Ren et al. Military Medical Research (2020) 7:36
https://doi.org/10.1186/s40779-020-00267-3

MMR MILITARY MEDICAL RESEARCH

LETTER TO THE EDITOR Open Access

Comparison of clinical laboratory tests between bacterial sepsis and SARS-CoV-2-associated viral sepsis

Chao Ren[1,2,3†], Ren-Qi Yao[1,2,3†], Di Ren[1,2†], Ying Li[1], Yong-Wen Feng[1*] and Yong-Ming Yao[1,3*]

Abstract

Sepsis is a life-threatening condition that is characterized by multiple organ dysfunction due to abnormal host response to various pathogens, like bacteria, fungi and virus. The differences between viral and bacterial sepsis are indeed of great significance to deepen the understanding of the pathogenesis of sepsis, especially under pandemics of SARS-CoV-2 infection.

Keywords: SARS-CoV-2, COVID-19, Sepsis, Bacteria, Virus, Infection, Host response

Dear editor,

The pandemics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have become a world health crisis that cause significant loss of life. The dysregulated host response to SARS-CoV-2 appears to be associated with the severity and poor outcomes of coronavirus disease 2019 (COVID-19) patients [1], hinting the critical involvement of SARS-CoV-2-induced sepsis based on Sepsis 3.0 definition [2–4]. The development of sepsis accounts for one of the leading causes of death in patients admitted to intensive care units (ICU), but evidences on viral sepsis remain scarce in current clinical practices, let alone its differences with bacterial sepsis. Given the pandemics of SARS-CoV-2 infection [5], the differences between viral and bacterial sepsis are indeed of great significance to deepen the understanding of the pathogenesis of sepsis.

In this study, we obtained the clinical data from two cohorts up to May 13, 2020, including 41 critically ill COVID-19 patients from the Third People's Hospital of Shenzhen and 194 non-COVID-19 patients admitted to ICU of the Second People's Hospital of Shenzhen, China. Demographic characteristics, comorbidities, and laboratory findings on ICU admission and clinical outcomes were collected. Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were calculated within the first 24 h since ICU admission. The bacterial and viral sepsis were identified by blood culture and metagenomic next-generation sequencing.

Twenty-one patients with SARS-CoV-2-induced sepsis and 46 patients with bacterial sepsis were finally recruited (Additional file 2). The median age was 64.0 years (IQR, 60.5–68.0) and 65.5 years (IQR, 49.3–77.3) for patients of SARS-CoV-2-induced sepsis and bacterial sepsis, respectively (Additional file 1). The prognostic scoring system, including SOFA [6.0 (IQR, 4.0–9.0) vs. 4.0 (IQR, 3.5–5.0), $P = 0.01$] and APACHE II [17.0 (IQR, 13.0–20.3) vs. 8.0 (IQR, 6.5–9.5), $P < 0.001$] were consistently higher among patients with bacterial sepsis than those with SARS-CoV-2-induced sepsis. Meanwhile, ICU mortality rates were significantly higher in patients with bacterial sepsis than those with viral sepsis [34.8% (16/46) vs. 4.8% (1/21), $P = 0.013$].

As presented in Table 1, absolute counts of T lymphocytes, cytotoxic T lymphocytes (Tc), and helper T lymphocytes (Th) were significantly lower among patients

* Correspondence: fengyongwen2008@126.com; c_ff@sina.com
†Chao Ren, Ren-Qi Yao and Di Ren contributed equally to this work.
[1]Department of Critical Care Medicine, the Second People's Hospital of Shenzhen, Shenzhen 518035, Guangdong, China
Full list of author information is available at the end of the article

Table 1 Comparison of laboratory findings between SARS-CoV-2- and bacteria-induced septic patients admitted to ICU

Item	Normal range	Total ($n = 67$)	SARS-CoV-2-induced sepsis ($n = 21$)	Bacteria-induced sepsis ($n = 46$)	*P*
Blood routine test					
White blood cell counts ($\times 10^9$/L)	3.5–9.5	9.6 (6.1–15.9)	7.0 (4.7–10.9)	11.7 (6.6–17.3)	0.007
Neutrophil counts ($\times 10^9$/L)	1.8–6.3	9.0 (4.3–13.9)	5.8 (3.6–8.9)	11.1 (5.5–15.3)	0.003
Lymphocyte counts ($\times 10^9$/L)	1.1–3.2	0.7 (0.5–1.0)	0.6 (0.6–0.8)	0.7 (0.5–1.0)	0.68
Neutrophil to lymphocyte ratio	NA	11.0 (4.8–21.5)	9.5 (4.5–13.1)	12.2 (6.0–24.6)	0.094
Monocyte counts ($\times 10^9$/L)	0.1–0.6	0.4 (0.2–0.8)	0.4 (0.2–0.5)	0.5 (0.2–0.9)	0.311
Platelet counts ($\times 10^9$/L)	125.0–350.0	186.0 (141.0–262.0)	181.0 (148.5–237.5)	191.0 (130.0–284.8)	0.71
Haemoglobin [g/L, mean (SD)]	130–175	113.7 (26.0)	131.5 (17.4)	105.6 (25.4)	< 0.001
Hematocrit (%)	40.0–50.0	33.8 (28.6–37.9)	37.3 (34.9–40.4)	30.8 (25.6–36.0)	< 0.001
Coagulation function					
Prothrombin time (s)	10.5–13.5	13.0 (11.9–14.1)	13.4 (12.3–13.9)	12.9 (11.8–14.5)	0.665
Activated partial thromboplastin time (s)	21.0–37.0	33.9 (29.1–40.4)	34.7 (32.5–40.2)	32.1 (29.0–41.6)	0.402
International normalized ratio	0.8–1.3	1.1 (1.0–1.2)	1.0 (0.9–1.1)	1.1 (1.0–1.3)	0.002
D-dimer (μg/L)	0–1.5	3.1 (1.6–8.0)	1.1 (0.7–2.8)	4.4 (2.6–9.6)	< 0.001
Blood biochemistry					
Albumin, median [g/L, mean (IQR)]	40.0–55.0	30.1 (25.6–33.7)	34.6 (31.3–36.5)	26.8 (24.2–31.6)	< 0.001
Alanine aminotransferase(U/L)	9.0–50.0	38.0 (27.8–60.1)	33.5 (22.0–54.3)	43.0 (28.8–70.0)	0.241
Aspartate aminotransferase (U/L)	15.0–40.0	48.4 (31.8–91.3)	47.0 (32.6–69.5)	48.5 (29.3–100.8)	0.567
Total bilirubin (μmol/L)	0.21.0	15.7 (10.7–22.2)	20.7 (12.8–27.6)	15.4 (8.6–21.0)	0.025
Serum creatinine (μmol/L)	57.0–111.0	77.0 (50.2–124.4)	75.1 (56.3–92.7)	77.0 (48.3–155.1)	0.727
Blood urea nitrogen (mmol/L)	3.6–9.5	7.1 (5.4–9.6)	6.6 (5.5–8.3)	7.4 (5.3–12.8)	0.151
Creatine kinase MB form (U/L)	0–5.0	2.0 (1.1–5.0)	0.8 (0.4–1.9)	2.8 (2.0–7.6)	< 0.001
NT-pro BNP (pg/ml)	0–125.0	1778.5 (223.8–6170.5)	133.5 (71.8–772.0)	3298.5 (473.8–7077.5)	< 0.001
Lactate dehydrogenase (U/L)	120.0–350.0	749.0 (427.0–1290.0)	693.0 (399.0–883.5)	936.5 (490.8–1535.5)	0.089
Arterial blood gas					
Sodium (mmol/L)	135.0–145.0	136.0 (132.0–141.0)	135.2 (132.5–141.6)	136.0 (131.8–141.0)	0.797
Potassium (mmol/L)	3.5–5.0	3.6 (3.4–4.1)	3.5 (3.2–3.6)	3.8 (3.5–4.3)	0.02
Chloride (mmol/L)	90.0–110.0	101.0 (97.8–106.0)	101.0 (98.0–106.5)	101.0 (96.8–105.3)	0.695
PaO_2 (mmHg)	83.0–108.0	81.0 (61.4–99.6)	65.3 (57.5–82.0)	86.5 (64.6–130.0)	0.02
$PaCO_2$ (mmHg)	35.0–48.0	33.6 (30.7–40.6)	33.3 (31.4–36.6)	34.0 (28.8–44.9)	0.72
PaO_2:FIO_2 (mmHg)	400.0–500.0	162.2 (119.4–219.3)	132.9 (116.2–174.9)	181.3 (119.0–279.9)	0.07
Glucose (mmol/L)	3.9–6.1	9.2 (6.8–13.8)	11.1 (8.3–14.9)	8.8 (5.9–13.0)	0.155
Lactate (mmol/L)	0.5–1.6	2.1 (1.5–2.9)	2.5 (1.6–3.0)	2.0 (1.5–2.6)	0.226
Immune-related biomarkers					
Absolute T lymphocyte counts (count/μl)	NA	440.0 (329.5–581.0)	329.5 (313.3–472.3)	492.0 (382.0–720.0)	0.004
Absolute helper T lymphocyte counts (count/μl)	NA	246.0 (188.0–372.0)	201.0 (156.0–264.5)	308.0 (208.0–420.0)	0.034
Absolute cytotoxic T lymphocyte counts (count/μl)	NA	152.0 (102.0–236.0)	101.0 (91.0–153.8)	180.0 (132.0–264.0)	0.003
CD4/CD8 ratio [mean (SD)]	0.9–3.6	1.8 (0.9)	1.9 (0.9)	1.8 (0.9)	0.709
Inflammation-related biomarkers					
C-reactive protein (mg/L)	0–10.0	104.7 (30.9–148.4)	119.2 (70.7–154.6)	37.2 (23.8–111.6)	0.008
Procalcitonin (ng/ml)	0–5.0	0.5 (0.2–3.8)	0.2 (0.2–0.3)	1.4 (0.3–5.5)	< 0.001

Data were median (IQR) if not otherwise specified. n (%) referred to the total number of patients with available data. *P* values indicated differences between SARS-CoV-2-induced sepsis and bacteria-induced sepsis, in which $P < 0.05$ was deemed as statistical significance
SD Standard deviation, *BNP* Brain natriuretic peptide, *NA* Not applicable

with SARS-CoV-2-induced sepsis at ICU admission, while elevated inflammation-related parameters, C-reactive protein (CRP) as an example, were observed in this cohort compared to patients with bacterial sepsis. In addition, obvious differences in organ functional parameters were noted between the two cohorts, including significantly increased levels of creatine kinase-MB and NT-pro BNP, and decreased albumin level in patients with developed bacterial sepsis.

In this study, ICU patients with SARS-CoV-2-induced sepsis and those with bacterial sepsis revealed comparable demographic characteristics, like age, gender distribution, and comorbidities, after rigorous screening processes. However, patients with bacterial sepsis were found with more severe organ dysfunction and poor outcomes when compared with those caused by SARS-CoV-2-induced sepsis, including higher values in SOFA and APACHE II, as well as more ICU deaths. The different patterns of immune responses might be the major cause of the divergent outcomes between viral and bacterial sepsis. We further found that failed homeostasis was characterized in both bacterial and viral sepsis but triggered by different pathogens. In the development of viral sepsis, the loss of T lymphocytes and their subsets was the dominant characteristics of dysregulated immune response, thereby contributing to the imbalance between innate and adaptive immune systems; while excessive inflammatory activation was the main feature of bacterial sepsis, which further resulted in intractable immune suppression and multiple organ dysfunction. This is the first report that compared clinical features and host responses between bacterial and SARS-CoV-2-induced viral sepsis. These findings might not only suggest divergent host responses to bacteria and virus but also provide novel insights into further researches on the development of sepsis with underlying etiology of various pathogens.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s40779-020-00267-3.

Additional file 1. Appendix Table 1. Baseline characteristics of critically ill patients with SARS-CoV-2- and bacteria-induced sepsis.

Additional file 2. Appendix Figure 1. Flow diagram of patient inclusion. COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SOFA: Sequential organ failure assessment; ICU: Intensive care unit; LOS: Length of stay; CAP: Community-acquired pneumonia.

Abbreviations

COVID-19: Coronavirus disease 2019; CAP: Community-acquired pneumonia; CRP: C-reactive protein; ICU: Intensive care units; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SOFA: Sequential organ failure assessment; APACHE II: Acute physiology and chronic health evaluation II

Acknowledgements

Not applicable.

Authors' contributions

All corresponding and first authors contributed to the study concept and design. CR and RQY analyzed the data and drafted this letter. DR and YL recruited patients and extracted epidemiological and clinical data. All authors reviewed and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (81730057 by YMY, 81801935 by CR), Sanming Project of Medicine in Shenzhen (SZSM20162011 by YMY and YWF), and the Military Medical Innovation Program of Chinese PLA (18CXZ026 by YMY).

Availability of data and materials

All data were presented in this manuscript or Appendix.

Ethics approval and consent to participate

This study was approved by the Committee on the Ethics of Medicine, the Second People's Hospital of Shenzhen, China (20200601026).

Consent for publication

Not applicable.

Competing interests

We declare no competing interests.

Author details

[1]Department of Critical Care Medicine, the Second People's Hospital of Shenzhen, Shenzhen 518035, Guangdong, China. [2]Department of Critical Care Medicine, the Third People's Hospital of Shenzhen, Shenzhen 518020, Guangdong, China. [3]Trauma Research Center, the Fourth Medical Center and Medical Innovation Research Department of the Chinese PLA General Hospital, Beijing 100048, China.

Received: 16 July 2020 Accepted: 29 July 2020
Published online: 04 August 2020

References

1. Xu Z, Shi L, Wang YJ, Zhang JY, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020. https://doi.org/10.1016/S2213-2600(20)30076-X.
2. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801–10. https://doi.org/10.1001/jama.2016.0287.
3. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. Lancet. 2020;395(10235):1517–20. https://doi.org/10.1016/S0140-6736(20)30920-X.
4. Ren D, Ren C, Yao RQ, Feng YW, Yao YM. Clinical features and development of sepsis in patients infected with SARS-CoV-2: a retrospective analysis of 150 cases outside Wuhan, China. Intensive Care Med. 2020:1–4. https://doi.org/10.1007/s00134-020-06084-5.
5. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7:4.