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LETTER TO THE EDITOR

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Could HIV infection alter the clinical course of SARS-CoV-2 infection? When less is better

To the Editor,

We read with real interest the article of Zhu et al[1] Here, the authors reported the first case of human immunodeficiency viruses (HIV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, in a 61-years-old male. After detection of SARS-CoV-2 infection by a real-time reverse-transcriptase polymerase chain reaction, anti-HIV drug (lopinavir/ritonavir, 400/100 mg per dose, twice daily for 12 days) was started. The patient also received moxifloxacin (400 mg once daily for 7 days), γ-globulin (400 mg/kg once daily for 3 days), and methylprednisolone (0.8 mg/kg once daily for 3 days). Despite the patient's comorbidities such as type II diabetes and mild lymphopenia (lymphocyte count of 1.1×10^9/L), that worsened during the acute phase of the disease (0.56×10^9/L), the patient had a good outcome, and he was discharged at home.

As noted by Joob and Wiwanitkit,[2] the patient did not receive antiviral therapy for HIV infection before. Presently, antiretroviral drugs are widely used for the treatment of HIV and SARS-CoV-2 infections.[3] However, the clinical efficacy of lopinavir/ritonavir for the treatment of SARS-CoV-2 infection needs to be confirmed by further clinical trial.[4] In addition, in this case report, the patients received other drugs that could alter the clinical outcome.

Although Nixon[5] raised doubts about the veracity of the mentioned case and the debate is still ongoing,[6] we would like to focus our attention on the correlation between immune system impairment and clinical manifestation of SARS-CoV-2 infection.

Another explanation of the good clinical outcome in this case report could be the relationship between HIV-related immunosuppressive status and clinical manifestations. As we stated in our previous article,[7] we hypothesized that patients with conditions that impair the state of the immune system, as immunosuppression for solid organ transplantation or HIV infection, could be protected against severe clinical manifestations, despite the susceptibility to SARS-CoV-2 infection.

It could be possible that the activation of the immune system enhances the injury caused by SARS-CoV-2 infection, with patient's worst outcome. The activation of the immune system, especially T cells, represents a landmark of the histological picture of lung injury related to COVID-19. Xu et al[1] investigated the pathological characteristics of SARS-CoV-2 infection by human post-mortem biopsies. They found that a histological picture of lung injury related to SARS-CoV-2 infection is similar to acute respiratory distress syndrome (diffuse alveolar damage, cellular fibromyxoid exudates, desquamation of pneumocytes, and hyaline membranes). In addition, they analyzed the characteristics of peripheral CD4 and CD8 T cells. They found a hyperactivated status, with an increased concentration of highly proinflammatory CCR6+ Th17 in CD4 T cells. The authors concluded that overactivation of T cells accounts for, in part, the severe immune injury.

In this case report, the patient had lymphopenia, but it could be related to the latent HIV infection rather than to a clinical manifestation of SARS-CoV-2. Also, we suppose that lymphopenia could represent a protective factor. It is clear that, in healthy patients, the development of lymphopenia during SARS-CoV-2 infection represents a factor for the progression in the severe clinical form.[8] In untreated HIV infected patients, the uncontrolled viral replication causes lymphopenia and alters the hyperactive response of the immune system to SARS-CoV-2 infection. When the antiretroviral treatment started (lopinavir/ritonavir) as management of SARS-CoV-2 infections, it could play a double effect: inhibition of SARS-CoV-2 replication, facilitating the viral clearance; inhibition of HIV replication, that could allow a slight activation of the immune response, just enough to contrast the SARS-CoV-2 infections without the beginning of the hyperinflammatory state.

Therefore, based on these assumptions, despite nontreated patients with HIV could be more susceptible to SARS-CoV-2 infection, at the same time, lymphopenia HIV-related could protect them from severe clinical manifestation, and the lopinavir/ritonavir administration could be more useful for the above-hypothesized activities than for a potential and not yet confirmed direct anti-SARS-CoV-2 antiviral effect. Moreover, the clinical course of the SARS-CoV-2 infection in patients under chronic antiretroviral therapy for HIV without lymphopenia could be extremely relevant. As a consequence, further studies are urgently required to face this lack of data.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All the authors wrote the article.

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