Cyclo-Mensa Therapy in a Patient with Systemic Lupus Erythematosus (SLE) and Class II Lupus Nephritis

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Cyclo-Mensa Therapy in a Patient with Systemic Lupus Erythematosus (SLE) and Class II Lupus Nephritis

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Abstract

Background: Lupus nephritis is a serious complication of systemic lupus erythematosus (SLE) caused by immune complex deposition in the glomeruli, leading to glomerulonephritis and renal impairment. Cyclophosphamide is a potent immunosuppressant widely used for severe lupus nephritis, but its toxic metabolite, acrolein, may induce hemorrhagic cystitis. The Cyclo-MENSA protocol, which combines cyclophosphamide with MESNA, sodium bicarbonate, and adequate hydration, is designed to reduce this risk.

Case Presentation: A 13-year-old female (36.05 kg) presented with class II lupus nephritis, positive ANA, proteinuria, and hematuria, with preserved renal function (serum creatinine 0.49–0.62 mg/dL). Physical examination revealed edema of the lower extremities and face. She received intravenous Cyclo-MENSA (cyclophosphamide 1 g + MESNA 0.5 g), but the regimen was given twice within less than one week, contrary to protocol.

Conclusion: This case highlights the importance of adhering to standard Cyclo-MENSA protocols. Early repeat dosing may elevate the risk of adverse effects, particularly hemorrhagic cystitis from acrolein toxicity

Keywords: Systemic lupus erythematosus, Lupus nephritis, Cyclophosphamide, Cyclo-MENSA, Treatment protocol

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with diverse clinical manifestations, typically associated with anti-dsDNA and anti-Sm antibodies (Calderon-Valverde et al., 2024; Hajji et al., 2023; Hindosh et al., 2022; Khormi & Hijazi, 2023). The pathogenesis involves immune complex formation and deposition in various tissues, leading to inflammation and organ damage. The kidney is one of the major target organs in SLE. The kidney's high blood flow and complex glomerular structure make it prone to immune complex deposition (Couser, 2012). When antibody–DNA/nucleoprotein immune complexes deposit in the glomerulus, complement activation occurs, inducing inflammation and lupus nephritis (Hahn, 2003; Whelband et al., 2023).

Clinically, nephritic syndrome is characterized by hematuria, proteinuria, hypertension, reduced glomerular filtration rate (GFR), and edema (Yuan et al., 2019). Lupus nephritis is one of the most serious complications of SLE and, if left untreated, may progress to chronic kidney disease (Saxena et al., 2011). Early detection is possible through urinalysis, proteinuria assessment, serum creatinine measurement, and renal biopsy (Hajji et al., 2023). Lupus nephritis affects approximately 35–45% of patients with SLE and remains a therapeutic challenge (Martínez Ávila et al., 2023; Roccatello et al., 2023).

CASE REPORT

A 13-year-old female weighing 36.05 kg presented with dizziness and a prior history of methylprednisolone pulse therapy. She had multiple hospital admissions in the preceding months for recurrent fever, abdominal pain, constipation with hematochezia, alopecia, malar rash, and edema of the lower limbs and face. On this admission, she was diagnosed with class II lupus nephritis.

Details of the patient's vital signs, laboratory test results, and prescribed medications are summarized in Tables 1–3.

Table 1. Patient vital signs data

Parameter	Normal Values	Day 1	Day 2	Day 3	Day 4	Day 5
Temperature (°C)	36	36,9	36,5	36,5	36,8	36,5
BP (mmHg)	100-120/60-80	98/65	98/60	98/60	98/67	92/61
Pulse (x/minute)	60-100	124	111	111	88	87
RR (x/minute)	12-18	21	21	21	21	21

Table 2. Patient laboratory examination data

Parameter	Normal Values	Day 1	Day 2	Day 3	Day 4
Erythrocytes	**4,0-5,4**	**3**	**3,23**		
Hemoglobin	**12,0-15,0**	**7,7**	**8,6**		
Hematocrit	**35,0-49,0**		**25,7**		
Urine Protein Negative	**Negative**		++		
Blood in Urine Negative	**Negative**		+		
Urobilinogen	**< 2,0 mg/dL**		**Normal**		
Potassium	**3,5-5,1**			**2,3**	**3,1**
Calcium	**2,10-2,55**			**1,97**	
Sodium	**136-145**			**132**	
BUN	**5-18**	**15**		**24**	
Creatinine	**0,49-0,62**	**0,49**		**0,62**	
ANA	**Negative**	**+++**			

C3	**90-180**	**24,9**			
C4	**10-40**	**3,91**			
Current glucose	**74-106**	**75**			

Table 3. Data on medication use by patients

Drug name	**Dosage**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**
HCT	25 mg/12 hours	**V**	**V**	**V**	**V**	**V**
Spironolaktone	25 mg/12 hours	**V**	**V**	**V**	**V**	**V**
KCl	125 mg/8 hours	**V**	**V**	**V**	**V**	**V**
Vit D	2000 IU/ 12 hours	**V**	**V**	**V**	**V**	**V**
Methylprednisolone pulse	30 mg/ kgBW/24 hours		**V**	**V**	**V**	
Folic acid	2 mg/12 hours	**V**	**V**	**V**	**V**	**V**
Cyclo, mensa	1 gram, 0,5 gram	**V**				**V**
Irbesartan	150 mg/24 hours	**V**	**V**	**V**	**V**	**V**
Hydroxychloroquine	200 mg/24 hours	**V**	**V**	**V**	**V**	**V**
Sodium muchophenolate	540 mg/ 12 hours	**V**	**V**	**V**	**V**	**V**
Methyl prednisolone	32 mg/ 24 hours	**V**				**V**

Laboratory findings revealed ANA positivity (+++), proteinuria (++), hematuria (+), hypocomplementemia (C3: 24.9, C4: 3.91), anemia (Hb 7.7–8.6 g/dL), hypoalbuminemia with edema, mild electrolyte disturbances (Na 132, K 2.3–3.1, Ca 1.97), and normal serum creatinine (0.49–0.62 mg/dL).

Therapeutic regimen included antihypertensives (HCT, spironolactone, irbesartan), immunosuppressants (hydroxychloroquine, mycophenolate sodium), corticosteroids (methylprednisolone pulse, oral methylprednisolone), vitamin D, folic acid, and Cyclo-Mensa

(cyclophosphamide 1 g and MESNA 0.5 g). Notably, Cyclo-Mensa was administered twice within less than one week.

DISCUSSION

The case of SLE with nephritic syndrome was indicated by positive ANA, proteinuria, and hematuria. Renal function was preserved, as shown by normal serum creatinine levels (0.49–0.62 mg/dL), although the patient presented with clinical edema in the lower extremities and face. As described by Hindosh et al. (2022), in SLE, autoantibodies form immune complexes with nuclear antigens that deposit in the glomeruli, leading to inflammation (glomerulonephritis) and impaired glomerular filtration, which results in proteinuria. Massive proteinuria may subsequently cause hypoalbuminemia. Since albumin maintains plasma oncotic pressure, its reduction facilitates fluid extravasation into the interstitial tissue, manifesting as edema.

Immunosuppressive therapy remains a cornerstone in SLE management. Cyclophosphamide is widely used because it is a potent immunosuppressant that effectively suppresses pathological immune responses, especially in lupus nephritis and other severe manifestations not adequately controlled by corticosteroids alone. Its mechanism of action targets both B and T lymphocytes, which play central roles in the pathogenesis of SLE.

In B cells, cyclophosphamide exerts its effect by alkylating DNA, thereby inhibiting proliferation and differentiation into plasma cells. This results in reduced production of pathogenic autoantibodies, such as anti-dsDNA and ANA, which are involved in immune complex formation. Cyclophosphamide also suppresses immunoglobulin class switching, leading to fewer high-affinity antibodies. Consequently, autoantibody levels and immune complex deposition in glomeruli are reduced, mitigating glomerular injury.

In T cells, cyclophosphamide inhibits proliferation and induces apoptosis, particularly in CD4+ T helper subsets. This decreases the secretion of proinflammatory cytokines (IL-2, IFN-γ, and TNF-α) and limits B-cell stimulation. In addition, suppression of cytotoxic CD8+ T cells further reduces tissue damage mediated by immune responses.

In clinical practice, cyclophosphamide is often combined with the **Cyclo-MENSA protocol**, which integrates cyclophosphamide with MESNA, sodium bicarbonate, and adequate hydration. MESNA (2-mercaptoethane sulfonate sodium) binds the toxic metabolite acrolein, thereby preventing hemorrhagic cystitis. Sodium bicarbonate alkalinizes urine, enhancing drug excretion and reducing urothelial irritation, while hydration provides additional protection.

The standard intravenous pulse therapy includes 0.5–1 g/m² every 4 weeks (NIH protocol) or a lower dose regimen such as the Euro-Lupus protocol (500 mg every 2 weeks for six doses). MESNA is administered intravenously before, during, and after cyclophosphamide infusion for bladder protection. In this case, Cyclo-MENSA was administered outside the recommended protocol, as it was given twice within less than one week. Such deviation may increase the risk of adverse effects, particularly hemorrhagic cystitis associated with acrolein toxicity.

CONCLUSION

Cyclophosphamide therapy that does not adhere to established protocols—for example, when administered too frequently or at excessively short intervals—may significantly increase the risk of acute complications such as hemorrhagic cystitis, myelosuppression, and infection, as well as long-term complications such as infertility and secondary malignancies.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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