

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



To the Editor:

Crees and Stockerl-Goldstein<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> COVID-19 has been associated with a potent thrombo-inflammatory milieu that causes thromboembolic complications.<sup>3</sup> An overlapping multiorgan involvement in AL amyloidosis and COVID-19 has several implications with respect to the drug administration.<sup>3</sup>

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<sup>3-6</sup>](#) 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.

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**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 <sup>3</sup>	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 <sup>3,4</sup>	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 <sup>4</sup>	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 <sup>3</sup>	Maintain COVID appropriate behaviour in the dialysis units	1. Stagger patients requiring dialysis 2. Consider peritoneal dialysis after nephrology consultation
Diagnostic considerations <sup>3</sup>	Avoid organ biopsies for the diagnosis of AL amyloidosis	Consider biopsy from alternate sites (abdominal fat pad)
Therapeutic measures Treatment modifications <sup>3</sup>	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.
	<u>B-NHL associated AL amyloidosis</u> 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. <sup>555</sup> 3. Consider SC rituximab
Management of AL amyloidosis in patients infected with COVID-19 Therapeutic measures <sup>3</sup>	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 <sup>3</sup>	COVID-19 could cause cardiorenal decompensation in AL amyloidosis patients	Consider meticulous supportive care
Response assessment <sup>2,3</sup>	1. COVID-19 infection could cause elevation of free kappa and lambda light chains <sup>2</sup> 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 <sup>3,5,6</sup>	1. Remdesivir - cardiac and renal toxicity 2. Baricitinib - renal toxicity <sup>5</sup> 3. Molnupiravir - no cardiorenal toxicities <sup>6</sup> 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 <sup>3</sup>	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**

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