# USE OF INTRAVENOUS IMMUNOGLOBULINS IN TREATMENT OF LUPUS PSYCHOSIS: A CASE REPORT

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*Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease. Its manifestations are protean and virtually any organ system can be involved. The disease in children is generally more acute and more severe than that in adult.*

*Recently it has been notified that intravenous immunoglobulins (IVIG) in patients with cerebral lupus have improved fairly. In this report, we present a case of systemic lupus erythematosus involving multiple organ systems, including psychosis which did not respond to high-dose intravenous corticosteroid therapy. After application of IVIG (400 mg/kg/24 hr, 5 day/month) as an adjunctive agent, psychosis of the patient was completely improved. This report supports the finding that IVIG therapy may successfully be used for nonresponders to conventional treatments of SLE, especially for those with cerebral complications.*

***Key words***: *Systemic Lupus Erythematosus, intravenous immunoglobulins, child.*

***Lupus psikozu tedavisinde intravenöz immünoglobulinlerin kullanımı: olgu sunumu***

*Sistemik lupus eritematosus (SLE) otoimmun bir multisistem hastalığıdır. Belirtileri çok yönlüdür ve hemen her organı tutabilir. SLE genellikle çocuklarda erişkinlerden daha akut başlar ve ağır seyreder.*

*Son zamanlarda serebral lupuslu hastalarda intravenöz immunglobülinlerin oldukça iyi sonuçlar verdiği bildirilmektedir. Bu makalede, psikoz ve birden fazla organ tutulumu olan; yüksek doz intravenöz kortikosteroide yanıt vermeyen, IVIG uygulamasını takiben (400 mg/kg/gün, 5 gün/ay) psikoz tablosu tamamen düzelen bir SLE olgusu sunuldu.*

*Bu bulgu, IVIG'in SLE'nin konvansiyonel tedavisine yanıt vermeyen olgularda, özellikle de serebral lupus da başarılı bir şekilde kullanılabileceğini desteklemektedir.*

***Anahtar kelimeler***: *Sistemik lupus eritematosus, intravenöz immunglobülin, çocuk.*

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Systemic Lupus Erythematosus (SLE), although has unclear etiology, is a disease that most likely occurs because of immune regulation disturbance[1,2]. It may cause neuropsychiatric signs in 18% of patients, such as personality changes, seizures, cerebrovascular accidents, polyneuropathies and psychosis. The psychosis signs are seen at the rate of 4% and following seizures (7%) and brain system dysfunction (5%) in cerebral SLE. Neurological signs indicate poor prognosis, and require acute and active management[3,4].

Recently, many studies have reported the advantages of IVIGs in treatment of all severe forms of SLE[5-8] including cerebral lupus[9-12] besides its employment in many other autoimmune diseases.

We report a case of SLE with multiple organ involvement, presenting with a clinical picture of psychosis which was not responsive to high-dose corticosteroids treatment but improved with IVIG treatment and discuss the importance of IVIG treatment in SLE with central nervous system involvement.

## CASE REPORT

The patient, 12-year-old girl, had the symptoms of fever, pain and swelling at joints, rashes swelling on the skin for a month ago. Additionally, she exhibited abnormal behaviors, and lack of interest of during last month. Family history revealed no special feature. Vital signs were as follows; fever 38.7 °C (axillary), heart rate 160/min, arterial blood pressure 140/110 mmHg, breathing rate 30/min. Physical examination revealed rashes on face (Fig.1) and whole body surface, hepatosplenomegaly, generalized lymphadenopathy, arthritis at both knee joints and the left ankle joint, abnormal behaviors, incoherence and agitation. Laboratory results were as follows: hemoglobin 8 g/dl, white blood cell count 3800/$mm^3$, erythrocyte sedimentation rate 115 mm/hour, BUN 78 mg/dl, creatinine 2 mg/dl, uric acid 11.8 mg/dl, total lipid 1100 mg/dl, cholesterol 270 mg/dl, SGOT 570 U/L, SGPT 142 U/L, alkaline phosphatase 1171 U/L, ammonia 30 μgN/dl, total protein 5.1 g/dl, albumin 2 g/dl and $Ca^{+2}$ 7.1 mg/dl. Urine examination showed microscopic hematuria and proteinuria (1.7 g/L/day). Glomerular filtration rate (GFR) was 40 ml/min/1.73$m^2$. l. As other diagnostic tests, ds-anti-DNA was 136 (0-6) IU/ml, $C_{33}$was 13 (50-90) mg/dl and anti-Sm antibodies was 42 (<25) IU/ml. Rheumatic factor, anti-nuclear antibody, direct coombs, CRP, Salmonella and Brucella agglutination, and cultures (blood, throat, urine, cerebrospinal fluid) were negative. The cerebrospinal fluid (CSF) protein was 160 mg/dl. Cranial tomography was normal, and magnetic resonance imaging could not be done. Electroencephalography (EEG) disclosed diffuse irregularity in background activity. Mild mitral insufficiency on echocardiography and sinus tachycardia (166/min) on Electrocardiography were detected. The psychosis picture of the patient was evaluated as lupus psychosis because of normal blood ammonia level though high liver enzymes, absence of cerebral hemorrhage and infarct, GFR which was not consistent with uremic encephalopathy, abnormal EEG and increased protein level in cerebrospinal fluid. The patient was diagnosed as SLE with multiple organ involvement. High-dose of methylprednisolone therapy (30mg/kg/day, maximum 1 g/day) was administered for three days with standard steroid therapy in addition to symptomatic treatment[1,2]. No response was observed at the end of 15 days of treatment. For this reason the steroid dose was decreased to 1 mg/kg/day and IVIG (400 mg/kg/day, 5 day/month/, consecutive days a month ) was added to the therapy schedule[10,11]. Fever and acute phase

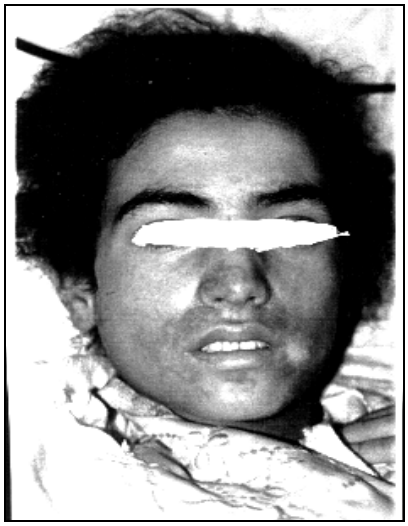

**Figure 1.** The patient showing the rash involving the malar area and extending over the bridge and the upper lip.

reactants were decreased and the signs of psychosis was improved on the 5th day of IVIG treatment. Also her EEG has returned to normal. The patient was discharged in a stable condition at the end of hospitalization period. She has been followed for three months as an outpatient with no neurological complaints but a few complaints related to other systems. A progressive clinical and laboratory improvement was observed in the patient during IVIG therapy.

## DISCUSSION

The most important criteria determining the prognosis of SLE are patient's age (more serious in children) major organ involvement and efficacy of treatment[2,3]. The aim of treatment is to suppress the immune reactivity and inflammation. The best indicator of that is patient's well condition both as clinical and laboratory findings[1]. The main drugs used for treatment are nonsteroid anti-inflammatory drugs (NSAID) and antimalarial agents, steroids and cytotoxic drugs[1-3]. Additionally, plasmapheresis and IVIG may be applied in treatment[8]. The treatment should be designed according to organ involvement in SLE.

Lupus psychosis appears the poor and active forms of the disease. It may be episodic and may not be recurrence when the active stage is treated successfully[2,3]. For this reason, it should be started acute treatment. There are many reports which reveal efficacy of steroids and oral or intravenous cyclophosphamide in cerebral lesions due to SLE[1,3,4].

Recently, IVIG has been successfully used in many autoimmune diseases[13]. Its mechanism is controversial. However, it is suggested that it acts on the impaired T and B cells producing antibodies which affect the pathologic antibodies [6,13]. There are many articles about the successful application of IVIG in systemic SLE[3,5-8] and SLE with CNS involvement[9-12]. Horoshovski et al[9] reported a case with pseudotumor cerebri due to SLE which was unresponsive to steroids but responded to the IVIG treatment. Tomer et al[19] successfully treated a patient with lupus psychosis with IVIG.

Our patient was a SLE case with major organ involvement. The most striking finding of the patient was psychosis. Lupus psychosis may be due to organ-spesific antibodies which are detected in SLE. Circulating antibodies against neurones were demonstrated in patients with cerebral SLE[3,4]. We started high-dose corticosteroids treatment besides the general symptomatic approach. During this treatment, sings of psychosis become worse and there was no improvement in the other symptoms. It is known that steroids have some adverse effects on CNS. These effects are EEG changes, decreasing convulsion threshold, appearing the psychiatric picture such as depression and psychosis, and occurring pseudotumor cerebri in high-doses of steroids[2,14]. So, we decreased steroid dose and started IVIG. Improvement in other systemic symptoms as well as in the psychotic picture were observed 5 days after the initiation of IVIG therapy. The decrease in acute phase reactants was correlated with response to the treatment. Our findings were consistent with those of the Horoshovski's[9] and Tomer's[11].

Persistence of the clinical and laboratory improvement in this patient supports the rapid and persistent efficacy of IVIG in cerebral lupus. Therefore IVIG therapy may be used for non responders to conventional treatments, especially for those with cerebral complications. However, more studies are needed to show efficacy of IVIG on lupus psychosis.

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