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# Varicella Infection Triggering Childhood Lupus Erythematosus: A Case Report

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**Abstract**
*Childhood-onset systemic lupus erythematosus (cSLE) is a rare disease with an incidence of 0.3-0.9 per 100,000 children-years and a prevalence of 3.3-8.8 per 100,000 children. Approximately 80% of patients with cSLE are female as in adult onset SLE. Etiology is unknown, but may be associated with genetic factors, non-organ specific humoral antibodies, impaired cell mediated immunity, environmental factors e.g. infections, stress etc. In recent decades, many researchers have focused on the role of viral infection in the etio-pathogenesis of systemic lupus erythematosus (SLE); cytomegalovirus (CMV) is considered to be most common virus reported, that may trigger SLE. We are reporting a male child with cSLE who suffered from varicella infection prior to the onset of severe SLE with lupus nephritis. Any patient with post viral exanthum, fever, photosensitive rash, arthralgia or arthritis should be investigated in detail to rule out underlying more serious autoimmune disease i.e. childhood lupus erythematosus.*
*Varicella zoster infection (chickenpox) is a very rarely reported trigger of cSLE.*
**Keywords**- *varicella zoster virus, childhood lupus erythematosus, infectious trigger, etiopathogensis.*

## Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that can involve any organ system and may lead to significant morbidity and even mortality. Childhood-onset SLE (cSLE) is a rare disease with an incidence of 0.3-0.9 per 100,000 children-years and a prevalence of 3.3-8.8 per 100,000 children.(1) Approximately 80% of patients with cSLE are female as in adult onset SLE. Most studies report a median age of onset of cSLE between 11-12 years; the disease is quite rare under the age of 5 years.(2,3) Etiology is unknown, but may be associated with genetic factors, non-organ specific humoral antibodies, impaired cell mediated immunity, environmental factors e.g. infections, stress etc. In recent decades, many researchers have focused on the role of viral infection in the etio-pathogenesis of systemic lupus erythematosus (SLE); cytomegalovirus (CMV) is considered to be most common virus reported, that may trigger SLE.

Here we report a case of 9 year old male child who had varicella infection which later on precipitated onset of SLE.

**Case Report**

A 9-year old male child presented with fever, arthralgia, malaise, weakness and skin lesions on face (malar area, bridge of nose and ear lobules) and upper trunk from last 15 days. Initially it started as red raised non itchy, non oozy lesion followed by appearance of oozy lesion subsequently covered with black crust. Child complained exacerbation of redness, itching and burning on exposure to sunlight. Two weeks prior to onset of above symptoms, he himself, his younger sister and their father had episode of varicella infection. Patient and his family members took treatment for same from nearby health facility. Both sister and his father recovered well from the varicella infection without any complications, but he had onset of new lesions with photosensitivity as mentioned above. He was admitted in the department of dermatology in our institution for detailed workup. There was no history suggestive of SLE or any other connective tissue disease in family.

On cutaneous examination over face and upper trunk there were multiple, discrete, erythematous, papulo-plaques lesions of varying size 1x1 cm to 5x4 cm with overlying brownish black crust and atrophy in few lesions at places. Malar region revealed fixed erythema. Over upper trunk, there were post varicella scars at places. He had multiple erythematous erosions on hard palate. No other mucosa revealed any lesions, nails and hair showed no abnormality.

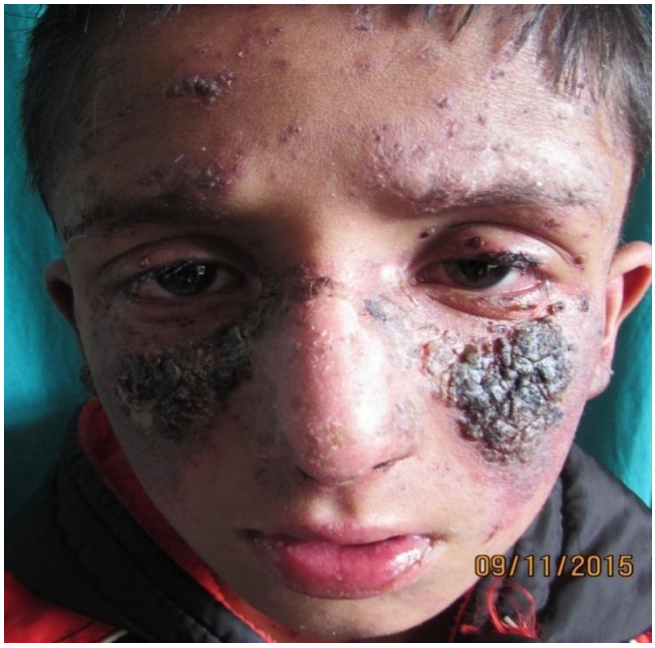


**Figure 1.** Erythematous, papulo-plaques lesions of varying size with overlying brownish black crust and malar erythema over face.

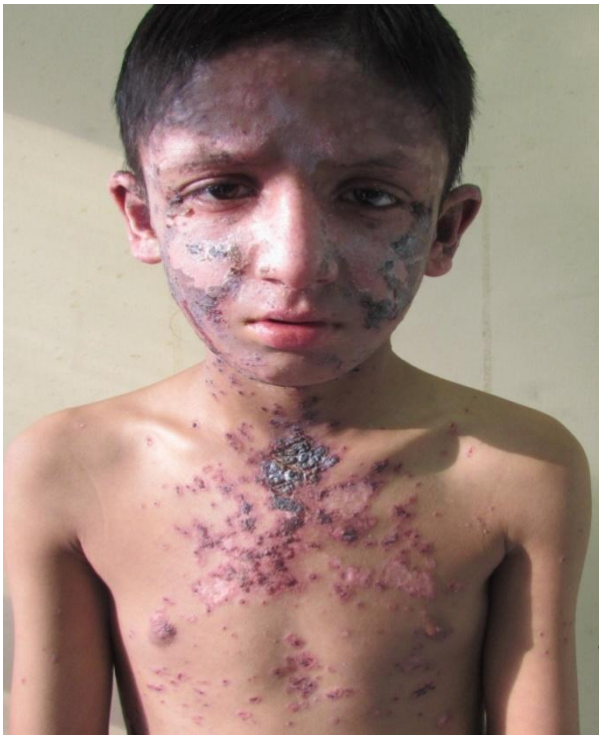

**Figure 2.** Erythematous, papulo-plaques lesions of varying size with overlying brownish black crust over face and chest on treatment in recovery phase.

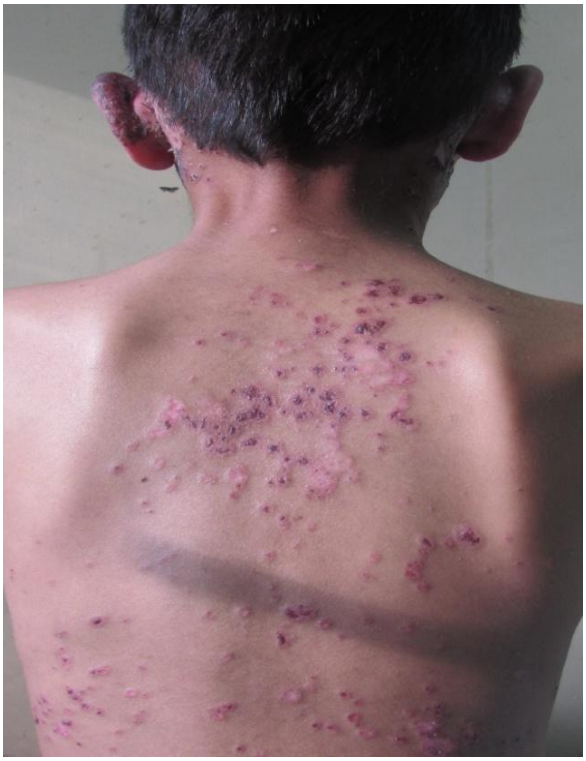

**Figure 3** Multiple erythematous papulo-plaque lesions with crust on the back and ears

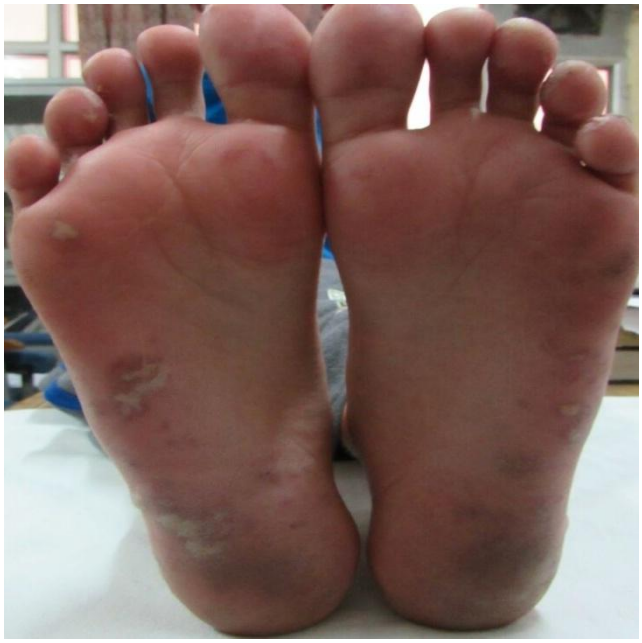

**Figure 4** Vasculitic lesions on both soles

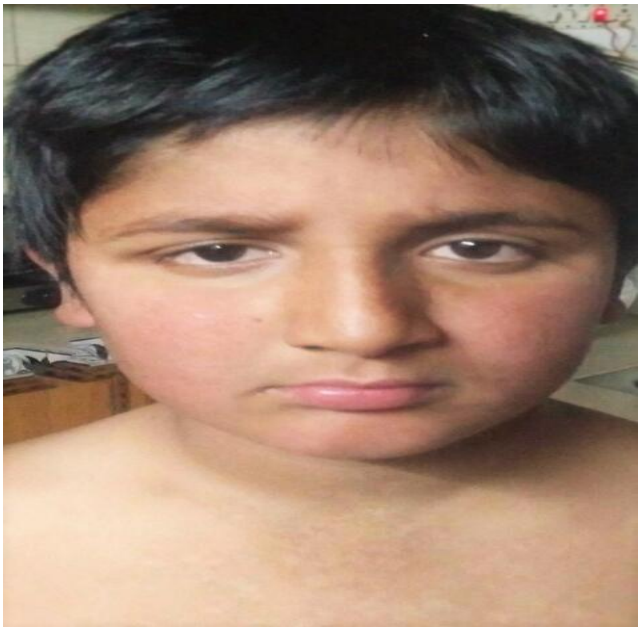

**Figure 5** Complete recovery of the rash after treatment.

On systemic examination, vital signs were normal, he had with low-grade fever and bilateral submandibular lymphadenopathy. Abdominal examination did not reveal hepato-splenomegaly. Neurologic exam was also normal.

Laboratory investigations showed: Hb% -13.9 gm%; TLC of 6,300/mm$^3$; Platelet 20 700/mm$^3$, ESR -11 mm in the first hour; FBS- 100 mg%; Urea 28 mg%, Cr 0.5 mg%; Urine routine examination showed trace of albumin; Chest X-Ray and USG abdomen were normal; liver function tests were normal; HBsAg and HCV serology were non reactive. Varicella zoster serology could not be done due to unavailability of this test in our institution. Lipid profile was normal; other tests showed PT/INR 15.1/1.29; ANA by indirect immunofluorescence (Hep2 method) was positive in high titre (1:1280) with a speckled pattern. Anti-dsDNA (Hep2) was negative; C3 levels reduced, 24 hour urine for protein was high i.e 1719mg. Renal biopsy could not be performed as child was uncooperative and the parents did not gave consent for the same. Echocardiography was normal.

Diagnosis of SLE with renal involvement was kept, according to Revised ARA criteria, patient fulfilling more than 4 criteria. SLE in this case was precipitated by varicella infection. He was started

on treatment with 1 mg/ kg/ day prednisolone and 200 mg hydroxychloroquine daily for 1week but patient developed new vasculitic lesion over trunk, hands and feet, thus dose of prednisolone was increased to 1.5mg/kg/day and concomitantly started on mycophenolate mofetil 250 mg two times a day as advised by nephrology department and continued on hydroxychloroquine. Improvement in lesions was noted as well 24 hour urinary proteins reduced to 485 mg and thereby prednisolone was tapered down to 1mg/kg/day after 2 weeks. Patient was discharged on same doses and to be reviewed in our OPD and nephrology OPD after 1 month. Now no fresh admissions in dermatology department he is now doing well and is on follow up from nephrology department of our institution (Figure 5).

**Discussion**

Systemic lupus erythematosus (SLE) is considered clinically and serologically the most diverse systemic autoimmune disease because it may affect any organ with a broad spectrum of manifestations. The disease mainly involves the skin, joints, kidneys, blood cells, and nervous system.[4] This disorder is characterized by the production of autoantibodies and polyclonal activation of B lymphocytes. Many studies have focused on the role of viral infection in its etiopathogenesis, which is often called the viral hypothesis[5]. EBV and CMV are commonly implicated viruses.[6] The mechanisms that lead to the aberrant autoimmune responses related to viral infection are not clearly understood,[7] and have been related to the capacity of viruses to induce autoantibodies[8,9] a defective functioning of some innate immune system molecules such as MBL or TLR[10,11] , interferon-related mechanisms[12] or abnormal T-cell mediated responses.[13] Ramos-Casals et al [14]reported that various viruses, especially CMV and B19, EBV, varicella, hepatitis A virus, norovirus, measles, and mumps, may be involved in inducing clinical symptoms mimicking lupus flares in patients with SLE. They also observed that in active SLE may be having a viral infection can easily confuse it with a lupus flare, SLE itself being an immunocompromised state.

The search has been always for the external agent that could trigger the autoimmune response and the development of lupus. However, a viral causal agent of lupus has not yet been discovered, but many interesting findings on the complex interactions between viruses and lupus in clinical practice have been made. In this child also SLE was precipitated after varicella zoster virus infection, suggesting a role of viral trigger in etiopathogenesis of cSLE. Infectious agents, including viruses are a key factor for induction of autoimmunity. These pathogens contribute toward abnormal immune responses in genetically susceptible individuals through molecular mimicry, epitope spreading, bystander activation, or other mechanisms.[15]

Varicella being very common childhood viral infection but being the trigging infection in childhood SLE is very rare to the best of our knowledge.

Most studies report a median age of onset of cSLE between 11-12 years. Our patient developed it at the age of 9 years. As in adult onset SLE, approximately 80% of patients with cSLE are female which is in contrary to this patient. Male gender, early onset of age, reduced complement level (C3 level) and renal involvement are risk factor for poor prognostic outcome, as the case in this child. The outcome of the treatment of lupus nephritis could be varied, although with aggressive treatment, prognosis can be improved.

We could not do the viral serology for varicella zoster virus, EBV and CMV due to non-availability of these investigations in our institution. But clinical diagnosis of varicella zoster infection (chickenpox) in the family members and in this child was straight forward.

Children have a more fulminant disease onset and course than adults with SLE, resulting in two to three times higher mortality. Adult SLE is about 10 times more common than cSLE in the United States but children with cSLE have a more severe disease than their adult counterparts. Lupus nephritis has a profound negative impact on survival

and results in high healthcare expenditure of both children and adults.[16] Some infectious agents, such as malaria, Toxoplasma gondii and Helicobacter pylori, may have a protective effect in induction of SLE. Vaccinations may play dual roles by protecting against friend and foe alike. [17,18]

This case had renal involvement with proteinuria and high 24 hour urinary proteins, reduced complement levels and thrombocytopenia as systemic finding but no other organ was involved. Severity of cSLE is a common finding as compared to adult onset SLE. There are reports from Canada suggesting a higher frequency of neurological and renal involvement at the time of diagnosis among children as compared with adults with SLE. [19,20]

A recent meta-analysis of a total of 905 cSLE patients and 5,993 aSLE patients concluded that fever; thrombocytopenia, mucocutaneous involvement, urinary casts, seizures, and hemolytic anemia are all more commonly encountered in cSLE than aSLE. [21]

Similar findings were seen in the present case.

## Conclusion

Childhood-onset SLE is a lifelong autoimmune disease that may be difficult to diagnose due to its multisystem involvement, and heterogeneity of clinical manifestations. It follows a more aggressive disease course than adult-onset SLE, with greater disease activity at presentation and over time, and consequently leads to greater morbidity and mortality than adult-onset SLE. Genetically predisposed children with viral infections are at a higher risk of triggering the onset of cSLE in fulminant form with systemic involvement especially lupus nephritis. Common viral exanthum like varicella zoster exanthum can lead to a complicating onset of childhood SLE. High index of suspicion must be there while dealing patients with post viral illness developing severe photosensitive rash, fever, proteinuria, thrombocytopenia etc. These cases must be worked up in detail to rule out cSLE. So that early diagnosis and treatment could decrease the morbidity and mortality of this chronic relapsing serious autoimmune illness.

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