Clinical Rheumatology (2023) 42:1723–1725
https://doi.org/10.1007/s10067-023-06611-x

LETTERS OF BIOMEDICAL AND CLINICAL RESEARCH

Rescue treatment of severe lupus myocarditis and proliferative lupus nephritis with immunoadsorption

Sandra Karanović Štambuk[1,2] · Ivan Padjen[1,3] · Nikolina Bašić Jukić[1,2] · Jadranka Šeparović Hanževački[1,4] · Branimir Anić[1,3]

Received: 6 January 2023 / Revised: 19 April 2023 / Accepted: 22 April 2023 / Published online: 27 April 2023
© The Author(s), under exclusive licence to International League of Associations for Rheumatology (ILAR) 2023

Dear Editor!

We report a patient with severe systemic lupus erythematosus (SLE) with myocarditis and proliferative glomerulonephritis successfully treated with immunoadsorption (IA) and intravenous immunoglobulins (IVIG) as an addition to cyclophosphamide.

The 45-year-old Caucasian female with an unremarkable previous medical history presented to her general practitioner with a 2-month history of low-grade fever (up to 37.8 °C), fatigue, polyarthralgias, and unintentional weight loss of 5 kg. Normocytic anemia (Hb 104 g/L) and elevated erythrocyte sedimentation rate (64 mm/h) were revealed as well as left-sided pleural effusion. She received empiric co-amoxiclav due to suspected left-sided pleuropneumonia. Since there was no clinical improvement, a second antibiotic (clarithromycin) was prescribed and the patient was referred for further workup. Meanwhile, she noticed gradually progressive lower extremity oedema and dyspnoea necessitating a visit to the hospital emergency department where she was admitted to the nephrology ward due to newly established renal insufficiency. At the point of admission, the patient had diffuse alopecia, a malar rash, acute heart failure (orthopnoea, sinus tachycardia, systolic precordial murmur) and generalized oedema. Initial workup revealed microcytic anaemia (Hb 95 g/L), an elevated erythrocyte sedimentation rate (105 mm/h), renal insufficiency with nephrotic range proteinuria and active urine sediment, low C3 and C4 complement levels, hypoalbuminemia, increased troponin and NT-proBNP, left-sided pleural effusion, enlarged hypoechogenic kidneys, and ascites. There were no signs of acute coronary syndrome in the electrocardiogram. Echocardiography revealed diffuse myocardial hypocontractility with reduced left ventricular ejection fraction (LVEF) of 31% combined with severe functional mitral and moderate tricuspid regurgitation without signs of endocarditis and a hemodynamically insignificant pericardial effusion. Increased troponin and severe global systolic dysfunction were consistent with acute nonischemic myocardial involvement, coronary artery disease was ruled out by CT-coronarography. A day after admission, in the midst of the COVID-19 pandemic, the patient became febrile, however the SARS-CoV-2 PCR testing came negative. She received appropriate antibiotic treatment according to the blood culture result revealing *Streptococcus pneumoniae* and became afebrile three days thereafter. ANA and anti-dsDNA antibodies in the meantime came positive in a high titer, while antiphospholipid antibodies were negative. Given a high suspicion of SLE the patient was started on 1 mg/kg methylprednisolone, in addition to hydroxychloroquine and supportive treatment. Kidney biopsy revealed lupus nephritis class IV with mild chronic glomerular and tubulointerstitial changes. Cardiac MRI (performed while the patient was already on glucocorticoids, at an estimated glomerular filtration rate, eGFR, of 35 ml/min/1.73m^2) revealed neither replacement fibrosis nor postcontrast imbibition. Despite the lack of typical MRI signs for acute myocardial inflammation, the clinical context with acute heart failure and myocyte injury was consistent with acute lupus myocarditis. Since a comprehensive viral serological workup came negative and the patient had no elements of systemic infection, hypersensitivity reaction, drug cardiotoxicity or other systemic disorders apart from SLE, lupus myocarditis (LM) was the

✉ Ivan Padjen
ivan_padjen@yahoo.ca

1 School of Medicine University of Zagreb, Zagreb, Croatia

2 University Hospital Center Zagreb, Department of Internal Medicine, Division of Nephrology, Arterial Hypertension, Dialysis and Transplantation, Zagreb, Croatia

3 University Hospital Center Zagreb, Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, National Referral Centre for Systemic Lupus Erythematosus and Related Disorders, Zagreb, Croatia

4 University Hospital Center Zagreb, Department of Cardiovascular Diseases, Zagreb, Croatia

most likely diagnosis. LM is a rare but potentially dangerous feature of SLE and its clinical manifestations can vary from unexplained tachycardia, cardiac arrhythmias to fulminant congestive heart failure, with no single clinical or imaging modality being diagnostic [1].

Due to the affection of two major organ systems, three pulses of 500 mg methylprednisone were administered, followed by cyclophosphamide and gradual methylprednisolone taper (cyclophosphamide 500 mg iv, Eurolupus protocol) [2]. Eplerenone was introduced, ACEI was replaced by valsartan sacubitril, SGLT2 inhibitor was added as well as 20% serum albumin substitution. Her 24h diuresis was preserved (around 3 L per day); however, she was constantly in volume overload and heart failure despite high-dose intravenous loop diuretics. Global kidney function was decreased, but stable, with eGFR around 30 ml/min/1.73m^2. Her volume overload progressed with increase in pulmonary congestion and finally pulmonary oedema, so she was temporarily treated with non-invasive mechanical ventilation. Despite all the undertaken measures within the next few days, the patient's myocardial function declined further (LVEF 28%), with an increase in serum troponin and NT-proBNP levels. In order to prevent irreversible myocardial damage and to accelerate her recovery, we introduced IA sessions aiming to specifically remove circulating IgG immunoglobulins, while avoiding potential downsides of classic plasma exchange in an already immunocompromised patient. IA is an extracorporeal treatment modality that removes circulating autoantibodies and immune complexes. It is usually performed using citrate anticoagulation, being associated with a low risk of bleeding. Additionally, no replacement fluid is needed, meaning there is no significant risk of volume overload and serum protein removal other than immunoglobulins [3, 4]. Beneficial effects of extracorporeal treatments have been observed thus far in refractory SLE, pregnancy and during contraindications to standard immunosuppression [5–7]. However, no large randomized trials have been conducted so far to evaluate IA and the experience is limited to open-label observational studies and single case reports [8–10]. We combined IA with slow continuous ultrafiltration (SCUF) procedures to deplete the patient of extra volume since IA procedures do not allow negative fluid balance. Nine IA procedures using Globaffin adsorber system (Fresenius Medical Care, Bad Homburg, Germany), were performed mostly every other day (with 20 grams of IVIG on the days without IA, a total of 9 applications), as well as three SCUF procedures prior to IA sessions. There were no complications of the procedure and the patient's myocarditis and laboratory parameters improved rapidly, with final recovery of global left ventricular systolic function (LVEF 55%) and heart failure symptoms within the following weeks (Table 1). The patient received six cyclophosphamide doses with a glucocorticoid taper. Four months after initial presentation the patient even reached renal remission.

To our knowledge, this is the first report of LM accompanied by nephritis treated with IA. IA may represent a potential choice of rescue therapy of life-threatening SLE, not responding fast enough to standard immunosuppression. In our patient, IA reverted the detrimental course of lupus myocarditis in a patient that had previously been started on a standard cyclophosphamide regimen.

Table 1 Laboratory values during clinical course of the patient

	Admission 28/1/2022	Cyclophosphamide 1st pulse 14/2/2022	After 1st IA 20/2/2022	After 4th IA 1/3/2022	After 6th IA 10/3/2022	After 9th IA 4/2022	6/2022
Serum creatinine (μmol/l) N: 49–90	191	155	188	128	147	119	115
Proteinuria (g/dU) N: < 0.15	5.02	6.9	4.8	NA	4.8	2.0	0.25
Troponin I (ng/l) N: < 5	12.9	56	54.5	11	8	5	5
NTproBNP (ng/l) N: < 300	18312	35000	35000	33573	11317	721	456
ANA N: < 1:100	1:51200	NA	NA	1:6400	1:6400	1:3200	NA
dsDNA (IU/mL) N: negative	3534	NA	NA	705	654	337	NA
C3 (g/l) N: 0.90–1.80	0.45	0.4	NA	0.58	0.7	0.64	0.92
C4 (g/l) N: 0.10–0.40	0.08	0.08	NA	0.12	0.14	0.12	0.24
LVEF N: 54–74%	31%	28%	NA	NA	40-44%	60%	NA

ANA antinuclear antibodies, *dsDNA* double strain DNA antibodies, *IA* immunoadsorption, *LVEF* left ventricular ejection fraction measured by ultrasound, *N* normal range, *NA* not available

Compliance with ethical standards

Consent for publication Informed consent for publication of the case was obtained from the patient.

Disclosures None.

References

1. Miner JJ, Kim AH (2014) Cardiac manifestations of systemic lupus erythematosus. Rheum Dis Clin North Am 40(1):51–60. https://doi.org/10.1016/j.rdc.2013.10.003
2. Houssiau FA, Vasconcelos C, D'Cruz D, Sebastiani GD, de Ramon GE, Danieli MG et al (2002) Immunosuppressive therapy in lupus nephritis: the Euro-Lupus Nephritis Trial, a randomized trial of low-dose versus high-dose intravenous cyclophosphamide. Arthritis Rheum 46(8):2121–2131. https://doi.org/10.1002/art.10461
3. Schneider KM (1998) Plasmapheresis and immunoadsorption: different techniques and their current role in medical therapy. Kidney Int Suppl 64:S61–S65
4. Richter WO, Donner MG, Selmaier A, Hiller E, Schwandt P (1997) Efficacy and safety of immunoglobulin apheresis. ASAIO J 43:53–59
5. Stummvoll GH, Aringer M, Jansen M, Smolen JS, Derfler K, Graninger WB (2002) Immunoadsorption (IAS) as a rescue therapy in SLE: considerations on safety and efficacy. Wien Klin Wochenschr 116:716–724. https://doi.org/10.1007/s00508-004-0232-8
6. Dittrich E, Schmaldienst S, Langer M, Jansen M, Horl WH, Derfler K (2002) Immunoadsorption and plasma exchange in pregnancy. Kidney Blood Press Res 25:232–239. https://doi.org/10.1159/000066343
7. Schmaldienst S, Jansen M, Hollenstein U, Graninger W, Regele H, Horl WH et al (2002) Treatment of systemic lupus erythematosus by immunoadsorption in a patient suffering from tuberculosis. Am J Kidney Dis 39:415–418. https://doi.org/10.1053/ajkd.2002.30564
8. Stummvoll G, Aringer M, Handisurya A, Derfler K (2017) Immunoadsorption in autoimmune diseases affecting the kidney. Semin Nephrol 37:478–487. https://doi.org/10.1016/j.semnephrol.2017.05.020
9. Kronbichler A, Brezina B, Quintana LF, Jayne DRW (2016) Efficacy of plasma exchange and immunoadsorption in systemic lupus erythematosus and antiphospholipid syndrome: a systematic review. Autoimmun Rev 15:38–49. https://doi.org/10.1016/j.autrev.2015.08.010
10. Yang M, Liao C, Zhu Q, Lin X, Yang B, Zhao D et al (2020) Meta-analysis on the efficacy and safety of immunoadsorption for systemic lupus erythematosus among Chinese population. Clin Rheumatol 39:3581–3592. https://doi.org/10.1007/s10067-020-05156-7

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.