

Letter to the Editor

Lung ultrasound signs and cytokine profile in Covid-19 patients: a case series

Dear Editor,

We read with interest the article by Wang et al¹ in which they managed a case of COVID-19 critically ill patient treated with tocilizumab, an anti-interleukin-6 drug. The case report presents several reasons for interest^{2,3}. The authors propose a hypothesis of "cytokine storm" that has been successfully taken up by several authors, and that has had a vast fortune in the COVID-19 literature^{4,5}. In our case series (Table I) we found no differences in the cytokine profile between the surviving and deceased patients. In particular, the levels of IL-6 at intensive care unit (ICU)

Table I. Compared characteristics between discharged or transferred and deceased ICU patients suffering from COVID-19. In brackets, the 1st and 3rd percentiles or percentage.

	Survivors (n = 13)	Non-survivors (n = 4)	p-value
Age (years)	63.0 [56.0-72.0]	68.0 [63.0-75.5]	0.281
Sex (male)	11 (84.6%)	2 (50%)	0.219
Days from symptoms onset	10.0 [6.00-13.0]	10.0 [6.50-13.8]	1.000
Dyspnea	10 (76.9%)	3 (75%)	1.000
Cardiopulmonary comorbidities	5 (38.5%)	3 (75%)	0.294
Lymphocytes absolute count reduced	10 (76.9%)	4 (100%)	0.541
PiO ₂ /FiO ₂	120 [100-238]	115 [90.0-140]	0.427
SaO ₂ (%)	95.0 [94.0;-9.0]	93.0 [90.0-96.5]	0.390
FiO ₂ (%)	60.0 [21.0-100]	60.0 [53.8-70.0]	0.728
Chest X-ray suggestive	11 (84.6%)	3 (75%)	1.000
LU positive	1 (7.7%)	1 (25%)	0.426
LU intermediate	10 (76.9%)	3 (75%)	1.000
LU negative	2 (15.4%)	0	1.000
Light beam sign	1 (7.7%)	1 (25%)	0.426
B lines separated	13 (100%)	3 (75%)	0.235
B lines coalescent	10 (76.9%)	2 (50%)	0.538
Irreg. or fragmented pleural line	13 (100%)	4 (100%)	*
Small peripheral consolidations	8 (61.5%)	4 (100%)	0.261
Large consolidation	3 (23.1%)	0	0.541
Large effusion	0	1 (25%)	0.235
LU focal	2 (15.4%)	0	1.000
LU multifocal monolateral	1 (7.7%)	0	1.000
LU multifocal bilateral	11 (84.6%)	4 (100%)	1.000
Days from admission (days)	2.00 [1.00-3.00]	2.50 [1.75-4.00]	0.408
CRP (mg/dL)	151 [58.0-188]	144 [83.5-239]	0.571
Procalcitonin (ng/mL)	0.21 [0.14-0.51]	0.21 [0.14-0.51]	0.251
Creatine-kinase (ng/mL)	173 [110-298]	182 [140-309]	0.794
LDH (U/L)	766 [657-1030]	679 [536-928]	0.571
White Cells Count (× 10 ³ /μL)	6.11 [4.96-15.0]	5.42 [4.44-6.36]	0.365
Neutrophils Count (× 10 ³ /μL)	4.77 [4.32-8.17]	4.60 [3.60-5.78]	0.461
Lymphocytes (μL)	370 [290-480]	425 [352-502]	0.692
IL-6 (pg/mL)	92.0 [53.0-164]	104 [78.5-169]	1.000

Table Contiend

Table 1 (Continued). Compared characteristics between discharged or transferred and deceased ICU patients suffering from COVID-19. In brackets, the 1st and 3rd percentiles or percentage.

	Survivors (n = 13)	Non-survivors (n = 4)	p-value
T cells CD3+ (/μL)	238 [165-418]	232 [206-304]	0.734
T cells CD4+ (/μL)	165 [108-248]	190 [157-219]	0.821
T cells CD8+ (/μL)	67.0 [39.0-78.0]	44.0 [39.8-88.5]	0.821
CD4+/CD8+ ratio	3.20 [1.90-4.80]	3.20 [1.90-4.75]	0.821
NK cells CD56+ CD16+ (/μL)	36.5 [27.5-48.8]	30.0 [20.5-50.5]	0.499
Lymph. T act CD3+ HLA-DR+ (/μL)	35.0 [26.0-47.0]	26.5 [16.8-89.2]	0.650
Lymph. B CD19 (/μL)	67.5 [38.8-105]	150 [86.0-172]	0.612
Tocilizumab	11 (84.6%)	3 (75%)	1.000
Hydroxychloroquine	12 (92.3%)	4 (100%)	1.000
Darunavir	10 (76.9%)	3 (75%)	1.000
Steroid	8 (61.5%)	3 (75%)	1.000
Amiodarone	3 (23.1%)	1 (25%)	1.000
Lopinavir/ritonavir	5 (38.5%)	1 (25%)	1.000

*All cases had irregularities in the pleural line. *Abbreviations:* LU (lung ultrasound); CRP (C reactive protein); LDH (lactate dehydrogenase); IL-6 (interleukin 6).

admission presented substantially comparable values in the two groups of patients. Tocilizumab has been widely used in our critically ill patients, yet we did not find a striking effect. The same can be claimed for the other drugs used. Liu et al⁶ highlighted a similar increase in IL-6 found by Wang et al¹ and a recent meta-analysis seems to agree with this hypothesis⁷. Yet we suggest that there are insufficient elements to assign IL-6 a direct role in the determinism of death of critically ill patients COVID-19^{8,9}. IL-6 could represent only an association, a manifestation of an increased inflammatory response, and, therefore, have a positive prognostic meaning, rather than, conversely, negative. In our analysis, the use of tocilizumab does not seem to change the clinical course of these patients.

Although we did not find an association between the cytokine profile and lung ultrasound (LU) patterns in our sample, we underline the finding of pleural line alterations in all patients. This finding highlights the role of LU in the diagnosis of COVID-19^{10,11}.

Ultimately, we consider the hypothesis of Wang et al¹ interesting, but we suggest that we are still far from having evidence of its effective response.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethical Approval

Ethical approval was obtained from Comitato Etico Unico Regionale (CEUR-ID #3336) on 23rd June 2020.

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