Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

THE AMERICAN JOURNAL of MEDICINE®

Comments on COVID-19 and AL Amyloidosis, the Missing Links

To the Editor:

Crees and Stockerl-Goldstein[1] recently reviewed the management of light chain (AL) amyloidosis during the coronavirus disease 2019 (COVID-19) pandemic. While the literature discussed by authors is pertinent, certain lacunae in the diagnosis, prevention, and management need attention.

Monoclonal protein in AL amyloidosis could be secreted by either plasma cells or, rarely, B-cells.[2] In addition to direct organ toxicity due to tissue deposition, monoclonal protein could cause 1) immunoparesis leading to increased risk and severity of infections, and an impaired vaccination response; and 2) coagulation disturbance leading to bleeding, thrombosis, or reduced antithrombin levels.[3] COVID-19 has been associated with a potent thrombo-inflammatory milieu that causes thromboembolic complications.[3] An overlapping multiorgan involvement in AL amyloidosis and COVID-19 has several implications with respect to the drug administration.[3]

In light of these observations and the current evidence, additional points are addressed below:

1. Diagnostic challenges for AL amyloidosis during COVID-19.
2. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) booster vaccination in patients with AL amyloidosis.
3. Management of indolent B-cell non-Hodgkin lymphoma-associated AL amyloidosis during the COVID-19 pandemic.
4. Management and response assessment in patients with AL amyloidosis infected with COVID-19.
5. Toxicity consideration of anti-COVID drugs in patients with AL amyloidosis.
6. Therapeutic implications of coagulation derangement of the 2 disorders.

These points are discussed in the Table[3-6] under 3 heads: 1) management of AL amyloidosis *during* COVID-19 pandemic; 2) management of AL amyloidosis *in* patients with COVID-19; and 3) management of COVID-19 *in* patients with AL amyloidosis.

Ankur Jain, MBBS, MD, DM (Clinical haematology)
Department of Haematology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

https://doi.org/10.1016/j.amjmed.2022.02.011

Funding: None.
Conflicts of Interest: None.
Authorship: The sole author is responsible for all content.

Requests for reprints should be addressed to Ankur Jain, MBBS, MD, DM, Department of Haematology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India.
E-mail address: drankur589@yahoo.in

Table A Summary of Additional Management Considerations of AL Amyloidosis During COVID-19 Pandemic

Management of AL Amyloidosis During COVID-19	Comment (s)	Suggestion (s)
Prevention measures		
Prophylactic drugs[3]	1. Uncertain benefit of HCQ and macrolides 2. Cardiac (HCQ and macrolides) and renal (HCQ) toxicity	Avoid using HCQ/macrolide prophylaxis for AL amyloidosis, particularly those with cardiorenal involvement.
SARS-Cov-2 vaccination[3,4]	Rituximab causes prolonged B-cell depletion lasting 6-12 months after the last dose Booster vaccination (mRNA vaccines) could augment antibody response following the second dose in patients with hematological malignancies[4]	Repeat SARS-CoV-2 vaccination at least 6-months after the last Rituximab dose Consider booster vaccination for patients with AL amyloidosis who have completed the 2-dose schedule.
Nephrological considerations[3]	Maintain COVID appropriate behaviour in the dialysis units	1. Stagger patients requiring dialysis 2. Consider peritoneal dialysis after nephrology consultation
Diagnostic considerations[3]	Avoid organ biopsies for the diagnosis of AL amyloidosis	Consider biopsy from alternate sites (abdominal fat pad)
Therapeutic measures		
Treatment modifications[3]	CyBorD	1. Reduce dexamethasone dose from 40 mg/week to 20 mg/week 2. Use renal-modified dose of cyclophosphamide
	DARA-based regimens	Consider 90-minute IV infusion following an uneventful first infusion, particularly in countries where SC formulation is not available
	HSCT and renal transplant cause prolonged immunosuppression	Defer both autologous HSCT and renal transplant for patients with AL amyloidosis, if feasible.
	B-NHL associated AL amyloidosis 1. Purine analogues cause prolonged lymphodepletion. 2. Rituximab can cause prolonged B-cell lymphopenia. 3. IV Rituximab infusions needs hospitalisation	1. Consider alkylator-based rituximab combinations 2. Consider 2-monthly infusions instead of 3-monthly infusions during maintenance. $$$ 3. Consider SC rituximab
Management of AL amyloidosis in patients infected with COVID-19		
Therapeutic measures[3]	Chemoimmunotherapy is potentially immunosuppressive	1. Withhold the treatment of AL amyloidosis after the detection of COVID-19 2. Resume treatment once COVID-19 is cured.
General measures[3]	COVID-19 could cause cardiorenal decompensation in AL amyloidosis patients	Consider meticulous supportive care
Response assessment[2,3]	1. COVID-19 infection could cause elevation of free kappa and lambda light chains[2] 2. COVID-19 could cause renal impairment and elevation of cardiac biomarkers	Re-evaluate for hematological and organ response after COVID-19 is cured
Management of COVID-19 in patients with AL amyloidosis		
Anti-COVID medications[3,5,6]	1. Remdesivir - cardiac and renal toxicity 2. Baricitinib - renal toxicity[5] 3. Molnupiravir - no cardiorenal toxicities[6] 4. Tocilizumab - may cause cardiac decompensation	1. Cautious use in patients with cardiorenal amyloidosis 2. Cautious use in patients with renal amyloidosis 3. Consider using as per local approvals 4. Cautious use in patients with cardiac amyloidosis
Hemostatic considerations[3]	1. Patients with AL amyloidosis have an inherent bleeding tendency 2. Renal excretion of LMWH 3. Reduced efficacy of heparin due to low AT	1. Judicious use of anti-coagulation 2. Anti-Xa-based LMWH dosing 3. Consider use of dabigatran or argatroban

AL = light chain; AT = antithrombin III; COVID-19 = Coronavirus disease 2019; CyBorD = cyclophosphamide, bortezomib, dexamethasone; DARA = daratumumab; HCQ = hydroxychloroquine; HSCT = hematopoietic stem cell transplant; IV = intravenous; LMWH = low-molecular-weight heparin; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = subcutaneous.

References

1. Crees ZD, Stockerl-Goldstein K. COVID-19 and light chain amyloidosis, adding insult to injury [online ahead of print]. *Am J Med* 2022 January 23. https://doi.org/10.1016/j.amjmed.2022.01.005.
2. Jain A, Haynes R, Kothari J, Khera A, Soares M, Ramasamy K. Pathophysiology and management of monoclonal gammopathy of renal significance. *Blood Adv* 2019;3(15):2409–23.
3. Jain A, Ramasamy K. Potential 'significance' of monoclonal gammopathy of 'undetermined significance' during COVID-19 pandemic. *Blood Cells Mol Dis* 2020;85:102481.
4. Avivi I, Luttwak E, Saiag E, et al. BNT162b2 mRNA COVID-19 vaccine booster induces seroconversion in patients with B-cell non-Hodgkin lymphoma who failed to respond to two prior vaccine doses. *Br J Haematol* 2022;196(6):1329–33.
5. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with Covid-19. *N Engl J Med* 2021;384(9):795–807.
6. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, et al. Molnupiravir for oral treatment of Covid-19 in non-hospitalized patients. *N Engl J Med* 2022;386(6):509–20.