Treatment of Posterior Reversible Encephalopathy Syndrome that Occurred in a Patient with Systemic Lupus Erythematosus by Plasmapheresis

Zehra İpek Arslan¹, Canan Kamile Turna¹, Çiğdem Yasemin Özerdem², Sara Yavuz³, Nur Baykara¹, Mine Solak¹

¹Department of Anaesthesiology and Reanimation, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

²Department of Neurology, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

³Department of Nephrology, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

Posterior reversible encephalopathy syndrome is characterized by visual and mental disturbances, nausea and vomiting and generalized or focal convulsions and often represents itself with parietal and occipital oedema formation. We want to report the treatment of posterior reversible encephalopathy syndrome with plasmapheresis, which developed in a 35-year-old woman with systemic lupus erythematosus diagnosed by renal biopsy 3 years ago. She has been followed up in the intensive care unit three times. However, she had been transferred to the nephrology department of our university hospital because of her uncontrolled blood pressure. Oral antihypertensive therapy, corticosteroid 500 mg 1 × 1 and cyclophosphamide were started for the activation of lupus. After the detection of low complement levels, systemic lupus erythematosus activation was suspected. She developed mental deterioration after her first plasmapheresis treatment and was then consulted by the neurology and intensive care unit doctors. Diffusion cranial magnetic resonance imaging was found compatible with posterior reversible encephalopathy syndrome. The patient was transferred to our intensive care unit. The patient gained consciousness after her second plasmapheresis. After 5 days of follow-up in our intensive care unit and after significant regression was observed in the magnetic resonance imaging analysis, the patient was transferred to the nephrology service conscious, cooperated and orientated. At the nephrology service, after a total of 13 times of plasmapheresis, complement levels were increased and she was discharged with corticosteroid therapy. Posterior reversible encephalopathy syndrome can be observed in patients with systemic lupus erythematosus and intensive care unit treatment may be required. To control the hypertension, plasmapheresis should be kept in mind in addition to the multiple antihypertensive therapy in these patients.

Keywords: Systemic lupus erythematosus, posterior reversible encephalopathy syndrome, plasmapheresis, intensive care unit

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical condition that often manifests with many neurological symptoms (headache, seizures, impaired consciousness, hypertension, nausea and vomiting, visual disturbances and aphasia) and with symmetrical white matter, mainly in the parieto-occipital region; rarely, it manifests with cortex abnormalities and oedema or haemorrhage. PRES is an acute or a subacute neurological condition that can develop as a result of eclampsia, seizures, mitochondrial disease, end stage renal failure, organ transplantation, systemic lupus erythematosus (SLE), acute intermittent porphyria or autoregulation disorder and endothelial dysfunction due to immunosuppressive drugs; it is generally seen as a vasogenic type of oedema secondary to hypertensive encephalopathy and can generally be remediated with proper treatment (1-3).

Systemic lupus erythematosus is an inflammatory disease due to cell and tissue damage caused by antibodies circulating in the blood, immune complex and. It generally manifests with weight loss, fever, nausea and weakness among young women and progresses with single or multiple organ involvement. Due to central nervous system (CNS) involvement, cerebrovascular incidents, seizures, meningitis, cognitive dysfunction, psychosis, dementia, anxiety and depression can be seen (4).

Plasmapheresis is currently used in the treatment of many autoimmune diseases. According to manuals, plasmapheresis is used in the treatment of diseases such as myasthenia gravis, multiple sclerosis, Guillain-Barre syndrome, haemolytic

uremic syndrome, thrombotic thrombocytopenic purpura and SLE (5, 6).

In this case report, we wish to present an end-stage renal failure SLE case that progresses with neurological disorders, oedema, multi-drug-resistant hypertension and PRES and that was treated with plasmapheresis.

Case Presentation

We obtained the patient's oral and written consent. A 35-year-old female patient with no prior complaints had applied to another health centre with the complaint of swelling in the feet in 2010; upon the detection of proteinuria, she was referred to the nephrology department of our university. Upon the detection of antinuclear antibody positivity, a renal biopsy was performed as SLE was suspected. Because the histopathology was compatible with membranoproliferative glomerulonephritis or class 4 lupus nephritis, the patient was given oral cyclophosphamide (endoxan, 50 mg, Baxter, Illinois, USA) and oral steroids (prednol, 32 mg, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey) for lupus for four months; the treatment continued for 2 years with gradually reduced doses, and the patient's proteinuria was reduced to 12 g from 26 g. Immunofluorescence analysis results were as follows: Ig A: membranous 3+ granular accumulation, Ig M: membranous 2+ granular accumulation and C₃: membranous 3+ granular accumulation. Within that period, the patient saw a rheumatology specialist in another health centre and used oral hydroxychloroquine sulphate (Plaquenil, 200 mg, Sanofi Aventis, Paris, France). Because the patient's 220/120 mmHg arterial blood pressure (ABP), syncope, seizures and right upper extremity weakness could not be brought under control, the patient applied to the emergency department of a private hospital twice and was given valsartan (Co-Diovan, Novartis, Basel, Switzerland) 1 x 1; the patient was monitored for five days in the intensive care unit (ICU) and was discharged when her ABP returned to normal. The patient was referred to our nephrology department on 27th December, 2013, because her blood pressure could not be regulated.

Because the patient's antinuclear antibodies, anti-dsDNA, ribosomal p-protein and anti-cardiolipin antibodies tested negative in her blood samples upon arrival, and because very low C₃ and C₄ levels (respectively 23 mg dL⁻¹ and 3.6 mg dL⁻¹) were detected in her disease activity follow-up, lupus activation was believed to have occurred. On the first day, the patient was started on albumin replacement 2 x 1, carvedilol 12.5-mg tablets 2 x 2 (Carvexal, Sandoz Inc., Istanbul, Turkey), doxazosin 4 mg 2 x 1 (Cardura, Pfizer Pharmaceuticals Inc., New York, USA), nifedipine 30 mg 2 x 2 tablets (Adalat Crono, Sesame Pharmaceutical Industry, Istanbul, Turkey), intravenous (IV) 500-mg steroid (prednol, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey), oral omeprazole 40 mg (Lansor, Sanovel, Istanbul, Turkey), and Aldactone 100-mg tablets. Plasmapheresis was performed (liquid was not drawn from the patient during the procedure). Upon regaining consciousness after the first plasmapheresis, she was consulted with neurology. The re-

sults of the neurology consultation were as follows: her vital signs were stable and neurological examination was normal, her pupils were isochoric, her deep tendon reflexes (DTR) were interpreted as normal, and oedema was only observed in the right arm and feet. Eight hours after this assessment, the patient became sleepy, and another neurological examination was performed. The patient became unconscious; weak flexor response was present in her four limbs, and she was able to open her eyes with painful stimuli with no verbal response. Her left eye was mydriatic, and her DTR were indifferent. She had no seizures. A diffusion cranial magnetic resonance (MR) scan was performed on 1st February, 2014; when hyperintensity and volume growth were discovered in the T₂ sequence that holds the deep grey matter and corpus callosum in the patient's bilateral cerebral and cerebellar hemispheres, and because the results were assessed as significant in terms of PRES (Figure 1), the following anti-oedema treatments were initiated: IV mannitol 4 x 1 (mannitol 20% 150 mL Mediflex, IE Ulugay Inc, Istanbul, Turkey), IV furosemide 4 x 1 (Lasix, Sanofi Aventis, Paris, France), and IV glyceryl trinitrate infusion (Perlinganit, Sesame Pharmaceutical Industry, Istanbul, Turkey). Since there was no decrease in the patient's blood pressure and she was in a state of unconsciousness, she was transferred to ICU on the same day with a 10 lt min⁻¹ oxygen mask for close monitoring. EEG taken in ICU was reported as a common bioelectrical hitch. The patient's Glasgow Coma Scale (GCS) when she was taken to ICU on 1st March, 2014: the 6 light reflex was bilaterally negative and the left eye was dilated; the right eye was mitotic and anisocoric. Her ABP was 240/120 mmHg, and the saturation in room air (SaO₂) was 92%. The patient continued to receive oxygen via an oxygen mask, and an IV esmolol (Brevibloc, Baxter, Illinois, USA) infusion was started. The arterial blood gas and biochemical results were as follows: PaO₂: 59 mmHg, PaCO₂: 34 mmHg, PH: 7.58, SaO₂: 95%, Glu: 144 mg dL⁻¹, Na: 134 mmol L⁻¹, K: 4.7 mmol L⁻¹, Ca: 1.24 mmol L⁻¹, Cl: 98 mmol L⁻¹, HCO₃: 32.2 mmol L⁻¹, urea: 54 mg dL⁻¹, creatinine: 2.12 mg dL⁻¹, Ca: 10.3 mEq L⁻¹, Na: 138 mEq L⁻¹ and OSM: 293. The patient's arrival APACHE II score was determined to be 37. Moreover, 1 x 500-mg steroid (prednol, Mustafa Nevzat Industry, Istanbul, Turkey), omeprazole 40 mg 2 x 1 (Eselan, Dem Pharmaceutical Industry, Istanbul, Turkey), mannitol 4 x 150 cc (mannitol 20% 150 cc Mediflex, IE Ulugay Inc, Istanbul, Turkey) and furosemide 20 mg 4 x 1 (Lasix, Sanofi Aventis, Paris, France) treatment continued for three days. Blood and urine cultures were obtained, and no reproduction took place. When the patient's ABP was approximately 170/90 despite esmolol (Brevibloc, Baxter, Illinois, USA) infusion, antihypertensive treatment was arranged in consultation with the cardiology department as carvedilol 300 mg 1 x 1 (CoAprovel, Sanofi Aventis, Paris, France), doxazosin 4 mg 1 x 1 (Cardura, Pfizer Pharmaceuticals Inc., New York, USA) and amlodipine 10 mg 1 x 1 (Norvasc, Pfizer Pharmaceuticals Inc., New York, USA). After a while, the esmolol and perlinganit infusions were stopped. The patient was monitored in our ICU for 5 days and underwent plasmapheresis 4 more times during the period of her intensive care stay. As the patient became conscious, on 1st January, 2014, she was trans-

Figure 1. Diffusion magnetic resonance image showing the patient's posterior reversible encephalopathy

Figure 2. Improved cranial magnetic resonance image of the patient after plasmapheresis

ferred back to the nephrology department for antihypertensive treatment in a conscious, orientated and cooperative state; her light reflex was +/+, her pupils were isochoric and her ABP was 120/80 mmHg stable. The patient's second diffusion cranial MRI, which was taken on 16th January, 2014, revealed a T₂ signal increase in the supratentorial white matter; a significant decrease was detected compared with the diffusion cranial MRI performed on 2nd January, 2014 (Figure 2). The results of the kidney biopsy of the patient performed on 1st February, 2014, indicated class 5 lupus nephritis. The patient had a total of 13 plasmapheresis sessions during hospitalization for 3 days, 1 g 1 x 500-mg IV steroid (prednol, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey), and then oral 64-mg 1 x 1 as a steroid follow-up, and finally, as of 13th February, 2014, 32-mg 1 x 1 as the last steroid treatment. Upon the observation of significant increases in her complement C₃ and C₄ levels (63 mg dL⁻¹ and 16.3 mg dL⁻¹), she was discharged to the nephrology department in a conscious, orientated and cooperative state.

Our patient returned to our emergency department two more times with clouding of consciousness and seizure complaints with ABP: 170/90 mmHg and GCS: 6 on 21st April, 2014 and 2nd June, 2014. She was readmitted to ICU, and anti-epileptic treatment and intravenous steroid (prednol, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey) 60 mg 1x1 were started and tapered afterwards.

The hyperintense areas in the cerebellar white matter and supratentorial white matter in the diffusion cranial MRI were reported to be compatible with PRES. Perlinganit and esmolol infusions were started in the ICU, and in consul-

tation with cardiology, dual antihypertensive therapy was rearranged; the patient was taken to plasmapheresis without being given anti-oedema treatment. Although her place and person orientation decreased occasionally after perlinganit and esmolol were terminated, she was transferred to the nephrology department with GCS: 15.

Discussion

The prevention of hypertension is the most important factor in the treatment of posterior reversible encephalopathy syndrome. Multiple intravenous and oral antihypertensive agents and diuretics are used in the treatment. Opioid therapy is performed for the pain. We also used multiple oral and intravenous anti-hypertensives with anti-oedema treatment for our patient. Furthermore, the addition of analgesics to the treatment and the necessity of anticoagulant treatment are also emphasized (4). Our patient received anticoagulant treatment on her arrival. PRES is more frequently seen among women. Our patient was a woman. PRES developing with infection in a SLE patient has been reported (5). Despite the lack of reproduction in the patient's blood and urine cultures, empirical antibiotic treatment was started.

The treatment of central nervous system involvement is one of the most important problems discussed regarding SLE, because neuropsychiatric manifestations are the major causes of lupus activation induced mortality and morbidity. Other systemic involvements caused by SLE activation are often concomitant with neurological involvement (6). Serum C₃ levels are more sensitive and specific than serum C₄ levels in terms of SLE activation (7). The conventional treatment re-

gime comprises a combination of corticosteroids and immunosuppressives; plasmapheresis is added to the treatment in some refractory patients who do not respond to conventional treatment (8). Thus, in our lupus cerebritis case, despite the long-term combination of corticosteroids and various immunosuppressive therapies, remission could not be achieved; therefore, the combination of therapies was replaced by plasmapheresis treatment. During the disease activity monitoring period, after the treatment, normal serum C₃ and C₄ levels, as well as clinical improvement, were obtained. Following plasmapheresis treatment, the patient's treatment continued with intravenous immunoglobulin treatment. The patient was admitted to our emergency department with clouded consciousness and hypertension every other month after her discharge and only responded to plasmapheresis treatment.

In the literature, headache developing in a postpartum pregnancy case with severe pre-eclampsia and PRES cases resistant to multiple antihypertensive treatments have been reported. It was reported that both neurological and radiological improvements were observed in patients following anti-oedema treatment and multiple antihypertensive treatments (9). In PRES syndrome, intracranial lesions are usually symmetrical and occipitally localized (10). In our patient, the lesion was symmetrically localized; however, the localization was atypical. In our patient's MRI, we observed cerebral and cerebellar oedema, oedema involving the corpus callosum, and deep grey matter from the bilateral frontal to the occipital lobes.

In our case, in addition to the patient's treatment, plasmapheresis was performed; after this treatment, the patient displayed a dramatic improvement. That the patient returned twice with similar complaints and the treatment of the patient with plasmapheresis was successful in both of these instances is remarkable. The same who admitted two more times with similar complaints and these two applications are also engaging in treatment and. Upon her first admission, she was administered anti-oedema treatment, but despite the fact that mannitol was not used during her second admission, remarkable improvement was observed in her consciousness and regression was observed in her oedema.

Among the reported complications of plasmapheresis are a decrease in ABP, arrhythmias, hyperthermia, and the development of paraesthesia. In the SLE induced PRES patient, the effect of plasmapheresis on removing antibodies with complement-level raising effects and reducing ABP side effects might be useful. It seems necessary to conduct extensive research on this subject.

Conclusion

In SLE patients who develop advanced-stage renal disease, if resistant hypertension and neurological symptoms develop, PRES should be considered, the diagnosis should be supported by radiological imaging methods, and urgent intervention with a multidisciplinary approach should be performed; in addition to anti-oedema therapy, plasmapheresis should be

considered as a treatment option. However, more cases are required to determine that plasmapheresis is effective in treating PRES syndrome.

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References

1. Fugate JE, Claassen DO, Cloft HJ, Kallmes DE, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. *Mayo Clinic Proc* 2010; 85: 427-32. [\[CrossRef\]](#)
2. Feske SK. Posterior reversible encephalopathy syndrome: a review. *Semin Neurol* 2011; 31: 202-15. [\[CrossRef\]](#)
3. Leroux G, Sellam J, Costedoat-Chalumeau N, Le Thi Huong D, Combes A, Tieulié N, et al. Posterior reversible encephalopathy syndrome during systemic lupus erythematosus: four new cases and review of the literature. *Lupus* 2008; 17: 139-47. [\[CrossRef\]](#)
4. Zhang YX, Liu JR, Ding MP, Huang J, Zhang M, Jansen O, et al. Reversible posterior encephalopathy syndrome in systemic lupus erythematosus and lupus nephritis. *Intern Med* 2008; 47: 867-75. [\[CrossRef\]](#)
5. Thipisuttikul I, Phanthumchinda K. Recurrent reversible posterior leukoencephalopathy in a patient with systemic lupus erythematosus. *J Neurol* 2005; 252: 230-1. [\[CrossRef\]](#)
6. Sibley JT, Olszynski WP, Decoteau WE, Sundaram MB. The incidence and prognosis of central nervous system disease in systemic lupus erythematosus. *J Rheumatol* 1992; 19: 47-52.
7. West CD. Relative value of serum C3 and C4 levels in predicting relapse in systemic lupus erythematosus. *Am J Kidney Dis* 1991; 18: 686-8. [\[CrossRef\]](#)
8. Sanna G, Bertolaccini ML, Khamashta MA. Neuropsychiatric involvement in systemic lupus erythematosus: current therapeutic approach. *Curr Pharm Des* 2008; 14: 1261-9. [\[CrossRef\]](#)
9. Keskin HL, Uyanık G, Sivaslıoğlu AA, Çelen E, Aşar AF. Şiddetli preeklampsi olgusunda postpartum posterior reversibl ensefalopati sendromu. *Türkiye Klinikleri J Gynecol Obst* 2014; 24: 62-6.
10. Ahn KJ, You WJ, Jeong SL, Lee JW, Kim BS, Lee JH, et al. Atypical manifestations of reversible posterior leukoencephalopathy syndrome: findings on diffusion imaging and ADC mapping. *Neuroradiology* 2004; 46: 978-83. [\[CrossRef\]](#)