis of KD, but leukopenia and elevated ESR constitute the most characteristic findings[3, 15]. A definitive diagnosis can be made only by the histopathological examination of lymph node biopsy tissues[8]. Histologically the lymph nodes exhibit focal, well-circumscribed, paracortical, necrotic foci, surrounded by histiocytes, immunoblasts, and plasmacytoid monocytes, and an absence of neutrophils[13]. Recently, there have been reports to the effect that, when skin lesions are a component of the presentation of KD, a skin biopsy alone can be used to diagnose the disease, obviating the necessity for an invasive lymph node biopsy[16]. In general, the histopathological findings of positive KD skin biopsies constitute a mirror image of biopsied lymph nodes from KD patients[14, 16]. In this case, as the skin lesions appeared after KD had already been confirmed via lymph node biopsy, we did not see any need to conduct a skin biopsy.

This disease is often misdiagnosed as systemic lupus erythematosus (SLE) or lymphoma[5, 9]. However, with careful physical examination and identification of the characteristic histiocytes and abundant karyorrhectic debris, rather than malignant lymphoma cells, KD can be distinguished from lymphoma. It is, admittedly, difficult to differentiate between KD and SLE, as both diseases are associated with similar clinical features. There are, however, certain differences. Whereas the lymph node involvement in KD is focal, it tends to be more extensive in SLE. The presence of hematoxylin bodies, abundant plasma cells, and true vasculitis outside the areas of necrosis indicates SLE rather than KD[7]. Previous literature regarding KD has frequently addressed the association between KD and SLE, and the reported rate was 1.3% to 7% in the general population[17]. In our case, we diagnosed the case patient with KD, due both to the normal laboratory findings, and the lack of any other systemic signs or symptoms. As expected, the skin lesions exhibited by our patient gradually resolved within 3 weeks.

In general, most incidences of KD require no specific treatment, and spontaneously resolve without any treatment in 2-3 months, although the condition (and symptoms) can sometimes recur[8]. In the few cases of KD in which oral steroids or antibiotics have been administered as a thera-

peutic modality, no differences in the course of the disease were noted[18]. Cutaneous eruptions in cases of KD also tend to spontaneously resolve within a few weeks or months, and the course of this symptom is similar to that of the lymphadenopathy[7].

In conclusion, physicians should remain alert to the possibility of KD when a patient is admitted with complaints of developing neck lymphadenopathy. In addition, certain skin features, such as the transient erythematous maculopapular lesions evidenced by our patient, should be considered as possible cutaneous manifestations of KD.

한 글 요 약

일과성의 홍반성 피부병변을 동반한 소아 Kikuchi병 1례

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유 영 · 이광철 · 손창성

Kikuchi병은 주로 젊은 여성에서 호발하고 소아에서는 비교적 드문 질환으로 원인 및 발생기전은 자세히 알려진 바 없으나 특별한 치료 없이도 수개월 이내에 자연적으로 회복되는 양성질환이다. 진단은 침범된 림프절의 특징적인 병리조직학적 소견을 확인하면 가능하다. 대부분의 환자에서 임상증상으로 림프절 비대와, 발열이 나타나고 피부증상은 16-40%에서 동반되며 주로 안면부, 상지, 상부 체간에 발생하고 대부분 작은 반점, 구진, 드물게 판과 결절 형태로 나타난다. 국내에서는 1983년 아급성 괴사성 임파선염이라는 이름으로 처음 언급한 이래 드물지 않게 보고되어왔으나 기존의 보고들은 피부증상을 동반하지 않거나 얼굴과 상지에 국한된 피부병변을 가진 증례 보고가 대부분이었다. 저자들은 지속적인 발열과 우측 경부 림프절 비대를 주소로 내원한 9세 남아에서 림프절의 조직검사결과 Kikuchi병을 진단할 수 있었고 이후 하지를 포함한 전신에 반점과 구진형태의 홍반성 병변이 발생한 Kikuchi병 1례를 경험하였기에 문헌고찰과 함께 보고하는 바이다.

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