BEHIND THE CYTOKINES STORM OF SEVERE COVID-19, COULD BE HIDDEN MACROPHAGE ACTIVATION SYNDROME – A CASE REPORT

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BACKGROUND

Our objective was to point out that macrophage activation syndrome (MAS) is a serious complication in COVID-19, which must be early diagnosed once immediate treatment can contribute to patient's survival.

CASE REPORT

On May 4, 2020, a 73-year-old man was admitted to the hospital with COVID-19 (on the 10th day of disease evolution). He was given oseltamivir, ivermectin, azithromycin and hydroxychloroquine by a local clinic empirically at the first day. He had history of hypertension, diabetes, chronic kidney disease and gout. On admission he was febrile 37.8 °C and oxygen saturation (Sats) oscillating between 88 to 94% (breathing ambient air/prone position). Computed tomography (CT) showed multiple ground-glass opacities dispersed predominantly peripheral pulmonary lobes affecting about 50% (Figure 1A). Laboratory results (Table 1) reflected a significant lymphocytopenia, anemia and mild thrombocytopenia. His inflammatory markers were elevated: high-sensitive C-reactive protein (hsCRP) 159 mg/L (0–3), a mild high erythrocyte sedimentation rate (ESR) 48 (4.5–11) mm/h, and D-dimer 2.88 µ/mL (<0–0.5). On the same day of admission heparin in full dose, methylprednisolone 80 mg and ceftriaxone were given. On May 6, drop in hemoglobin was noted and erythrocyte sedimentation rate did not increase proportionally, ferritin 1136 (22–320) ng/mL and a myelogram had done. The myelogram had shown hemophagocytic activity (Figure 2). On May 7, the patient developed shortness of breath and his Sats decreased to 88% when breathing ambient air, and 92–94% on 10 L of oxygen by nasal catheter. A CT was repeated and showed progressing infiltrations bilaterally reaching about 80% (Figure 1A). The patient was admitted to the ICU, ceftriaxone was changing by Piperacilina-tazobactam and teicoplanin, 2g/kg IVIg was started, and methylprednisolone was increased for 1000 mg on the first day, 250 mg on the second and third day, and then maintained with 80 mg/day completing ten days. After the last IVIg infusion, CT has repeated and already showing improvement (Figure 1B). Supplemental oxygen was discontinued on May 14, and his Sats level returned to 97–98% on ambient air. The result of laboratory tests on May 14 showed recovered lymphocyte count and reduced hsCRP 2.39 mg/L.

Figure 1. Chest computed tomography scan of patient: (A) 1st day of admission in the hospital and three days after, (B) before and after infusion intravenous immunoglobulin with days of illness, (C) day after the last day of infusion intravenous immunoglobulin and eight days after.

Figure 2. Myelogram. (A) and (B) both images show histiocytes phagocytosing red blood cells; (C) image shows a histiocyte phagocytosing a leukocyte; however, the leukocyte degeneration does not allow what kind of leukocyte is it; and (D) shows histiocyte in phagocytic activity with the presence of two polymorphonuclear cells (red arrows) and one red cell (blue arrow).

Table 1. Laboratory tests.

Measures (Normal ranges)	Illness days								
	5th	1st Hosp 10th	11th	12th	1st ICU 13th	14th	18th	20th	26th
WBC ($10^9/L$) 4.5–11	4.8	7.5	11.5	9.9	8.7	9.8	7.8	8.2	10.4
RBC ($10^{12}/L$) 4.5–5.9	4.53	3.48	3.63	3.47	3.44	3.8	3.34	3.6	3.31
Hb (g/dL) 13.5–17.5	13.5	10.8	11.2	10.8	10.5	11.5	10.4	11	10.4
PLT ($10^9/L$) 150–450	163	109	131	160	172	205	224	252	292
NEUT ($10^9/L$) 1.6–7.7	2.6	6.3	9.6	8.81	7.48	8.42	6.2	6.3	9.15
LYM ($10^9/L$) 1.1–3.9	1.6	0.6	1.38	0.59	0.78	0.68	0.99	1.19	1.0
ESR (mm/h) < 20	NR	48	69	36	NR	NR	NR	35	NR
hsCRP (mg/L) 0–3	11.94	159.1	187.8	124.7	92.7	80.4	14.3	2.39	3.5
SF (ng/mL) 22–320	426	NR	1136	1300	876	869	585	NR	NR
Tn (ng/L) 0–14	NR	NR	14	10	NR	NR	NR	NR	NR
LDH (U/L) 120–246	180	386	NR	NR	360	375	NR	256	190
ALB (g/dL) 3.4–4.8	4.1	2.8	NR	NR	2.4	NR	NR	NR	NR
TBIL (mg/dL) 0.3–1.2	NR	NR	0.23	NR	0.3	0.4	NR	NR	NR
ALT (U/L) 6–41	24	17	16	NR	19	29	NR	25	NR
AST (U/L) 15–37	34	35	38	NR	42	52	NR	24	NR
γ -GT (U/L) 15–85	NR	NR	141	NR	179	NR	NR	NR	NR
CRE (mg/dL) 0.5–1.3	0.9	2.23	1.99	1.64	1.8	1.69	1.66	1.63	1.44
Ur (mg/dL) 15–50	40	60	61	62	58	49	80	80	82
CK (U/L) 39–308	55	NR	115	NR	NR	NR	NR	NR	43
D-dimer ($\mu g/mL$) 0–0.5	2	2.88	> 20	2.61	NR	1.59	1.81	1.35	0.97
FIB (mg/dL) 200–400	347	NR	616	647	NR	NR	NR	NR	NR

WBC: white blood cell count; RBC: red blood cell count; Hb: hemoglobin; PLT: platelet count; NEUT: absolute neutrophil count; LYM: absolute lymphocyte count; ESR: erythrocyte sedimentation rate; NR: not realized; hsCRP: hypersensitive C-reactive protein; SF: serum ferritin; Tn: troponin; LDH: lactate dehydrogenase; ALB: albumin; TBIL: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; γ -GT: γ -glutamyltransferase; CRE: creatinine; Ur: urea; CK: creatine kinase; FIB: fibrinogen.

CONCLUSION

It is necessary to keep in mind that severe COVID-19 is a hyperferritinemic syndrome and can degenerate into MAS without the classic signs of primary MAS, such as organomegalies. The assessment of each patient individually and the interpretation of clinical and laboratory signs are the key to for early and correct diagnosis, which implies an effective therapy.

KEYWORDS

COVID-19, MAS, IVIG, Methylprednisolone.