Case Report

Juvenile Systemic Sclerosis/discoid Lupus Erythematosus Overlap Syndrome: A Case Report

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Abstact:

Juvenile systemic sclerosis is rare and the association of systemic sclerosis with discoid lupus erythematosus is uncommon. To date, no juvenile systemic sclerosis with discoid lupus erythematosus has been reported. We described a case of 15-year-old girl diagnosed as juvenile diffuse systemic sclerosis/discoid lupus erythematosus overlap syndrome with initial presentation of Raynaud's phenomenon, digital pitted scar, and skin sclerosis. She developed multiple atrophic scars on her both dorsum of hands and wrists two years later. Skin histopathology showed vacuolar degeneration of basal cell layer, superficial and deep perivascular lymphoplasmacytic infiltration, together with periadnexal inflammation. In addition, sclerosis of collagen is also identified. Direct immunofluorescence revealed C3, IgA, IgG, and IgM deposition along dermal-epidermal junction in granular pattern. Antinuclear antibodies and anti topoisomerase-I antibody were positive, while anti-double-stranded DNA, anti-U1RNP were negative. The patient fulfills the criteria for juvenile systemic sclerosis, while histopathology and direct immunofluorescence revealed finding consistent with discoid lupus erythematosus. Chest radiography and transthoracic echocardiogram were normal. The treatment was started with antimalarials, antifibrotic agents, calcium channel blocker, antiplatelet and topical corticosteroid. There was improvement in skin sclerosis and Raynaud's phenomenon during 2-year follow up.

Keywords: ● *Overlap syndrome* ● *Juvenile systemic sclerosis* ● *Discoid lupus erythematosus*

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รายงานผู้ป่วย

ผู้ป่วยโรคหนังแข็งเกิดร่วมกับรอยโรคลูปัสที่ผิวหนังชนิดเรื้อรังในผู้ป่วยเด็ก

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บทคัดย่อ

รายงานผู้ป่วยโรคหนังแข็งเกิดร่วมกับรอยโรคลูปัสที่ผิวหนังชนิดเรื้อรังในผู้ป่วยเด็ก โรคหนังแข็งในเด็กเป็นโรคที่พบได้น้อย และการเกิดขึ้นร่วมกับโรคลูปัสที่ผิวหนังชนิดเรื้อรังนั้นมีโอกาสขึ้นเกิดน้อยมาก ในปัจจุบันยังไม่มีรายงานการเกิดโรคหนังแข็งร่วมกับรอยโรคลูปัสที่ผิวหนังชนิดเรื้อรังในผู้ป่วยเด็ก รายงานฉบับนี้เป็นการนำเสนอผู้ป่วยเด็กหญิงอายุ 15 ปี ได้รับการวินิจฉัยเป็นโรคหนังแข็งร่วมกับโรคลูปัสที่ผิวหนังชนิดเรื้อรัง ผู้ป่วยมาด้วยอาการผิวหนังแข็งทั่วตัวร่วมกับปลายมือปลายเท้าซีดเย็น และแผลที่ปลายนิ้วมือสองปีถัดมาผู้ป่วยมีผื่นผิวหนังขึ้นเพิ่มที่หลังมือและข้อมือหลายรอยโรค ลักษณะทางพยาธิวิทยาและอิมมูโนพยาธิวิทยาพบว่าเข้าได้กับรอยโรคลูปัสที่ผิวหนังชนิดเรื้อรัง ได้ทำการส่งตรวจเลือดพบ antinuclear antibodies และ anti topoisomerase-I ให้ผลบวก ในขณะที่ anti- double-stranded DNA และ anti-U1RNP ให้ผลลบ ผู้ป่วยรายนี้จึงได้รับการวินิจฉัยว่าเป็นโรคหนังแข็งที่เกิดร่วมกับโรคลูปัสที่ผิวหนังชนิดเรื้อรังในผู้ป่วยเด็ก การตรวจภาพถ่ายรังสีทรวงอกและตรวจหัวใจด้วยคลื่นความถี่สูงอยู่ในเกณฑ์ปกติ หลังได้รับการรักษาด้วยกลุ่มยาต้านมาลาเรีย ยาลดการแข็งตัวของผิวหนัง ยาลดความดันโลหิตกลุ่มปิดกั้นแคลเซียม ยาต้านเกร็ดเลือด และยาทากลุ่มคอร์ติโคสเตียรอยด์ พบว่าอาการหนังแข็งและอาการมือซีดเย็นดีขึ้นในช่วงระยะเวลา 2 ปีที่มาติดตามการรักษา

คำสำคัญ: ● *โรคหนังแข็ง* ● *โรคหนังแข็งในเด็ก* ● *รอยโรคลูปัสที่ผิวหนังชนิดเรื้อรัง*

เวชสารแพทย์ทหารบก 2561;71:279-301.

Introduction

A 15-year-old girl first visited Institute of Dermatology, Bangkok, in February 2016. She had noticed skin sclerosis on her fingers, arms, and upper back with Raynaud phenomenon since the age of 14. She developed multiple atrophic scars on her both dorsum of hands and wrist from May 2018. She had no history of fever, arthralgia, or general fatigue. Physical examination showed swelling and stiffness of the fingers, forearms, legs, and abdomen (Figure 1). In addition, erythematous atrophic plaques with scaling distributed bilaterally on both dorsum of hands and both wrists.

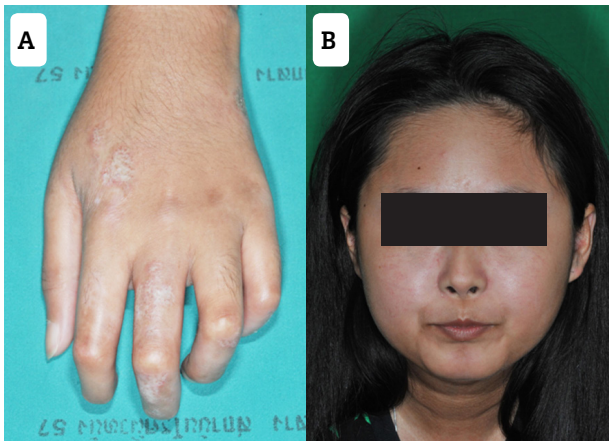

Figure 1 A) Erythematous atrophic plaques with scaling distributed on left dorsum of hands and fingers, **B)** skin sclerosis on face with microstomia

She also had diffuse hypopigmentation on her abdomen, hands, forearms, and legs. Multiple digital pitting scars, and microstomia were also observed. There were calcifications on both elbows. A biopsy specimen from erythematous atrophic plaque on left wrist revealed vacuolar degeneration of basal cell layer, hyperkeratosis, superficial and deep perivascular lymphoplasmacytic infiltration, together with periadnexal inflammation. In addition, sclerosis of collagen is also identified (Figure 2). Immunofluorescence study of erythematous atrophic plaque on the same site revealed C3, IgA, IgG, and IgM deposition along dermal-epidermal junction in granular pattern. Antinuclear antibodies (ANA) were positive (> 1:2560 homogeneous type), anti-topoisomerase I antibody (anti-Scl-70) was positive, while anti-double-stranded DNA, anti-U1RNP were negative. Chest radiography and transthoracic echocardiogram were normal. Blood tests revealed normal complete blood count, and blood chemistry. Urine examination showed no proteinuria, hematuria or cellular cast. These finding led to the diagnosis of discoid lupus erythematosus and juvenile systemic sclerosis.

The treatment was started with antimalarials, antifibrotic agents, calcium channel blocker, antiplatelet

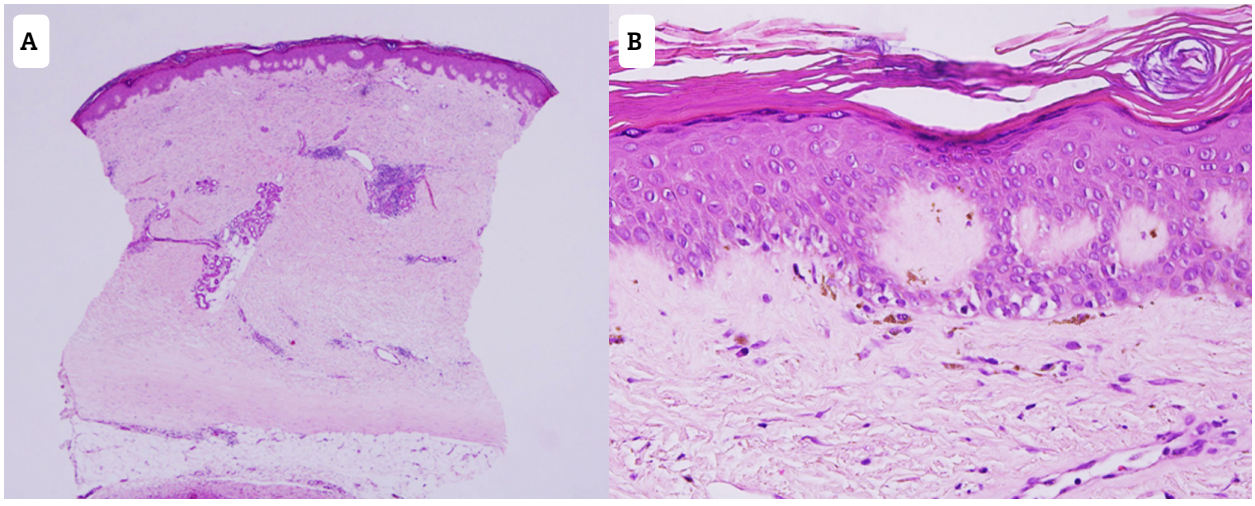

Figure 2 Histopathology shows vacuolar degeneration of basal cell layer, hyperkeratosis, superficial and deep perivascular lymphoplasmacytic infiltration, with periadnexal inflammation and sclerosis of collagen.

and topical steroid. During 2-year follow-up period, her skin sclerosis has improved.

Discussion

Overlapping systemic sclerosis and discoid lupus erythematosus is a rare disease. In a case series of 118 systemic sclerosis patients who had additional autoimmune diseases, only one patient (0.8%) has coexistence of discoid lupus erythematosus[1]. To our knowledge, only two juvenile systemic sclerosis/systemic lupus erythematosus overlap cases have been reported till now[2,3]. However, there is no reported case of juvenile systemic sclerosis/discoid lupus erythematosus overlap. A case series of 20 adult Japanese systemic sclerosis/discoid lupus erythematosus overlap cases has been reviewed. Mean age of patients was 48.8 years and four times more common in female patients. The DLE followed scleroderma in 10 cases (50%). The localized type of scleroderma was the most frequent type (60%), DLE was most often the localized type (65%). The most frequent areas involved were the face, followed by the head, back, and limbs. ANA was found in 18 patients (80%). Anti topoisomerase-I antibody was found in 12 patients (60%). In contrast, anti-centromere antibody was detected in one patient and anti-RNP antibody was observed in nine patients[4]. Another six case series of systemic sclerosis/discoid lupus erythematosus overlap from Japan showed that the mean age of onset of DLE was 40.2 years preceded systemic sclerosis in all cases. Three patients had diffuse scleroderma. Locations of DLE were in front of the auricle, back, and forehead. Although, chilblain lupus-type DLE was observed in one case. Three patients had both anti topoisomerase-I and anti RNP antibodies. Lung fibrosis was found in three patients and esophageal dysfunction in five patients[5].

Juvenile systemic sclerosis is a rare disease. A study from the United Kingdom reported an annual incidence rate of 0.27 per million children under the age of 16 years. Mean age of onset is 8.1 to 11 years[6,7]. There are two types of scleroderma, localized scleroderma and systemic sclerosis, with localized scleroderma ten times more common than systemic sclerosis[6].

For systemic sclerosis, isolated Raynaud's phenomenon is the frequent presenting symptom. Cutaneous changes are preceding with edema, followed by induration and atrophy. During the sclerotic phase, the skin becomes waxy and shiny with areas of hypo- or hyperpigmentation. Telangiectasia is uncommon in children. Nail fold capillary abnormalities may show capillary dropout, tortuous dilated loops, and distorted capillary architecture. Digital pitting, ulceration and gangrene, occur as a result of a distal artery ischemic event. Subcutaneous calcification, especially over the elbows, MCP joints and knees can be found. Arthritis and myositis may occur in up to 30% of children. The esophagus is often involved but usually asymptomatic. Cardiac fibrosis may lead to conduction defects, arrhythmias, and impaired ventricular function. Cardiac involvement is one of the major prognostic factors in juvenile systemic sclerosis as the main cause of death, and pericarditis was the major predictor of mortality. Unlike adults, renal and pulmonary involvements are rarely reported[7].

Compared to adults, juvenile systemic sclerosis has overall better outcome. Children show a significantly less frequent internal organ involvements. Overlaps were significantly more frequent among the juvenile systemic sclerosis than in adult[6,8]. The most frequent overlap juvenile systemic sclerosis is idiopathic inflammatory myositis (IIM) and inflammatory arthritis[8,9].

Provisional classification criteria for juvenile systemic sclerosis was developed by Pediatric Rheumatology European Society and American College of Rheumatology in 2007 (PRES/ACR/EULAR 2007), which require all subjects to have skin thickening proximal to the

metacarpal phalangeal joints, and at least two additional (minor) criteria. Minor criteria include several types of organ involvement (e.g. pulmonary, cardiac, gastrointestinal, renal, vascular, musculoskeletal, neurological, and serological involvement).

ANA usually present is 80-97% of juvenile systemic sclerosis, although anti-topoisomerase I antibody was found 20-40% of patients[6].

Treatment of juvenile systemic sclerosis is based on organs affected, with medications based on adult studies including vasodilators, antiplatelet and immunosuppressive drugs. Nonpharmacologic management is also important and includes physical therapy and cold avoidance[6].

We present our case due to the rare coexistence of systemic scleroderma with discoid lupus erythematosus in children. In our report, the patient fulfilled the criteria of PRES/ACR/EULAR 2007 provisional classification criteria for juvenile systemic sclerosis and histopathologically compatible with discoid lupus erythematous, but there were no other findings suggestive of SLE. The patient has a good response to antimalarials, topical corticosteroids, antifibrotic agents, calcium channel blocker and antiplatelet therapy.

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