

A case of Juvenile Systemic Lupus Erythematosus in a pre-pubertal child with atopic eczema

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Abstract

Juvenile Systemic Lupus Erythematosus (JSLE) is a subset of SLE, with onset before eighteen years of age and associated with increased mortality and morbidity. JSLE is a complex autoimmune disease with respect to its underlying genetics. It is characterised by the disruption of immune tolerance, resulting in cascade of immune responses including the Th2 response with production of interleukins (ILs) 4,5,10, as seen with allergic disorders. Along with this, polyclonal activation of B lymphocytes results in the production of autoantibodies, particularly of the IgG, IgM and antinuclear IgE autoantibodies. JSLE is frequently recognized in girls. The purpose of this case report is to share an uncommon presentation of JSLE in a 8-year-old boy who was diagnosed as a case of atopic eczema at the age of 8 months and later on, at the age of 4 years, he was presented with the case of full blown JSLE with early development of stroke within one year of diagnosis of JSLE.

Keywords: IgE therapy, Atopic dermatitis, Juvenile autoimmune connective tissue disease, Serum IgE, Neuropsychiatric.

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Introduction

Juvenile Systemic Lupus Erythematosus (JSLE) is a subset of SLE, with onset before 18 years of age and associated with increased mortality and morbidity. It accounts for 20% of all SLE patients.¹ The global prevalence of JSLE is 206,931 per 2,069,000,000 children less than 16 years of age. The highest number of cases are seen in Asia.² Atopic eczema is a chronic condition characterised by eczematous dermatitis, predominantly involving flexures in children and adults. It is mainly caused by serum immunoglobulin E reactivity and there are also chances of development of immunoglobulin E sensitivity against self-antigen.³ Here The case of a 8-year-old boy is reported who was a known case of atopic eczema but later on, he developed classical

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features of systemic lupus erythematosus with early onset of stroke.

Case Report

The reported patient was the first child born to a non-consanguineous couple; the mother's pregnancy was uneventful. According to the parents, the boy developed dry skin at the age of 8 months; predominantly involving the flexures. At that time his serum IgE levels were >12000 IU/ml when he was diagnosed as a case of atopic eczema. At the age of four years, he gradually developed pustular and maculopapular rashes involving the face and gradually spreading over both the upper limbs and back associated with oral ulcers for which he visited a teaching hospital (Liaquat National Hospital, Karachi). His labs depicted ANA ++ (homogeneous pattern) rheumatoid factor and positive RNP/anti-smith/anti-Scl-70, while, antiphospholipid and anti-dsDNA antibodies were negative (Table).

He was then diagnosed as a case of JSLE and was discharged on topical and systemic treatment. After one year of diagnosis, he was re-hospitalised with extensive rash and high-grade fever. During his admission period, he developed an episode of altered level of consciousness with left sided weakness and transient facial weakness. MRI brain showed subarachnoid haemorrhage, Magnetic Resonance Venography (MRV) displayed thrombosis in the proximal part of the right transverse sinus. His recovery was achieved with intravenous pulse therapy using 500 mg of injection methylprednisolone for 3 days. According to the parents, they tried to taper off his medicines (steroids and

Table: Investigations.

S. No	LAB	Patient value	Normal values
01	CBC	Hb 12.8 gm/dl TLC 8,000 / μ l Platelet 150,000/ μ l	14 to18 gm/dl 40000-11000/ μ l 150,000-450,000/ μ l
02	ESR	55mm in 1st hour	0 to 15 mm/hr
03	Antinuclear antibodies	++homogenously positive	
04	Antismooth muscle antibodies	negative	
05	Anti mitochondrial antibodies	negative	
06	Anti dsDNA antibodies	negative (1.82)	< 10 IU/mL
07	Rheumatoid factor	58.70	<15 IU/mL
08	SS-A/Ro antibodies	66,9U/ml positive	
09	SS-B/La antibodies	0.54 negative	
10	Sm antibodies	>40U/ml positive	
11	Scl-70 antibodies	>60U/ml positive	
12	RNP antibodies	>60U/ml positive	



Figure: Shows A). livedo reticularis. B). scarring of conchae. C, D). multiple erythematous scaly atrophic plaque of variable size and shape involving face and back.

azathioprine) as advised by a local medical practitioner which led to these symptoms. They also admitted to missing medication frequently.

The patient's disease activity was well-controlled on oral steroid therapy but tapering off steroids to less than 10 mg/day led to relapse and worsening of his symptoms. Being on steroids for a long time, he also had developed iatrogenic Cushing's syndrome followed by weight gain, truncal obesity, abdominal striae and stunted growth.

Family history for any autoimmune disease was not significant. He has two brothers both are alive and healthy.

On cutaneous examination there was multiple erythematous scaly atrophic plaque of variable size and shape involving the face and back (Figure 1.C&D). Figure 1A is showing a net like pattern of red-blue discoloration of the hand (Livedo Reticularis) Erythematous scaly plaques are seen involving the whole helix of the ears with scarring of both conchae (Figure 1B).

Physical examination revealed that he was below height for age/short stature with truncal obesity and moon faced; Temperature: 37.0°C; Heart rate: 85 beats per minute; Respiratory rate: 20 breaths per minute; Blood pressure: 110/70 mmHg and Body weight: 30 kg. He was limping on the left side while walking, decreasing left arm swing and slight deviation of angle of the mouth towards the right side. Whereas, cardiovascular, gastrointestinal and respiratory examinations were unremarkable. On follow up the child developed one flare, because he stopped taking medicine for which he was again counselled since then he has remained in remission.

Discussion

JSLE is a disease having a vast variety of presentations especially, when seen for the first time.

JSLE is a chronic autoimmune disease of children. Pre-pubertal onset (<7 years) of this disease is reported in 10.3% of the children, whereas, 57.4% present with peri-pubertal onset (8-13 years) and 32.3% are diagnosed during adolescent (14-18 years).³ JSLE affects females more than males. Approximately 44% patients of JSLE present with mucocutaneous involvement, 40% with neuropsychiatric disorders and 30% with constitutional symptoms. In the reported case, the 8-year-old child presented with an atopic eczema which progressed to full blown JSLE with early onset of subarachnoid haemorrhage within one year of clinical diagnosis. Common neuropsychiatric symptoms evidenced in decreasing order are headache, mood disorder, cognitive impairment, seizures, movement disorders and cerebrovascular accidents. Venous sinus thrombosis is a rare and fatal entity affecting 6% of the children (between 3-11 years of age).⁴

In the reported case, the patient was having early onset of subarachnoid haemorrhage diagnosed on MRI/CT scan brain. Only 30-40% of SLE patients are tested positive for APLA (anti-phospholipids antibodies)⁵ 19-89% and 10-62% of JSLE patients are tested positive for anti-cardiolipin antibodies and lupus anticoagulant respectively.⁶ In this case, APLA antibodies were negative. Vasculitis can be one of the cause of subarachnoid haemorrhage in this patient. The reported patient was initially presented with excessively dry skin, predominantly involving flexures and exceptionally high levels of serum Ig-E which skewed the diagnosis more towards atopic eczema. This association of atopic eczema with high level of serum Ig-E further delayed the diagnosis. Thrombosis in the right transverse sinus, ultimately lead to increased venous pressure resulting in subarachnoid haemorrhage in this patient despite of having negative APLA. Immune complex mediated endothelial injury is proposed to be the pathogenesis of cerebral venous sinus thrombosis in SLE.⁷

Moreover, presence of elevated total serum Ig-E levels demonstrate the pathogenic role of auto reactive Ig-E in SLE.⁸ A possible link between atopic dermatitis and JSLE is evident by the presence of auto reactive Ig-E, that activates basophils by binding to high affinity receptors FcεRI. Basophils will then release IL-3, IL-4 and IL-17 that increase survival and differentiation of plasma cells, which in return synthesizes immunoglobulins.

There is also a low affinity receptor CD23 located on mature B cells responsible for binding Ig-E. Soluble CD23 levels were found to be elevated in a range of autoimmune

diseases like SLE.^{9,10}

Conclusion

The presented case of a 8-year-old child concludes that it is important to do detailed testing of a patient who presents with skin lesions and excessive high levels of serum Ig-E. And to think on the lines of autoimmune disorders generally and JSLE specifically. As, elevated levels of serum Ig-E are related to auto reactivity and to the development of JSLE. Some Ig-E targeted therapies are under trials and include Omalizumab, ligelizumab, quilizumab for the treatment of JSLE. The steroids are the life-saving drugs that play a significant role in preventing complications. Therefore, detailed counselling of the parents regarding the importance of treatment and follow up visits to the doctor is crucial. Patients should be advised to never stop or miss a dose. Tapering off the medicines should only be done on the physician's recommendation.

Consent: Consent to publish the case report on the child for enhancement of science, was obtained from the parents.

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Author Contribution:

GA: Concept, design, drafting, final approval and accountable for all aspects of the work.

SJ: Concept, revision, final approval and accountable for all aspects of the work.

FZ: Data interpretation, revision, final approval and accountable for all aspects of the work.