COVID-19 among Malaysian patients with systemic lupus erythematosus on hydroxychloroquine

We read with interest the letter by Mathian A *et al*[1] describing the clinical course of COVID-19 in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine. The COVID-19 Global Rheumatology Alliance registry[2] shows that 19 (17%) of 110 patients with rheumatic diseases who have been diagnosed with COVID-19 as of 1 April 2020 were patients with lupus. Bozzalla Cassione *et al*,[3] Romão *et al*[4] and Ye *et al*,[5] respectively, described patients with SLE in their papers. The latest paper by D'Silva *et al* reported ten cases of lupus in their cohort.[6] We would like to share the clinical course of COVID-19 among patients with SLE in Malaysia.

As of 30 March 2020, there were five cases of SLE from a total of 2626 cases of COVID-19 in Malaysia. Clinical data were obtained through a review of medical records. COVID-19 was diagnosed in the patients based on a positive result on a reverse transcriptase PCR testing that detected severe acute respiratory syndrome coronavirus 2 from nasopharygeal swab specimen. All five patients were women with a mean age of 52.80±4.46 years and a mean disease duration of 13.20±3.92 years. All the patients were on long-term hydroxycholoroquine at baseline. Two patients were on conventional disease modifying antirheumatic drugs (DMARDs) (sulfasalazine and azathioprine), and one patient was on biological DMARDs (belimumab). Only one patient was on prednisolone during the diagnosis of COVID-19 infection. Majority of the patients were hypertensive and obese; 60% of them were on ACE inhibitor or angiotensin II receptor blocker treatment. The most common presentations were fever and cough. One patient was having active lupus shortly before COVID-19 diagnosis, while two patients were having flares of disease concurrently with COVID-19. Most patients have lymphopenia (lymphocyte count $<1500\,mm^3$). Radiologically,

Table 1 Demographic, clinical characteristics, outcome and laboratory findings

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Demographic					
Age (years)	46	50	57	53	58
Gender	Female	Female	Female	Female	Female
SLE					
SLE manifestations	Malar rash, arthritis, ANA, dsDNA	Malar rash, photosensitivity arthritis, Raynaud's phenomenon, ANA, dsDNA	Arthritis, autoimune haemolytic anaemia, low complement, ANA, dsDNA	Discoid rash, photosensitivity, oral ulcer, arthritis, leucopenia	Arthritis, pancytopenia, oral ulcer, ANA
Disease activity	Stable	Flare during admission	Flare during admission	Active	Stable
Hydroxychloroquine at baseline	Yes, 8 years	Yes, 12 years	Yes, 12 years	Yes, 20 years	Yes, 14 years
Prednisolone at baseline	No	No	No	Yes, 10 mg daily	No
Medications	Sulfasalazine	Azathioprine	No	Intravenous belimumab	No
ACE-I/ARB	Losartan	No	Losartan	Perindopril	No
Comorbidities	Hypertension, Obesity	No	Hypertension, dyslipidaemia, obesity	Hypertension, diabetes, obesity	Hypertension, Graves' disease postradioactitive iodine, obesity
Body Mass Index (kg/m^2)	35.2	20.5	32.3	36.8	30.4
Clinical					
Symptoms at disease onset	Fever, diarrhoea, cough, runny nose, dyspnoea	Fever, cough, multiple cervical lymph nodes	Lethargy, loss of appetite, arthralgia, haemolytic anaemia	Fever, cough dyspnoea	Fever, cough, myalgia
Imaging features	Bibasal lungs consolidation	Bilateral lower zone recticular opacities	Focal air space opacities in the right middle and lower zones	Bilateral air space opacities in the midzone and right base	Right perihilar infiltrates
Clinical stage of COVID-19	5 (ARDS)	3B	3B	5 (intubated)	3A
Treatment					
Hydroxychloroquine	Yes	Yes	Yes	Yes	Yes
Lopinavir/ritonavir	No	Yes	Yes	Yes	Yes
Subcutaneous interferon beta	No	No	No	Yes	No
Intravenous antibiotic	Yes Augmentin/azithromycin/ piperacillin/tazobactam	Yes Ceftriaxone	Yes Piperacillin/tazobactam	Yes Ceftriaxone	No
Intravenous hydrocortisone/intravenous methylprednisolone	No	Yes	Yes	Yes	No
Outcomes	Death	Home well	Home well	Home well	Home well

Clinical staging of COVID-19: 1, asymptomatic; 2, symptomatic, no pneumonia; 3, symptomatic, pneumonia; A, without fever; B, with fever; 4, symptomatic, pneumonia, requiring supplemental oxygen; 5, critically ill with multiorgan failure.
ACE-I, ACE inhibitor; ANA, antinuclear antibody; ARB, angiotensin II receptor blocker; ARDS, acute respiratory distress syndrome; dsDNA, double-stranded DNA; od, once a day; SLE, systemic lupus erythematosus.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2020-218154 on 31 July 2020. Downloaded from http://ard.bmj.com/ on January 16, 2021 by guest. Protected by copyright.

Table 2 Laboratory findings

Laboratory findings	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
White cell count (10^3/µL)	7.90	2.95	4.20	7.9	5.50
Differential count (10^3/µL)					
Absolute lymphocyte count	0.72	0.50	1.87	0.80	1.50
Platelet count (10^3/µL)	296	353	332	151	232
Haemoglobin (g/L)	139	94	73	129	129
Albumin (g/L)	40	34	42	24	44
Alanine aminotransferase (U/L)	24	13	29	19	37
Aspartate aminotransferase (U/L)	42	30	36	24	27
Lactate hydrogenase (U/L)	344	420	496	–	–
Sodium (mmol/L)	136	133	138	135	136
Potassium (mmol/L)	4.2	3.9	4.4	3.6	3.7
Urea (mmol/L)	3.5	2.9	10.2	3.5	8.3
Creatinine (µmol/L)	70	55	117	56	81

all the patients had pneumonia in the chest X-rays. Demographic characteristics, clinical features, treatments and outcomes of five cases are illustrated in tables 1 and 2.

The ongoing, rapidly evolving COVID-19 pandemic poses a real threat to patients with SLE. As illustrated in the cases, COVID-19 is fast becoming a cause for morbidity and mortality in patients with SLE who are immunosuppressed. COVID-19 might mimic SLE flare as well as occur concurrently with SLE flare as demonstrated by cases 2 (arthritis) and 3 (autoimmune haemolytic anaemia).

Early diagnosis and treatment of COVID-19 is of paramount importance to ensure a good outcome. As illustrated by the cases, all patients presented with moderately severe to severe COVID-19 but responded well to treatment except the first case, which presented very late and was diagnosed posthumously. Only case 4 needed invasive ventilation and this patient received intravenous belimumab 1 week prior to contracting COVID-19. She needed more intensive treatment compared with the others. The role of belimumab in the clinical course of COVID-19 awaits further research. Three of them were also received intravenous corticosteroids during their hospitalisations; two received intravenous hydrocortisone as treatment of their concurrent SLE flares. Interestingly, case 3 received intravenous methylprednisolone for severe haemolytic anaemia at a very early stage; her COVID-19 was not worsening with this early use of corticosteroids but responded to standard treatment and she recovered well. The role of corticosteroids in the treatment of COVID-19 is controversial.

In summary, COVID-19 among our patients with SLE on hydroxychloroquine has a severe disease course needing aggressive therapy. Background hydroxychloroquine treatment for SLE did not prevent COVID-19 among our patients. Early diagnosis and treatment of COVID-19 resulted in good outcome in our patients with SLE.

Cheng Lay Teh ,[1] **Yaw Kiet Cheong,**[1] **Wan Rosmaiza Wan Musa,**[2] **Sharifah Aishah Wan Mohd Akbar,**[1] **Noraini Mat Husin,**[3] **Suk Chyn Gun**[4]

[1]Department of Medicine, Sarawak General Hospital, Kuching, Sarawak, Malaysia
[2]Department of Medicine, Hospital Putrajaya, Putrajaya, Malaysia
[3]Department of Medicine, Hospital Ipoh, Ipoh, Perak, Malaysia
[4]Department of Medicine, Hospital Tuanku Ja'afar Seremban, Seremban, Negeri Sembilan, Malaysia

Correspondence to Dr Cheng Lay Teh, Medicine, Sarawak General Hospital, Kuching 93450, Malaysia; tehchenglay@yahoo.com

Acknowledgements The authors thank the Director General of Health, Malaysia, for technical support for this research paper.

Contributors CLT and SCG: study conception and design. YKC, WRWM, SAWMA and NMH: data acquisition and data analysis. CLT, YKC and SCG: manuscript preparation and critical revision. All authors read and approved the final version.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.

Check for updates

To cite Teh CL, Cheong YK, Wan Musa WR, *et al*. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218154

Received 29 May 2020
Accepted 31 May 2020

Linked

► http://dx.doi.org/10.1136/annrheumdis-2020-218173

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-218154

ORCID iD
Cheng Lay Teh http://orcid.org/0000-0001-7897-3994

REFERENCES

1 Mathian A, Mahevas M, Rohmer J, *et al*. Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine. *Ann Rheum Dis* 2020;annrheumdis-2020-217566.
2 Gianfrancesco MA, Hyrich KL, Gossec L, *et al*. Rheumatic disease and COVID-19: initial data from the COVID-19 global rheumatology alliance provider registries. *Lancet Rheumatol* 2020. doi:10.1016/S2665-9913(20)30095-3. [Epub ahead of print: 16 Apr 2020].
3 Bozzalla Cassione E, Zanframundo G, Biglia A, *et al*. COVID-19 infection in a northern-Italian cohort of systemic lupus erythematosus assessed by telemedicine. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217717. [Epub ahead of print: 12 May 2020].
4 Romão VC, Cruz-Machado AR, Fonseca JE. No evidence so far on the protective effect of hydroxychloroquine to prevent COVID-19: response to the Comment by Joob and Wiwanitkit. *Ann Rheum Dis* 2020:annrheumdis-2020-217665.
5 Ye C, Cai S, Shen G, *et al*. Clinical features of rheumatic patients infected with COVID-19 in Wuhan, China. *Ann Rheum Dis*;26:annrheumdis-2020-217627.
6 D'Silva KM, Serling-Boyd N, Wallwork R, *et al*. Clinical characteristics and outcomes of patients with coronavirus disease 2019 (COVID-19) and rheumatic disease: a comparative cohort study from a US 'hot spot'. *Ann Rheum Dis*;16:annrheumdis-2020-217888.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2020-218154 on 31 July 2020. Downloaded from http://ard.bmj.com/ on January 16, 2021 by guest. Protected by copyright.