



## CASE REPORT

# A Children's Tale: Unusual Presentation of Juvenile SLE

Naisar Dilip Nahar<sup>1\*</sup> and Prachi Naisar Nahar<sup>2</sup>

<sup>1</sup>Consultant Rheumatologist, Arham Rheumatology Center, Nashik, India

<sup>2</sup>Clinical Associate, Arham Rheumatology Center, Nashik, India

\*Corresponding author: Naisar Dilip Nahar, Consultant Rheumatologist, Arham Rheumatology Center, Nashik, India



## Abstract

Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disease with multiple manifestations resulting in inflammation & damage to several organs. We report a case of young boy presented to us with features of meningoencephalitis with multisystem involvement (phenotype-constitutional symptoms, neuropsychiatric involvement, mucocutaneous involvement, serositis, renal affection, hematological manifestations). Detailed clinical examination with laboratory & imaging studies clinched the diagnosis of paediatric SLE. Patient showed remarkable response to steroid & immunosuppressive therapy.

patient was conscious but irritable with no meningeal signs. Reflexes were normal with normal fundoscopic examination. Other systemic examination reveals decrease air entry at both lung bases with no added sound & rest systemic examination were unremarkable.

On lab evaluation his Hb: 7.8gm/dl, total count 2300/cumm, platelet count 130000/cumm. His ESR was 40 mm per hour (westergren's method) with normal CRP (turbidometry), normal biochemistry and normal electrolytes. Urine showed 3+ proteinuria with red blood cell cast. On imaging, CXR showed bilateral pleural effusion and 2D ECHO showed mild pericardial effusion. USG abdomen & pelvis showed moderate ascites. MRI brain was normal and lumbar puncture performed with normal cytochemical marker. CSF bacteriological culture was negative. PCR testing for EBV HZV in CSF was negative. Serum ammonia and lactate levels were normal. Blood & urine cultures were negative. On immunological evaluation ANA was positive (1:1280-Homogenous pattern), dsDNA was positive with low complement level (C3, C4). 24 hr urinary protein was 3.5gm per 24 hours. Bone marrow studies showed hypocellular marrow with no evidence of malignancy. Renal biopsy and extractable nuclear antigen (ENA profile) was not done.

## Introduction

Paediatric systemic lupus erythematosus (pSLE) is one of the most common systemic autoimmune connective tissue disorders in children [1]. It is a great mimicker. Aetiology is not known as yet and pathogenesis is very complex. pSLE is more aggressive than in adult. In the pediatric age group, SLE represents a special challenge. Here we present a case of young boy with fever, headache, rash, convulsion and constitutional symptoms.

## Case Report

A 16-year-old boy first child of non-consanguineous marriage presented with low to moderate grade fever since 8 days and 2 episode of generalized tonic-clonic convulsion. He also has non projectile vomiting and an erythematous non blanching maculopapular rash all over body since 8 days. There was no significant past or family history. On clinical examination patient was toxic but his vitals were stable. CNS examination showed

## Treatment

Initially meningoencephalitis was suspected and empiric treatment with broad spectrum antibiotics and antiviral given. As investigation results ruled out different infectious etiology, neuropsychiatric lupus was considered and immunosuppressive therapy in terms of

IV methylprednisolone (1000mg daily for 3 days) were given followed by oral steroids and monthly pulses of IV cyclophosphamide were started (total 6 pulses given). He was also started on hydroxychloroquine (as per his weight). There was dramatic clinical improvement after beginning of above therapy. Steroids were gradually tapered & Azathioprine was started for maintenance. Patient is following up regularly with us for past 2 years.

## Discussion

Paediatric systemic lupus erythematosus (pSLE) is a chronic multisystem autoimmune disease with remitting, relapsing course and onset of symptoms before age 18 years. It accounts for approximately 20% of all SLE [2]. This clinically heterogeneous disease is characterized by a B-cell mediated autoimmune process leads to variety of clinical manifestations with distinct spectrum of autoantibodies (ANA, dsDNA and antibodies against extractable nuclear antigens). The American college of rheumatology (ACR) classification criteria for adults with SLE is commonly applied to children with pSLE [3]. The incidence across the world varies between 0.3 to 0.9 per 100,000 per year [1]. Although the exact prevalence of pSLE in a developing country is not known. There is scarce epidemiological data from India. A study from Eastern part of India found that 3.9% of all children presenting to a paediatric rheumatology OPD had pSLE [4]. In one population study from north India, a point prevalence of pSLE is 3.2 per 100000 is observed [5]. It is more common in girls with the peak age of presentation around puberty [1] and in India, mean age at diagnosis is 12.1years [6]. Earlier age of onset also correlates with more severe disease [7]. Antiphospholipid antibodies are found more commonly in pSLE [7]. Clinical features were depicted in the following table 1 [8].

Renal involvement is more common in Indian scenario [9] and neuropsychiatric features are not as common as presenting feature in pSLE.

The neuropsychiatric lupus (NPSLE) involvement

seems to be more serious in children than in adults which may lead to permanent organ damage [10]. It may occur in earlier stages of the disease without manifestations in other organs. The pathogenic aetiology of NPSLE is likely multifactorial and may involve a non-inflammatory vasculopathy of the small vessels, non-thrombotic effects of CNS-specific auto-antibodies and inflammation caused by intrathecal production of proinflammatory cytokines [11]. Other autoantibody which may play a decisive role in neuropsychiatric SLE pathogenesis include antiphospholipid antibodies. The prevalence of anti-beta 2 glycoprotein I antibodies is higher in SLE patients with neuropsychiatric manifestation compared with those without. In the pathogenesis of diffuse neuropsychiatric symptoms also antineuronal antibodies and antibodies against ribosomal P-protein have been documented to play a role [12]. The classification of neuropsychiatric SLE in children and adolescents remains a challenge. The neuropsychiatric manifestations of lupus are classified in 19 different syndromes by the American College of Rheumatology [13]. According to the prospective study of Sibbitt, et al. [14], the most common manifestations NPSLE in the paediatric population are headache (72%), mood disorder (57%), cognitive dysfunction (55%), seizures (51%), acute confusional state (35%), peripheral nervous system dysfunction (15%), psychosis (12%) and stroke (12%).

Up to 65% of pSLE patients develop NPSLE at any time during the disease course, and up to 85% of these patients will develop NPSLE within the first 2 years from diagnosis [14]. Agarwal, et al. [6] studied 70 patients with JSLE from 1987 to 2006 & reported 21% patients had NPSLE symptoms.

A diagnosis of NPSLE in children is based on clinical assessment including comprehensive neurocognitive testing, inflammatory markers and neuroimaging & American college of rheumatology SLE criteria which may not be present in early part of the disease [15].

The differential diagnosis of SLE is broad, and includes infection, malignancy and other inflammatory disorders as in our case. The adolescent female who presents with a photosensitive malar rash, painless oral ulcer, polyarthritis and pleural effusions is not a diagnostic challenge. However, initial symptoms may be vague which may poses a problem for early diagnosis to paediatrician. It includes an older child or adolescent with any combination of persistent fever, fatigue, anemia, cytopenia, lymphadenopathy, other rash, alopecia, raynaud's phenomenon, unexplained weight loss, headaches and other neuropsychiatric symptoms, or unexplained microscopic hematuria or proteinuria. We should consider more broad differential diagnoses in a patient presenting with systemic features.

The therapeutic approach in NPSLE includes symptomatic and immunosuppressive therapies.

**Table 1:** Common clinical features of pSLE.

TABLE1: COMMON CLINICAL FEATURES OF pSLE <sup>8</sup>		
	Clinical Feature	Prevalence
1.	Fever	37-100%
2.	Lymphadenopathy	13-45%
3.	Weight loss	21-32%
4.	Mucocutaneous	60-90%
5.	Musculoskeletal	60-90%
6.	Nephritis	48-78%
7.	Neuropsychiatric	15-95%
8.	Gastrointestinal	24-40%
9.	Hematologic	50-100%
10.	Cardiovascular	25-60%
11.	Pulmonary	18-81%

The first-line immunosuppressive treatment includes corticosteroids. Although a steroid has its own side effects profile in these age group. There are no published NPSLE treatment trials in paediatric population, but in some studies with NPSLE adult patients [16] cyclophosphamide appears as a good therapeutic option for induction therapy. Induction therapy with Mycophenolate mofetil was found to be safe, well tolerated & effective in small cohort of renal and non-renal pSLE patients [3].

Azathioprine has been used as an effective maintenance immunosuppressive agent, with good outcomes in some published cases [17]. Although there are some refractory cases to immunosuppressive treatment. Other therapies in SLE patients include Rituximab (anti CD 20 antibody) & Belimumab (B lymphocyte stimulator specific inhibitor) with potential benefits but needs large randomized trials. Adjuvant therapies include sunscreen lotions (SPF > 30), calcium and vitamin D, regular aerobic exercise, education. pSLE is associated with higher rate of morbidity and lower rate of remission [18]. Treatment must be tailored according to disease activity & severity, clinical phenotype & number of flares. Overall prognosis with pSLE has markedly improved over past few decades. However, therapy remains challenging due to an unpredictable disease course, long term therapy and compliance.

## Conclusion

SLE is commonly seen in young female but rarely it can also be seen in male children. In this clinical report, we describe a male child with primary central nervous system involvement. However, these clinical manifestations usually do not occur as the initial clinical presentation of the disease, leading to some difficult diagnostic challenges. Male gender with primary nervous system involvement is also unusual. pSLE is more severe disease, as compared to adults having significantly more renal & nervous system involvement. Team approach is a key for treatment of patients with pSLE.

## Learning Points

1. In an uncommon encephalitis presentation, a broad differential diagnosis has to be considered.
2. Dealing with the diagnosis of a lifelong, unpredictable and relapsing-remitting disease is challenging for pSLE patients and recognition of the specific needs of this age group is important for optimal outcome.
3. Neuropsychiatric systemic lupus erythematosus has variable clinical manifestation which leads to difficult diagnostic challenges but early recognition is important and it requires early and aggressive immunosuppressive treatment which may prevent permanent organ damage.

## Conflict of Interest

None.

## References

1. Chiewchengchol D, Murphy R, Edwards SW, Beresford MW (2015) Mucocutaneous manifestations in juvenile-onset systemic lupus erythematosus: A review of literature. *Pediatric Rheumatology*: 13.
2. Kamphuis S, Silverman ED (2010) Prevalence and burden of pediatric-onset systemic lupus erythematosus. *Nat Rev Rheumatol* 6:538-546.
3. Kelly RMT *Textbook of rheumatology*. 108:1771.
4. Mondal R, Nandi M, Ganguli S, Ghosh A, Hazra A, et al. (2010) A childhood lupus: Experience from eastern India. *Indian J Paediatr* 77:889-891.
5. Malviya AN, Singh RR, Singh YN, Kapoor SK, Kumar A (1993) Prevalence of systemic lupus erythematosus in India. *Lupus* 2:115-118.
6. Agarwal I, Kumar TS, Ranjini K, Kirubakaran C, Danda D (2009) Clinical features and outcome of systemic lupus erythematosus. *Indian Pediatr* 46: 711-715.
7. Font J, Cervera R, Espinosa G, Pallarés L, Ramos-Casals M, et al. (1998) Systemic lupus erythematosus (SLE) in childhood: Analysis of clinical and immunological findings in 34 patients and comparison with SLE characteristics in adults. *Ann Rheum Dis* 57: 456-459.
8. Levy DM, Kamphuis S (2012) Systemic lupus erythematosus in children and adolescents. *Pediatr Clin North Am* 59: 345-364.
9. Pande I, Sekharan NG, Kailash S, Uppal SS, Singh RR, et al. (1993) Analysis of clinical and laboratory profile in Indian childhood systemic lupus erythematosus and its comparison with SLE in adults. *Lupus* 2:83-87.
10. Ferrara N, Rocha S, Fernandes VS, Correia T, Goncalves E (2013) Juvenile systemic lupus erythematosus with primary neuropsychiatric presentation. *BMJ case reports*.
11. Joseph FG, Scolding NJ (2010) Neuro lupus. *Pract Neurol* 10:4-15.
12. Weiner SM, Peter HH (2002) [Neuropsychiatric involvement in systemic lupus erythematosus. Part 1: Clinical presentation and pathogenesis]. *Med Klin (Munich)* 97:730-737.
13. (1999) The American college of rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 42:599-608.
14. Sibbitt Jr WL, Brandt JR, Johnson CR, Maldonado ME, Patel SR, et al. (2002) The incidence and prevalence of neuropsychiatric syndromes in pediatric onset systemic lupus erythematosus. *J Rheumatol* 29:1536-1542.
15. Hochberg MC (1997) Updating the American college of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 40:1725.
16. Barile-Fabris L, Ariza-Andraca R, Olguin-Ortega L, Jara LJ, Fraga-Mouret A, et al. (2005) Controlled clinical trial of IV cyclophosphamide versus IV methylprednisolone in severe neurological manifestations in systemic lupus erythematosus. *Ann Rheumatic Dis* 64:620-625.
17. Joseph FG, Lammie GA, Scolding NJ (2007) CNS lupus: A study of 41 patients. *Neurology* 69:644-654.
18. Hersh AO, von Scheven E, Yazdany J, Panopalis P, Trupin L, et al. (2009) Differences in long-term disease activity and treatment of adult patients with childhood- and adult-onset systemic lupus erythematosus. *Arthritis Rheum* 61:13-20.