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Case Report
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Higher Cytokines Expression in Lower Respiratory Tract than Sera of Coronavirus Disease 2019 Case: A Case Report

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Abstract

Coronavirus Disease 2019 (COVID-19), an emerging infectious disease with significant morbidity and mortality, is caused by a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which mainly infects lung and bronchial tissues, leading to Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS).

Keywords: Inflammatory cytokines; Lower respiratory tract; Coronavirus Disease 2019

Introduction

Although most of the COVID-19 patients have mild or moderate courses, characterized by flu-like symptoms, up to 16% to 19% can have severe, potentially life threatening disease [1-3]. The most common presentations in severe/critical COVID-19 patients are underlying comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes, and "cytokine storm" [4,5]. "Cytokine storm" is characterized by the excessive production of massive inflammatory cytokines and chemical mediators, such as Interleukin-1 (IL-1), IL-6, IL-8, Tumor Necrosis Factor-α (TNF-α), Interferon-γ (IFN-γ), IFN-γ Induced Protein-10 (IP-10), Chemokine C-C ligand-2 (CCL2), CCL3 and CCL5, postulated to be due to over activation of immune cells [5]. While "cytokine storm" often refers to the systemic response, it is still unclear if the composition and expression of cytokines differs between the Lower Respiratory Tract (LRT) and systemic compartment.

Case Presentation

A 74-year-old man with chronic kidney disease was diagnosed with a severe acute lower respiratory infection, requiring admission to intensive care units (ICU, received invasive mechanical ventilation on 8th to 83th day post infection). He was confirmed to be infected with SARS-CoV-2 by Dongguan Center for Disease Control and Prevention's (CDC). Four specimens including sputum and serum samples were collected from this critical COVID-19 case on 37th day and 57th day post infection (SARS-CoV-2 positive from 5th to 37th day post infection). The ethics committee of the Dongguan's People's Hospital (KYKT2020-005-A1) approved the sampling procedure and the use of patient samples for this study, and informed consent was obtained from patient. All the clinical specimens were handled at the Dongguan People's Hospital, Dongguan, China. Here, we compared the inflammatory cytokines expression between lung tissue and serum. The 48 cytokines and chemokines' level in Sputum Supernatant (SS) and serum (25 ul-volume samples) were quantified by the Bio-Plex method using the Bio Plex 2200 Multiplex Testing System (Bio-Rad, Hercules, CA, USA) according to the manufacturer's instructions. A high-speed digital processor managed the data output, and the Bio-Plex Manager™ 6.0 software presented the concentration results in pg/ml. As shown in Figure 1, it is shown that inflammatory cytokines expression in sputum samples more precisely reflect "cytokine storm" in lung tissue than serum samples, for most of inflammatory cytokines levels, including IL-1α, IL-1β, IL-5, IL-6, IL-7, IL-8, IL-12p40, IL-15, IL-16, IL-17, IP-10, TNF-α, Eotaxin, b-FGF, M-CSF, LIF, MIP-1β, VEGF, GROa, monokine induced by Interferon (IFN)-γ (MIG), macrophage Migration Inhibitory Factor (MIF), Hepatocyte Growth Factor (HGF), Granulocyte-Colony Stimulating Factor (G-CSF) and Tumor Necrosis Factor (TNF) - Related Apoptosis-Inducing Ligand (TRAIL), were higher in LRT than sera, especially during the SARS-CoV-2 positive period (37th day). The IL-6 level in sputum supernatant was over 10^3 times higher

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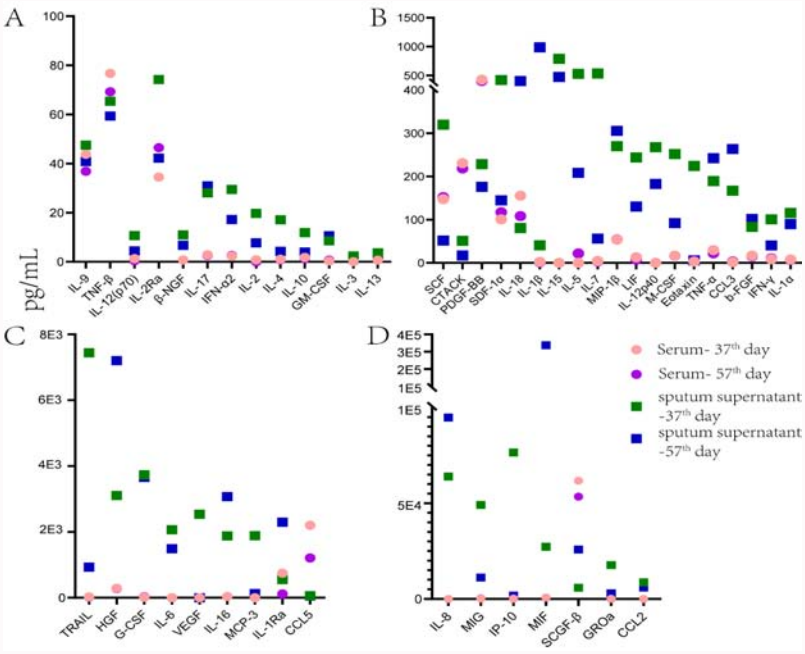

Figure 1: Levels of 48 protein cytokine in acritically ill COVID-19 patient in thesputum or serumsample according to days after symptom onset (37th and 57th day).

than that in serum (Figure C). The levels of IL-8, MIG, IP-10, MIF in LRT were significantly higher than serum, over 1×10^4 pg/ml (Figure D). In addition, in the cytokine levels were still high even when the patient was no longer positive for SARS-CoV-2. However, we do note the limitations of our research. Only four SS and serum samples were collected in the middle and late course of disease, for it cannot be collected at other time points, such that there was no information on the early phase of the disease.

Complications or ultimately death arising from COVID-19 have been associated with hyper induction of proinflammatory cytokine production [5]. Here we compared the expression levels of cytokines and chemokines in the LRT and serum of a critically ill case with COVID-19 on 37th and 57th day, and results indicated that higher proinflammatory cytokines levels in SS than serum samples. While we acknowledge the difficulty in collecting LRT samples monitoring the responses in the site of infection, when permissible, may be more informative of a patient's clinical status than sera.

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