



ORIGINAL ARTICLE

Coagulation and Immune Characteristics in a COVID-19 Case

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Abstract

An outbreak of respiratory illness, officially named Coronavirus Disease 2019 (COVID-19), has spread rapidly worldwide. The domestic situation has been controlled, now the resumption of production and work as well as people's normal life has been accelerating. We focused this article on laboratory changes in the infection confirmed case of COVID-19 hospitalized to clarify the immune characterizations and coagulation system. Coagulation dysfunction is common in patient with COVID-19, especially fibrinogen and APTT, and the degree of elevation is related to immune characteristics. As the disease recovers, fibrinogen, APTT and CD8+ T cells also return to normal.

Keywords

Coagulation, Immune, COVID-19

Introduction

COVID-19 is caused by SARS-CoV-2 infection and was first reported in central China on 30th December 2019 [1]. As of 11:13 am CET, 21 June, 2021, there have been 180,517,492 confirmed cases of COVID-19, including 3,918,010 deaths globally [2], the case count has been rising daily, and raised a global health emergency.

It has been found that host humoral and cellular antiviral immune responses are indispensable to fight back and control infectious diseases [3]. The subsets of CD4+ T cells, CD8+ T cells, B cells, and natural killer (NK) cells play an important role in the maintenance of immune system function. After virus infection, alteration in the subsets varies with different virus types, indicating a potential association between lymphocyte subset alteration and viral pathogenic mechanisms [4]. Recent study has reported that T lymphocyte in the peripheral

blood is correlated with the severity of COVID-19 [5]. CD4+ and CD8+ T cells expression are interfered with via viral infection and can play crucial roles in the control of virus replication and the outcome of patients [3]. Coagulopathy in SARS-CoV-2 infection has been shown to be associated with high mortality, with elevated D-dimer levels and fibrinogen, those being particularly important markers for the coagulopathy. A comparative analysis between survivors and non-survivors COVID-19 patients revealed significantly longer PT and APTT compared to survivors on admission [6].

In this study, we recorded and analyzed the dynamics changes of coagulation function and peripheral CD8+ T immune cells, and the other important outcomes of a patient diagnosed with critical COVID-19 during the 13-day hospitalization when SARS-CoV-2 RNA confirmed positive and the day when the result returned to negative. The purpose of the present study was to explore the relationship between coagulopathy and immune characteristics in patients with COVID-19. This report was approved by Affiliated Chaohu Hospital of Anhui Medical University Institutional Review Board and the requirement for informed consent was waived.

Case Report

A 30-year-old man who was a frozen meat processor worker in Wuhan, with a history of cough, mild chills and low grade subjective fever was good physically healthy before had no underlying diseases before this onset. On checking into the outpatient clinic in our hospital, the patient put on a mask in the waiting room. After waiting approximately 30 minutes, he was taken into an



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examination room by a doctor. Owing to the outbreak of COVID-19 in Wuhan city and the announcement of related symptoms, he was immediately admitted to the isolation ward, received supplemental oxygen through a face mask and underwent examination. His vital signs remained stable, apart from the exertional dyspnea, intermittent dry cough and sore throat. The initial physical examination revealed a body temperature of 38.9 °C, blood pressure of 120/70 mmHg, pulse of 98 beats per minute, respiratory rate of 22 breaths per minute, and breathing sound was normal initially. Laboratory examinations results demonstrated a normal leukocyte count ($7.99 \times 10^9/L$), normal neutrophils (68.4%), normal lymphocytes (22.2%), elevated glucose (6.6 mmol/L) and C-reactive protein (29.88 mg/L). His procalcitonin level peaked at 0.1 (normal level: < 0.05 ng/mL), serum lactate dehydrogenase (LDH) at 485 U/L (normal level: 0~10 mg/L) and serum amyloid A protein (SAA) at 220.6 mg/L (normal level: 0~10 mg/L). The patient tested negative for influenza A and weakly positive for influenza B virus. *Mycoplasma pneumoniae* and adenovirus specific IgM antibodies were found to be positive in serum sample. CT results showed multiple consolidations and ground glass opacities in both lungs. The Centers for Disease Control (CDC) confirmed that the patient's oropharyngeal swab and sputum specimens tested positive for COVID-19 by rRT-PCR assay.

Analysis of lymphocyte subsets showed that the number of CD8+ T cells in the peripheral blood of a SARS-CoV-2-infected patient is significantly reduced, CD8+ T lymphocytes increased significantly after treatment. However, CD4+, B lymphocytes and natural killer (NK) cells showed no significant change after treatment. One day after admission to our hospital, his laboratory findings included elevated activated partial thromboplastin time (APTT) and elevated levels of fibrinogen. Interestingly, the platelet count remains minimally modified. If the T lymphocyte subsets count was lower, significant increases were found with respect to APTT and fibrinogen, CT images showed an enlarged lesion evidence of pneumonia in both lungs.

The patient was treated with antiviral drug and antibiotics for symptomatic treatment. After 8 days of treatment, the temperature of the patient dropped to normal and the symptoms disappeared. On the 13th day of admission, CT showed that the patient's bilateral pulmonary lesions improved. Repeat rRT-PCR was negative and patient was discharged.

Discussion

SARS-CoV-2 infection has become an urgent public health challenge in the world. Most of the infected patients had mild disease and recovered 2-3 weeks later. However, more than 10% of the infected patients died of multiple organ failure in a short period of time once they developed severe acute respiratory distress

syndrome [4]. Thus, a further understanding of related characteristics of the disease is urgently needed.

Response to viral infections is accompanied by activation of the innate and acquired immune system. The most effective response against a variety of viral infections is the activation of the cellular immune response especially T cell activation. CD8+ cytotoxic T cells (CTLs) by secreting a number of molecules, including perforin, granzyme, and interferons (IFNs) can eliminate viruses from the host body [4]. Lymphocytes and their subsets play an important role in the maintenance of immune system function. As with immune diseases and other infectious disease, virus infection can also lead to dysregulation in the levels of lymphocyte subsets [7]. Recent studies have reported that T lymphocytes are correlated with the severity of COVID-19 [5]. Lymphopenia has been considered as a poor prognostic factor for severe COVID-19 [8]. The percentage of lymphocytes level was normal, although this difference may be attributed to the milder symptoms of this patient. As a result, this case was prone to misdiagnosis in the clinic. In this patient, CD8+ cells gradually increased with the progress of treatment.

Patients with COVID-19 have a profound hypercoagulable state, and complicating venous thrombotic events are common [9]. Abnormalities in coagulation screening measures, including a prolonged APTT, have been reported in patients with COVID-19. This finding could be seen as a reason to avoid the use of anticoagulation at both therapeutic and prophylactic doses. Furthermore, the relevance of COVID-19-coagulation abnormalities are becoming increasingly clear as a substantial proportion of patients with severe COVID-19 develop, sometimes unrecognized, venous and arterial thromboembolic complications [10]. Fibrinogen, as an acute reactive protein, can be significantly increased in the course of mild COVID-19 patients and in the early onset of severe patients [11]. The Second day after admission, the prolonged APTT and elevated fibrinogen were measured in the COVID-19 patient. Using the available evidence, we suggest monitoring coagulopathy in patients with severe COVID-19 by measuring prothrombin time, APTT, platelet count, and D-dimer concentrations every 2-3 days. So they should be dynamically monitored, alert to hypercoagulable period and timely anticoagulant intervention. There is evidence supporting the use of prophylactic dose low molecular weight heparin as prophylaxis for venous thromboembolism in critically ill patients. In view of the hypercoagulable state of patients with severe COVID-19, and the potential increased risk of thrombosis, we suggest that all COVID-19 patients that are admitted to hospital should receive this prophylactic treatment in the absence of medical contraindications.

In this case, the patient had clear history of contact with the epidemic area, and the leukocytes were normal,

thus it was misdiagnosed as common pneumonia at first. Similar to viral pneumonia due to other etiologies, GGOs are the main CT findings of the patients with COVID-19. SAA is an acute phase-reactive protein and can be rapidly increased by about 1000 times within 4~6 h when the body is infected by pathogens, its sensitivity is higher than CRP [12,13]. Detection of COVID-19 RNA in specimens from the upper respiratory tract showed that viral loads in the patient are consistent with his coagulation and immune function. The case revealed rapid diagnostic assays, effective treatment and wide use of chest CT would be crucial to contain the worldwide outbreak of COVID-19 in the future. Combination with RNA test and other detective methods such as specific antigen, IgM antibody or the next generation sequencing, is also conducive to diagnosis.

We suggest that: 1) CD8+ T cells caused by immune imbalance following SARS-CoV-2 infection may be an important cause of progress; 2) APTT and fibrinogen may be associated with the disease process; 3) Coagulation dysfunction and immune characteristics have better consistency in reflecting the disease progression.

In the post epidemic era, CT scan has been used as a routine test item for admission, what's more, major medical institutions in various provinces are carrying out nucleic acid and antibody detection in an orderly manner before hospitalization, including the family members accompanying the bed in China.

Authors' Contributions

ZM and ZZJ co-designed the study and helped writing the manuscript. ZZJ and HKM gathered information and drafted the manuscript. All authors read and approved the final manuscript.

Competing Interests

The authors declare that they have no competing interests.

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