

A Rare Case of Pediatric Systemic Lupus Erythematosus in Saudi Arabia

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ABSTRACT

Pediatric-onset systemic lupus erythematosus (SLE) is a rare disease. The skin is involved in up to 85% of the cases and may be the only organ involved in cutaneous lupus erythematosus. A two years and eleven months old boy presented with a one-day history of vomiting and diarrhea five to six times per day. His condition began at the age of 7 months with bilateral wrist joint swelling and pain with interphalangeal Joint swelling with ankle swelling and pain. This was associated with fever, macular rash. He was treated with steroids. Then with a recurrent history of fever, arthritis and the rash, Methotrexate and multi injections of tocilizumab for ten months were added. Then over this time, he developed recurrent otitis media and had recurrent mouth ulcers. His lab results showed inflammatory markers Anti-ds DNA were 23.7k/uL equivocal and ANA antibody is 12.1ng/mL which is positive. Brain MRI showed generalized atrophy with associated white matter changes. Findings could be related to the previous treatment or Periventricular leukomalacia or white matter diseases due to non-specific etiology. On discharge, he was afebrile for more than seven days, vitally stable, the rash

was improved, and mouth ulcers also improved with good oral intake. He tried to walk, and joint swelling had decreased with no tenderness. In conclusion, although, childhood-onset SLE is rare, it should be suggested by clinicians in a differential diagnosis in a child with the suggestive clinical presentations as it has a greater risk of systemic complications in children.

Keywords: Systemic Lupus Erythematosus, Children, Dermatology, Skin Biopsy, Histopathology.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a rheumatic disease characterized by autoantibodies directed against self-antigens, immune complex formation, and immune dysregulation, resulting in damage to essentially any organ.¹ The natural history of SLE is unpredictable; patients may present with many years of symptoms or with acute, life-threatening disease.²

Pediatric-onset SLE is a rare disease with an incidence of 0.3-0.9 per 100,000 children.³ Prevalence rates are higher in females than in males. A female-to-male ratio of approximately 4:1 occurs before puberty.³

Disease onset has been reported as early as the first year of life. However, SLE remains uncommon in children younger than age 8 years.⁴

The skin is involved in up to 85% of systemic lupus erythematosus (SLE) cases and may be the only organ involved in cutaneous lupus erythematosus (CLE).⁵ Three major subtypes were identified: chronic cutaneous LE, subacute cutaneous LE, and systemic or acute cutaneous LE. Besides these three subtypes, other less frequent clinical varieties may occur.¹ The diagnosis of the cutaneous manifestations of LE is based on

clinical, histopathology, and immunohistology of skin lesions. Also, serum autoantibodies are considered immunologic markers for distinct clinical types of the illness.⁶

CASE REPORT

A two years and eleven months old boy presented to the emergency department (ER) with a one-day history of vomiting of whatever he ate and diarrhea five to six times per day. His condition actually started at the age of 7 months with bilateral wrist joint swelling and pain with interphalangeal Joint swelling with ankle swelling and pain. This was associated with fever, macular rash. The parents sought medical advice at another hospital and at the age of 9 months, and he was labeled as systemic juvenile idiopathic arthritis (SJIA). He was treated with steroids. Then with a recurrent history of fever, arthritis and the rash, methotrexate and multi injections of tocilizumab for ten months were added. Then over this time, he developed recurrent otitis media and had recurrent mouth ulcers. He had problems with his feet with regression of his milestones with an inability to walk and talk. His mother stopped methotrexate because of increasing mouth ulcers.

On physical examination, he looked ill, febrile with a temperature of 39 degrees C, pale, not in distress. Maintaining saturation on room air with a respiratory rate of 28 breaths per minute. His pulse was 178 beats per minute (tachycardia). He was mildly dehydrated. His blood pressure was 124/64 mmHg. Skin had marked red rash on the face and the neck. He had hair loss (alopecia areata). ENT examination revealed multiple mouth ulcers, foul smelling, with cracked lips. He had a crusted lesion behind the ear, oozing blood and ulcerated. Chest, abdominal and cardiovascular examinations were normal. He had weak hip girdle muscle with flexors 4+ all over and increased plantar reflex. He had hypertonia, especially in the lower limbs. There was no joint swelling, but there was tenderness with decreased range of movement.

His lab results showed inflammatory markers ESR 89 mm/hr, CRP 27.7 mg/L, Hb was low at 9.2 g/dL, with low MCV and MCH. WBC was 9.2 k/uL. Neutrophils 4.5 x 10⁹/L and Leukocytes 8.2 mls, platelets 263 x 10⁹/L. Anti-ds DNA is 23.7 k/uL equivocal, and ANA antibody is 12.1 ng/mL which is positive, normal complement C3 and C4. Rheumatoid factor was <10 which is negative. Virus serology results were all negative. Immunology work-up, including

the IgG level?. Brain MRI showed generalized atrophy with associated white matter changes. Findings could be related to the previous treatment or PVL? or white matter diseases due to non-specific etiology.

During his hospitalization, he received IV fluids for hydration. He continued steroids and was seen by multiple specialties. Our impression was that the rash is related to SLE diagnosis. Also, seen by Ophthalmologists and uveitis was ruled out and his examination was normal. The Immunology team saw him, and they requested immunology work-up. As he had been on steroids for a long time, it could interfere with the immunology moderator. ENT specialists saw him and had a mild conductive hearing loss due to chronic suppurative otitis media. He was reviewed by the neurology team, and he had upper and lower limb weakness and trunk muscle mostly related to prolonged steroid use and findings of upper motor neuron lesions. They requested a brain MRI. The findings of the brain MRI from the Neurology point of view showed atrophy is secondary to the prolonged methotrexate use. The patient was treated with antibiotics, Amoxicillin, for the otitis media for a total of seven days. The possibility of periodic fever syndrome raised and lab works for hyper IgD syndrome sent.



Figure 1: Multiple hyperpigmented plaques with central hypopigmentation and atrophy. (By Luai Mohammed Assaedi)



Figure 2: Discoid rash on the chin. (By Luai Mohammed Assaedi)

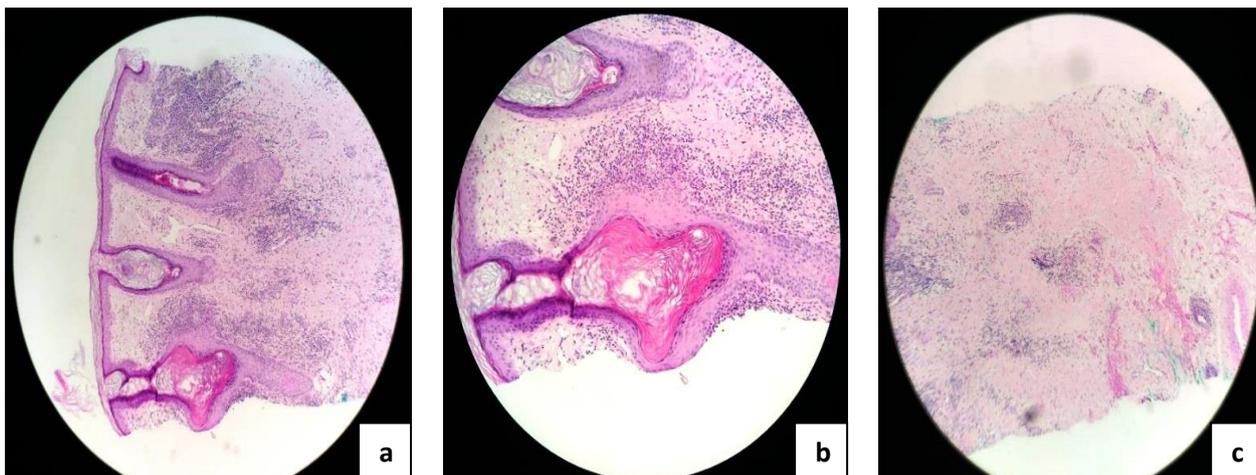


Figure 3(a-c): Skin biopsy showed epidermal atrophy with vacuolar interface degeneration of the basal layer and apoptotic keratinocytes. There are marked follicular plugging. The dermis showed characteristic perivascular and periadnexal lymphohistiocytic infiltration. (By Luai Mohammed Assaedi)

On discharge, he was afebrile for more than seven days, vitally stable, the rash was improved, and mouth ulcers also improved with proper oral intake. He tried to walk, and joint swelling had decreased with no tenderness. He was on physiotherapy with a waddling gait. He was clinically stable. He had been discharged on Prednisolone 5mgs am and 4mgs pm with tapering on the plan. He was given a follow-up appointment in one month with Paediatric Rheumatology and Paediatric Immunology. His final diagnosis was Hyper Immunoglobulin D syndrome and query SLE. He was admitted again for 18 days and was diagnosed to have systemic lupus erythematosus based on the skin findings and laboratory marker. He was presented to our emergency room with two weeks history of progressive erythematous rash all over the face, neck, and upper chest with bleeding and crusting, as well as mouth ulcer, in association with the two-day history of decreased oral intake and activity. There was no history of fever, abnormal movement, change in the level of consciousness, joint swelling or decreased range of joint movement.

He was diagnosed as having hyper IgD syndrome which was ruled out based on the normal immunological workup (possibility of prolonged 'effect of steroid) was raised especially in the presence of truncal weakness in addition to the questionable effect of Methotrexate on the white matter changes that appeared in MRI brain which showed generalized brain atrophy). On presentation to our ER, the patient was vitally stable, afebrile. He was conscious, alert, mildly dehydrated, not in distress. Erythematous rashes were distributed all over the face involving the nasolabial fold, forehead, chin, ears, neck, and chest. Swelling of the tongue was noticed in addition to whitish discharge on the mouth on the hard palate. ENT examination showed normal, clear bilateral tympanic membrane. Chest, abdomen, and heart examinations were normal. Rectal examination: Showed redness of the skin and fissure at 1, 6, and 11 o'clock. There was no bleeding or discharge. The neurological exam showed normal cranial nerve examination, tone, reflexes, and power. Musculoskeletal examination revealed no joint swelling, no wound, no redness, and no decreased range of motion. Skin biopsy was taken and examined histopathologically (figures 3)

On the second admission, he was started on Methylprednisolone, initially 2 mg/kg/day, but with two episodes of increased blood pressure, the Methylprednisolone was tapered down slowly until the patient was controlled on 1 mg/kg/day (5 mg bid). Plaquenil was added 100 mg every other day. In addition to topical ointment and cream including Nystatin, Lidocaine hydrochloride, Fusidic acid, mouthwash and petroleum white, and sunscreen which was advisable to protect the skin upon discharge from the hospital. During admission, blood culture was taken and showed *Staphylococcus Aureus*. The wound culture showed the same organism. The infectious team was involved, and they preferred to start the patient on cloxacillin after repeating the culture, which showed gram-positive cocci in the wound. The gram-positive cocci turned to be coagulase-negative *Staphylococcus Aureus*. The patient was continued on Cloxacillin for around ten days. During hospitalization, he showed no spike of temperature, no deterioration in the clinical parameters. He was evaluated by the infectious team, and they planned the patient to continue on oral Cephalexin for five more days. The patient, having stable vitals and clinical measurements, no spike of temperature, good oral intake improvement of the skin lesions, and with control of flare-up

of the disease, he was planned for discharge. On second discharge, the patient was in stable condition. Discharge plan consisted of Prednisolone 5 mg tid, Plaquenil 100 mg every other day and Sunscreen topical ointment as advised by dermatology team. He was asked to be evaluated in the rheumatology clinic, infectious disease clinic, and dermatology clinic two weeks from discharge. He was followed up till he reached 6 years. He developed new skin lesion over the face. By examination, there was multiple hyperpigmented plaques with central hypopigmentation and atrophy (figures 1 and 2)

Skin biopsy from this lesion showed epidermal atrophy with vacuolar interface degeneration of the basal layer and apoptotic keratinocytes. There are marked follicular plugging. The dermis showed characteristic perivascular and periadnexal lymphohistiocytic infiltration. Positive mucin deposition in the dermis. Which is consistent with Discoid lupus erythematosus (figures 3).

DISCUSSION

Early diagnosis and careful treatment of patients with symptoms of SLE have improved the prognosis in what was once perceived as an often-fatal disease. Pediatric-onset systemic lupus erythematosus is uncommon before 10 years and affects females predominantly than males with the peak age of onset being 12 years.^{7,8}

Contrary to that, the present case is a male aged 3 years. The definite etiology of SLE is unknown, but there is a suggestion of an interaction between many factors (immune complexes, autoantibodies, genetic, drugs and environmental factors) could play a significant role in causing inflammation and eventually damage to the organs and systems of the body.⁹

Pediatric-onset SLE patients have a less favorable prognosis as compared with adult-onset type, resulting in almost double higher mortality.¹⁰ Therefore, early diagnosis and prompt treatment are warranted for these cases.

The clinical presentation of pediatric-onset SLE is frequently more severe than adult-onset SLE with multiple organ involvements, particularly the kidney and central nervous system.¹¹ However, the present case was presented with mainly cutaneous manifestations with no renal or central nervous system involvement. Janwityanujit et al.¹² and Font et al.¹³ suggested that cutaneous changes particularly, the malar rash is more common in pediatric patients than adults. The present case confirmed this suggestion where the macular rash was a prominent figure in the present case. The same finding also has been reported in a case aged 7 years from India.¹⁴ Neuropsychiatric symptoms and signs have been reported in a considerable percentage of children with SLE (29-44%).¹⁵ However, in the present case, neurological or psychiatric findings were not present.

The diagnosis of SLE can be confirmed by histopathology and serology. Histopathological examination of a skin biopsy showed features specific for SLE. Serology showed a high titer of ANA (positive) and high Anti-dsDNA. Anti-dsDNA antibodies are highly specific for SLE and are present in about 61-93% children with the active disease. However, they may be absent in about 40% children with active lupus.¹⁶ Immunofluorescence study was not performed due to its nonavailability in our institution. The disease severity varies from mild to severe and requires long-term and often aggressive treatment.

To conclude, childhood-onset SLE is a challenging health problem both difficult to diagnose and to manage. Although it is rare, it should be suggested by clinicians in a differential diagnosis in a child with suggestive clinical as it has a greater risk of systemic complications in children. Also, children with SLE should be continually followed up, and appropriate therapy should be initiated as early as possible to minimize morbidity and mortality of the disease. Additionally, the family of the child with SLE must have a thorough understanding of the disease, its severity, the complications of the disease and its treatment.

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