Autoimmune Rheumatic Disease and COVID-19 : A Literature Review

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Abstract

The world has been dealed with COVID-19 pandemic for almost three years. It has brought challenges to humanity, especially in the face of health. Autoimmune rheumatic disease (ARD) covers amultiform group of conditions characterized by joint involvement with a broad scope of systemic manifestations. The altered immune system cause patients with ARD are known to have a higher chance and ill-fated outcomes of COVID-19. However, since various studies have continued to evolve, COVID-19 infection can also cause an autoimmunity process. Web-based literature search using related keywords was carried out. This literature review aims to collect data and articles related to these two topics.

Keywords: autoimmune rheumatic disease, COVID-19, humans and health, post-COVID-19

1. Introduction

The COVID-19 pandemic has touched lives around the world and presented new challenges to the face of medicine. Patients with autoimmune rheumatic disease are among the population at risk during the pandemic. In people with ARD, SARS-CoV-2 infection was twice as common compared to the general population [1]. After almost three years of the pandemic, cases of ARD post-COVID-19 infection were found and reported. COVID-19 cancause autoimmunity through a process of immune-mediated injuries which are present both in COVID-19 infection and autoimmune diseases [2]. The impaired immune function will lead to autoimmunity. Autoimmunity is the existence of antibodies and T lymphocytes directed against normal cells in the human body called autoantigens. Autoimmunity is the pathological basis for the occurrence of autoimmune rheumatic disease. The aims of this literature review is to elaborate the interplay between COVID-19 and ARD.

2. Method

A literature exploration was performed using PubMed and Google Scholar. The subsequent keywords were used, solely or in combination: ‘COVID-19’, ‘autoimmune rheumatic disease’, ‘post COVID-19’, ‘rheumatic diseases’. To maximize the search, reverse tracing of reference lists from retrieved articles was also carried out.

3. Findings

a. COVID-19

The World Health Organization (WHO) declared the outburst of COVID- 19 as a pandemic on 11 March 2020. Either asymptomatic or symptomatic patients, both are considered to be highly contagious. The disease is easily spread by human-to-human transmission with respiratory droplet as the main route. All population is generally susceptible of COVID-19 without tendency of a given sex or age. Based on data from Chinese Preventive Medicine Association, among all identified individual who are older (over 50 years old), recorded for 53.6% of the reported cases and there is a small predominance at 51.4%. Also it is reported that patients with underlying comorbidities such as hypertension (15–25%), diabetes (20–25%), obesity, and cardiovascular diseases (10– 15%), or chronic obstructive pulmonary disease (10– 15%) are have higher risk to be contracted the virus leading to the more serious profile of COVID-19 and developing complications. Overall, the probability of poor COVID-19 disease outcomes may be intensified in patients with jeopardized immune system [3].

The pathogenesis of COVID-19 is still widely unknown and needs to be discovered, but it may duplicate SARS infection to some degree. Identical to what was noticed in reaction to SARS-CoV, immune-mediated injury may appear to be a vital role in the pathogenesis of COVID-19, specifically among individuals who are in a life-threatening condition due to severe disease [4]. When the virus entry and binding with pneumocytes in the lung, it induces the local inflammatory response and encourage the deliver of cytokines including transforming growth factor-β1 (TGF-β1), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, including numbers of chemokines that work to attract circulating leukocytes [4].

b. Autoimmune Rheumatic Disease

Autoimmune rheumatic disease (ARD) covers a multiform group of conditions characterized by joint involvement with a broad scope of systemic manifestations [5]. Some of the diseases that are included in the ARD group are systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), and scleroderma. Most of the pathophysiology of the disease remains unknown, but there are various contributing factors such as genes, infection, and environment in the occurrence of autoimmunity.

c. COVID-19 and Autoimmune Rheumatic Disease

- Risk of patients with ARD to COVID-19

General explanation of autoimmune disease is that the underlying disarray immune function.Most of the patients with autoimmune disease receive immunomodulatory medications or biological agents. The drugs that are usually used are NSAIDs, glucocorticoids, hydroxychloroquine, and DMARDs. All of them have similar effects on suppressing the pro-inflammatory agents. Based on Akiyama S, et al. study, mainly found that COVID-19 was twofold as regular in autoimmune diseases patients contrasted to the public [1]. The study also found that there is an increasing risk of being infected with COVID-19 in patients taking glucocorticoid [1]. During pandemic situations, glucocorticoid is like a double-edged knife for patients with autoimmune disease. It needs to maintain the autoimmune disease progressivity, but on the other hand it can make the patients more likely infected with COVID-19. Moreover, a lot of patients with autoimmune disease avoid close contact with people and go to healthcare facilities to reduce the risk of developing COVID-19. Also, they may try to reduce the immunosuppressive effect of the drug. With such conditions, the suspended medication can trigger rheumatologic disease flares and worsen the disease activity. Obedience to treatment plans is a must to prevent flares that might lead to organ damages.

- Similarities in immune response

Autoimmune diseases are depicted by the presence of autoantibodies and preserved inflammatory responses in consequences of the deprivation of immune tolerance and disarray immune system, directing to target organ failure and breakdown [6]. Immune-mediated injuries present both in COVID-19 infection and autoimmune diseases. In SARS-CoV-2 infection, T cell immunity works a vital part in controlling the disease. Studies regarding the clinical laboratory test, lymphopenia (lymphocyte count < 1.5 x 10/l) which occurs in the clinical course of some autoimmune rheumatic diseases, corresponded with critical illness in COVID-19 patients. Also, abundant production and release of pro-inflammatory cytokines and chemokines which are observed in both COVID-19 and autoimmune disease patients, can lead to severe organ damage in critical cases. Unstoppable cytokine storm syndorme may continue to be macrophage activation syndrome (MAS) which leads to fatal conditions in COVID-19. Based on Conti et al. novel study, they suggested that activated mast cells in SARS-CoV-2 could release histamine to increase IL-1 levels to commence cytokine storm and provoke lung injury. In COVID-19, it was identified that lupus, antiphospholipid syndrome and ANCA-associated vasculitis, activated neutrophil, and production of neutrophil extracellular trap seem to have a pathogenic characteristic [2]. The immune response system in our body is a double-edged sword which may save us or harm us during the SARS-CoV-2 infection. The imbalance of cytokine and immune cells activation influence the prognosis of the disease.

- Autoantibodies in patient with COVID-19

Patients with COVID-19 have been identified to have autoantibodies, also appeared to happen in several autoimmune diseases. From Pascolini et al. [7], antinuclear antibodies (ANA), anti- cytoplasmic neutrophil antibodies (ANCA) and antiphospholipid (APL) antibodies was presented in 33 consecutive patients with COVID-19. Almost half of the patients were positive for at least one autoantibody and patients with positive autoantibodies have a tendency to be in a worse prognosis and a notably higher respiratory rate at admission [2]. Lupus anticoagulant in COVID-19 patients presents as a probable agent of higher rate of thrombosis. In addition, study demonstrated by Amezcua-Guerra et al. [8] antiphospholipid (APL) antibodies present in COVID-19 patients seems to be contributed with a hyperinflammatory condition with incredibly high levels of ferritin, C reactive protein and IL-6, and with pulmonary thromboembolism. The data presented above show a probable interpretation for the hypercoagulable course in worse and critical COVID-19 cases and indicate that SARS-CoV-2 may give rise to autoimmune reactions [2].

- COVID-19 outcomes in ARD

For most of the time, viral infection is a self-limiting disease. But in the course of severe SARS-CoV-2 infection, it can lead to cytokine storm which may cause multi-organ failure or even death. A study from UK primary care database involving 17 million adults indicate that the risk of COVID-19 associated death for the combined group of people with RA, SLE, or psoriasis were slightly higher than for the general population [9]. In a South Korean research of 8,297 patients with ARD, the risk of COVID-19- related death was greater than in a matched cohort without rheumatic disease (adjusted OR 1.69; 95% CI 1.01-2.84) [10]. Overall, compared with the general population, ARD patients are at an escalate threat of hospitalization, and has a potential of other COVID-19 severe outcomes, with some of the risk being attributable to comorbidities. However, elevated risk of bad outcomes in COVID-19 does not correlate with the consumption of conventional synthetic DMARDs and bDMARDs, which is parallel with the recommendation from the EULAR to continue ARD medications despite the SARS-CoV-2 exposure [11].

- ARD in Post COVID-19 Infection

Autoimmunity has arised as a characteristic of the post-COVID-19 syndrome [12]. Several studies around the world have been reported cases of autoimmune disease in post COVID-19 infection. In April 2020, Zhang et al. identified that patients with COVID-19, by coagulopathy and multiple thrombi, were positive for anti-Cardioloipin IgA antibodies, as well as anti-β2-Glycoprotein IgA and IgG antibodies [13]. In the article, the authors firlmy assisted that antiphospholipid antibodies might be the cause of the thrombotic events. Another study done in Greek by Vlachoyiannopoulos et al., analyzed 29 patients and reported that more than half of the participants had developed an autoimmune activation as a result of SARS-CoV-2 infection [14]. A cohort study done in Italy also presented a prominent regularity of ANA, ANCA, and ASCA IgA antibodies opposed with healthy individuals [11]. ANA antibodies are significant signals in the identification of the different autoimmune diseases, mainly ANA-associated rheumatic diseases.

All those studies reported that COVID-19 is associated with autoimmunity, in particular ANA, ASCA, and ANCA antibodies development [15]. Cañas [16] suggested that the occurance of autoimmune conditions following COVID-19 infection could be related (1) with the temporary suppresion of innate and acquired immunity directing to a self-tolerance and (2) with a process of unsuitable immune reconstruction in genetically susceptible individuals.

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