COVID- 19 AND THYROID INFECTION: LEARNING THE LESSONS OF THE PAST

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INTRODUCTION

Coronavirus disease (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has created a worldwide crisis that affects different facets of human life. The lung is a major target organ of the virus, but other organs such as kidneys, intestine and the thyroid can also be infected (1).

The capacity of virus dissemination in various organs is leading to multiple organ failure and different clinical manifestations. This characteristic is not limited to the SARS-CoV-2 and is observed in a number of other viruses such as hepatitis C virus (2).

To date, there are few reports about the effects of COVID-19 infection on the thyroid and there is no detailed histopathological examination of the thyroid gland in patients with SARS-CoV-2 infection. Nonetheless, recent researches have shown that thyroid disorders including hypothyroidism or subacute thyroiditis are more common in SARS-CoV-2- infected patients. These patients showed an altered thyroid function and signs of thyroid inflammation such as swelling and pain in the thyroid area (3).

At present it is difficult to distinguish whether altered thyroid function is a result of direct or indirect effects of viral infection. Moreover, the mechanism of action of this virus is unclear. In spite of these essentially unanswered questions, the study of literature helps identification of cellular and molecular changes that may contribute to virus pathogenesis. Viral infections are important environmental factors in the pathogenesis of different types of thyroid disorders such as autoimmune thyroid diseases and subacute thyroiditis and there is evidence that, thyroiditis may occur in response to viral infection of the thyroid. This

hypothesis is supported by several observations such as the presence of virus particles in the thyroid of patients and elevation of anti-virus antibodies in individuals with thyroid disorders.

Despite unique characteristics of SARS-CoV-2 that distinguish it from other viruses, evidence indicates that divergent viruses use similar mechanisms for invading the host.

Viruses are thought to act as triggering agents for the initiation and development of diseases in different ways. For instance, some viruses can induce host cell apoptosis and liberate cellular antigenic contents. Molecular mimicry is another mechanism by which the virus triggers an antiviral response which turns against autoantigens. It has also been shown that aberrant cytokine and chemokine production and secretion which can lead to aberrant expression of major histocompatibility complex class II molecules and activation of Toll-like receptors (the key players of the host innate immune system, that can recognize conserved molecular signatures of a wide range of microbial pathogens known as pathogen associated molecular pattern and are present on thyrocytes) participate in the pathogenesis of human viral diseases (4). Interestingly, molecular evidence suggests that all of these potential mechanisms may be involved in invasion success of SARS-CoV-2 and may partially explain the unusual manifestations of virus infection in organs such as the thyroid. It has been indicated that antibody against SARS-CoV-2 spike protein strongly reacts with thyroid peroxidase (5). These antibodies may have a role in initiating the autoimmune responses through molecular mimicry in susceptible individuals. In such scenario, autoantibodies may be generated against a virus epitope that bears similarity to one on the thyroid. The development of cross-reactive antibodies following exposure to SARS-CoV-2 may lead to thyroid pathology due to interaction with determinants on the thyroid cells.

Excessive production of cytokines, which

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appears to be critical in the pathogenesis of different viruses are also observed after infection with SARS-CoV-2. Analysis of cytokine profiles in COVID-19 patients have indicated that there is a direct correlation between the cytokine storm and multiorgan failure (6).

Induction of inappropriate apoptotic responses seems to be other common features of the virus-induced disease process. Therefore, this phenomenon may also play a role in the pathogenesis of SARS associated coronavirus infection in the thyroid gland. Currently, there is no clear statement about the importance of SARS-CoV-2-induced apoptosis in the thyroid dysfunction. However, some knowledge regarding this issue can be gathered from a previous coronavirus pandemic. For instance, during the SARS-CoV outbreak, the histopathological examinations of the thyroid have revealed that apoptosis plays an important role in thyroid injury (7).

All the above mentioned issues provide valuable insights into disease mechanisms but do not address the root of the connection between COVID-19 and thyroid dysfunction. To date, there are unresolved issues concerning the mechanisms of immunopathological changes in the thyroid gland of patients with COVID-19. The fact is, more research is still needed to elucidate mechanisms behind the possible relationship between SARS-CoV-2 and thyroid diseases. However, it seems that careful attention to thyroid manifestations of COVID-19 infection will be essential not only for a better understanding of disease mechanisms, but also for a proper diagnosis and appropriate treatment of patient's disease.

Conflict of interest

The author declares that he has no conflict of interest.

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