Refractory secondary thrombotic microangiopathy in two systemic disorders with remission after autologous haematopoietic stem cell transplantation: a case series

Supplementary materials

Supplementary Table 1. Laboratory results of Patient A at the time of admission in March 2017

Parameter	Value	Reference values
Creatinine (µmol/L)	123	44-97
eGFR (mL/min/1.73 m^2)	51	> 60
UPCR (g/g creatinine)	7.82	< 0.15
Erythrocyturia (x10^6/L)	655	< 10
CRP (mg/L)	56	0-5
SR (mm/h)	82	0-21
Leukocytes (x 10^9/L)	4.6	4.0-10.0
Haemoglobin (g/L)	87	120-150
Platelets (x 10^9/L)	75	150-410
Schistocytes	3.1%	Not defined
LDH (µkat/L)	7.67	< 4.12
Haptoglobin (g/L)	< 0.07	0.3-2.0
ANA	0	0
Anti-dsDNA*	0.68	< 0.35
C3 (g/L)	0.23	0.90-1.80
C4 (g/L)	0.04	0.10-0.40
Cryoglobulins (mg/L)	284	< 100
aCL IgG (AUG)	11	< 5
aPS/PT IgG (AUG)	> 100	< 5

Abbreviations: aCL, anticardiolipin antibodies; ANA, antinuclear antibodies; anti-dsDNA, anti-double-stranded deoxyribonucleic acid antibodies; aPS/PT, anti-phosphatidylserine/prothrombin antibodies; AUG, arbitrary units units (standard units used to quantify aCL and aPS/PT antibodies in our laboratory); C3, complement component 3; C4, complement component 4; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; IgG, immunoglobulin G; LDH, lactate dehydrogenase; SR, erythrocyte sedimentation rate; UPCR, urinary protein-to-creatinine ratio.

* Anti-dsDNA was measured with an in-house FARR-RIA assay. The result is a ratio of antibodies in the supernatants (S) and pellets (P) calculated as (P – S)/(P + S) [1].

Supplementary Table 2. Summary of treatment of SLE exacerbation in Patient A during hospitalization from March to August 2017

Medication	**Dose**	**Date**
Methylprednisolone	3 x 750 mg IV 32 mg per day PO* 3 x 125 mg IV	08/03/2017 – 10/03/2017 Starting on 11/03/2017 25/05/2017 – 27/05/2017
Cyclophosphamide	500 mg IV	13/03/2017
Rituximab	600 mg IV 600 mg IV 600 mg IV 600 mg IV	09/03/2017 17/03/2017 05/04/2017 12/04/2017
Eculizumab	900 mg IV 900 mg IV 900 mg IV 1200 mg IV 1200 mg IV 1200 mg IV	16/06/2017 23/06/2017 30/06/2017 17/07/2017 31/07/2017 14/08/2017
Cyclosporine	2 x 75 mg per day PO†	Starting on 28/06/2017
Intravenous immunoglobulins	420 g IV (all together)	During hospitalization
Plasma exchange	51 procedures‡ (all together)	During hospitalization

Abbreviations: IV, intravenous; PO, orally; SLE, systemic lupus erythematosus.

* Initial dose, subsequently lowered during hospitalization.

† Initial dose, adapted according to trough levels with goal of achieving 70-100 µg/L.

‡ Exchange fluid was fresh frozen plasma in 42 procedures and crystalloids with added albumin in 9 procedures.

Supplementary Table 3. Immunosuppressive and immunomodulatory treatment in Patient B

Medication	Dose	Date
Ravulizumab	3300 mg IV	13/12/2023
	3600 mg IV	28/12/2023
Methylprednisolone	64 mg per day PO	08/03/2024 – 08/04/2024
	60 mg – 0 mg per day PO*	09/04/2024 – 21/06/2024
Rituximab	800 mg IV	22/03/2024
	800 mg IV	29/03/2024
Daratumumab	1800 mg SC	17/05/2024
	1800 mg SC	24/05/2024
	1800 mg SC	31/05/2024
	1800 mg SC	07/06/2024
	1800 mg SC	21/06/2024
	1800 mg SC	28/06/2024
	1800 mg SC	05/07/2024
	1800 mg SC	12/07/2024
	1800 mg SC	02/08/2024
	1800 mg SC	11/10/2024
	1800 mg SC	08/11/2024
Bortezomib	2.9 mg SC	17/05/2024
	2.9 mg SC	24/05/2024
	2.9 mg SC	31/05/2024
	2.9 mg SC	07/06/2024
	2.9 mg SC	21/06/2024
	2.9 mg SC	28/06/2024
	2.9 mg SC	05/07/2024
	2.9 mg SC	12/07/2024
	2.9 mg SC	02/08/2024
	2.9 mg SC	09/08/2024
	2.9 mg SC	16/08/2024
	2.9 mg SC	23/08/2024
	2.9 mg SC	11/10/2024
Lenalidomide	10 mg per day PO	17/05/2024 – 07/06/2024
	10 mg per day PO	21/06/2024 – 12/07/2024
	10 mg per day PO	02/08/2024 – 23/08/2024
	10 mg per day PO	06/09/2024 – 27/09/2024
	10 mg per day PO	11/10/2024 – 01/11/2024
	10 mg per day PO	08/11/2024 – 29/11/2024
	10 mg per day PO	13/12/2024 – 03/01 2025
	10 mg per day PO	10/01/2025 – 31/01/2025
	10 mg per day PO	07/02/2025 – 19/02/2025

Abbreviations: IV, intravenous; PO, orally; SC, subcutaneous.

* Tapering from 60 mg to 0 mg in the given time

Supplementary Table 4. Timeline of disease progression in Patient B with main clinical events and key laboratory findings

Month-Year	**Clinical event**	**Creatinine** µmol/L	**eGFR** ml/min/1.73 m^2	**UPCR** g/g	**MI** g/L	**Hb** g/L	**Platelets** x 10^9/L	**SR** mm/h	**CRP** mg/L
May 2023	▪ Hospitalized for new-onset heart failure, MRI interpreted as myocarditis	81	110	N.A.	N.A.	164	489	N.A.	8
August 2023	▪ First nephrology consultation for proteinuria, high blood pressure, headaches, profuse night sweats and malaise ▪ MI identified	91	96	3.45	3.2	167	516	11	N.A.
November 2023	▪ First kidney biopsy: isolated glomerular TMA ▪ Bone marrow biopsy: no multiple myeloma ▪ Treatment with ravulizumab started in December	90	97	4.52	2.8	152	537	N.A.	8
March 2024	▪ Persistence of high blood pressure, recurrence of malaise and profuse night sweats ▪ Second kidney biopsy: progression, with glomerular and vascular chronic active TMA ▪ ^{18}F-FDG PET/CT scan: lytic lesions in right clavicle and left iliac bone and a soft lesion behind the right clavicle ▪ Treatment with MP and rituximab started	93	89	4.88	2.7	157	568	N.A.	8

Month-Year	**Clinical event**	**Creatinine** µmol/L	**eGFR** ml/min/1.73 m^2	**UPCR** g/g	**MI** g/L	**Hb** g/L	**Platelets** x 10^9/L	**SR** mm/h	**CRP** mg/L
April 2024	▪ Bone biopsy of lesion in right clavicle: confirms plasmacytoma	99	83	2.67	2.4	167	528	N.A.	< 5
May 2024	▪ Start of treatment with daratumumab, bortezomib, lenalidomide	83	107	2.03	2.0	147	466	N.A.	< 5
February 2025	▪ Lenalidomide maintenance discontinued due to diarrhoea	133	58	2.75	2.7	142	430	N.A.	26
June 2025	▪ Biopsy of a retroclavicular lymph node: Castleman disease-like histology	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
August 2025	▪ Worsening of kidney function, high blood pressure, bilateral papilledema, new-onset dyspnoea, profuse sweating and malaise, loss of 5 kg of BW ▪ Third kidney biopsy: progression of chronic active TMA with diffuse acute tubular injury ▪ Brain MRI: intracranial hypertension ▪ Cardiac MRI: cardiomyopathy with diffuse myocardial fibrosis and pericardial effusion ▪ ^{18}F-FDG PET/CT scan: expansion of retroclavicular soft tissue lesion and the left iliac bone lesion ▪ Bone biopsy of lesion in left iliac bone: confirms plasmacytoma	165	44	3.85	4.3	116	508	43	29

Month-Year	**Clinical event**	**Creatinine** µmol/L	**eGFR** ml/min/1.73 m^2	**UPCR** g/g	**MI** g/L	**Hb** g/L	**Platelets** x 10^9/L	**SR** mm/h	**CRP** mg/L
September 2025	▪ AHSCT performed, complicated by *Clostridium difficile* diarrhoea with no subsequent issues	203	35	2.05	4.6	117	536	48	40
May 2026	▪ **Last follow-up:** without major clinical complaints, blood pressure 140/77 mmHg	112	70	1.17	2.0	129	362	22	6

Abbreviations: ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; AHSCT, autologous haematopoietic stem cell transplantation; BW, body weight; CRP, C-reactive protein; CT, computed tomography; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; MI, monoclonal immunoglobulin; MP, methylprednisolone; MRI, magnetic resonance imaging; N.A., not available; PET, positron emission tomography; SR, erythrocyte sedimentation rate; TMA, thrombotic microangiopathy; UPCR, urinary protein-to-creatinine ratio.

Normal ranges of laboratory results: Creatinine 64-104 µmol/L, eGFR > 60 ml/min/1.73m^2, UPCR < 0.15 g/g, MI negative, Haemoglobin 130-170 g/L, Platelets 150-410 x 10^9/L, SR < 15 mm/h, CRP < 5 mg/L.

Supplementary references

1. Žigon P, Lakota K, Čučnik S, Švec T, Ambrožič A, Sodin-Šemrl S, et al. Comparison and evaluation of different methodologies and tests for detection of anti-dsDNA antibodies on 889 Slovenian patients' and blood donors' sera. Croat Med J. 2011;52:694–702. doi:10.3325/cmj.2011.52.694.