

New Prospect

COVID-19 and Sarcoidosis: A two-way possible association

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Abstract. Immunological impairments such as lymphopenia in patients with sarcoidosis and their treatment by glucocorticoids and cytotoxic drugs may increase the risk of severe bacterial and viral infections, so these people may be more susceptible to COVID-19 as a disease with viral source. On the other hand, many previous studies pointed to viral trigger in sarcoidosis but no specific virus was mentioned. A recent French cross sectional study on 482 patients, suggests that daily active tobacco smokers have a lower risk of developing severe or symptomatic COVID-19 as compared to nonsmokers. It should be mentioned that our primary observations during the first COVID-19 outbreak (February-April 2020) on 206 COVID-19 patients admitted in intensive care units in Shahid Sadoughi hospital, Yazd, Iran, showed a possible negative association between smoking and coronavirus-2 infection. An observation that was addressed in the literature for sarcoidosis. Some previous studies mentioned that current smokers also have less probability for developing sarcoidosis. According to all these comparable features in patients with COVID-19 and sarcoidosis, may be one day in future, it will be reported that a sarcoidosis-like disease found in patients with COVID-9 history in 2020. Who knows?

Keywords: COVID-19, sarcoidosis, association

Coronavirus Disease 2019 (COVID-19), caused by coronavirus-2 (COV-2), is a global happening. As of March twenty first, 2020 infected patients were present in 167 countries and there have been quite 285,000 cases worldwide with nearly 12,000 death [1]. At the end of the first month of 2020, the World Health Organization stated that CoVID-19 is a public-health emergency of worldwide importance [2]. So, it is critical to take steps to stop transmission and save lives. In this regard, it is important to spot the individuals which are at higher risk for this illness.

Age over 70 and underlying systemic conditions such as cardiovascular disease, diabetes and high blood pressure were all associated with an increased risk of death among COVID-19 patients [3]. The possible mechanism for these associations will be explained hereinafter. People with autoimmune or rheumatologic disease such as rheumatoid arthritis have also an increased risk due to the immune system impairment or to the immunosuppressive effects of corticosteroids and synthetic or biological disease-modifying drugs, although Chloroquine and hydroxychloroquine have now been included in COVID-19 pneumonia treatment protocols [4].

Studies showed that coronavirus-2 requires the angiotensin-converting enzyme 2 receptor (ACE2) as a port to enter host cells [5]. ACE2 is highly expressed in the

lung, heart and vascular endothelium, counteracting the effects of angiotensin II in states with excessive activation of the renin-angiotensin system such as hypertension and heart failure [1]. Consistent with a hypothesis, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may also increase the danger of severe COVID-19. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are commonly used medications for patients with cardiovascular diseases such as refractory high blood pressure and heart failure. These two families of drugs are also prescribed for the management of cardiovascular diseases in elderly patients and in patients with diabetes. Intravenous infusions of ACEIs and ARBs in animal models increase the numbers of angiotensin converting enzyme 2 (ACE2) receptors in the cardiopulmonary circulation. Patients taking ACEIs or ARBs chronically are assumed to have increased numbers of ACE2 receptors throughout their cardiopulmonary circulations which also results in an upregulation of ACE2 as observed in experimental animals [6]. A further point that should be noticed is the genetic predisposition for an increased risk of COVID-19, which might be due to ACE2 polymorphisms that have been linked to diabetes mellitus and hypertension, specifically in Asian populations. So, the predisposition of a patient might result from a combination of both drug therapy and ACE2 polymorphism [7]. An

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opposing hypothesis has suggested that increasing of ACE2 or infusion of human recombinant ACE2 might protect against CoV-2 infections. However, it has to be emphasized that the role of ACE2 in this protection, are not clear. Furthermore, it should be considered that ACEIs have been reported to modify the adaptive immune response, suggesting that long-term periods of ACEIs' usage might suppress the adaptive immunity, which has a key role against viral infections. Available published data indicate briefly that ACE2 is a double-edged sword, specifically when considering patients with CoVID-19 and comorbidities of hypertension, diabetes and cardiovascular disease [8]. Despite all of these controversies, during reading these articles, a question that comes to mind is: Could there be a link between other systemic diseases such as Sarcoidosis and the increased risk of Covid-19 and vice versa?

Angiotensin-converting enzyme (ACE) is elevated in sarcoidosis patients and may also be elevated in other certain pulmonary granulomatous disorders (silicosis and tuberculosis), hyperthyroidism and diabetes [9, 10] and Covid-19 as mentioned before. Polymorphism in the ACE gene that affects the ACE enzyme level in metabolic diseases like hypertension and sarcoidosis might be a genetic marker for predisposition of these diseases in some populations [11] similar to what mentioned recently for COVID-19 [7].

On the other hand, several studies mentioned an important role for Th17 cells besides Th1 in sarcoidosis, as the frequency of IL-17-producing T cells is increased in peripheral blood and lungs of subjects with sarcoidosis compared with controls [12]. Peripheral blood of patients with severe COVID-19 had a strikingly high number of TH17 cells, further supporting a Th17 type cytokine storm in this disease which results in lung tissue damage. Elevated Th17 as the same of Th-1 responses or enhanced IL-17-related pathways are also discovered in MERS-COV and SARS-COV patients [13].

According to the novelty of COVID-19 disease, genetic predisposing assessments has not been investigated yet but in MERS-COV infection, MHC II molecules, such as HLA-DRB1*11:01 are associated with the susceptibility to this infection [5]. HLA-DRB1*11:01 (OR, 1.69; 95% CI) is also associated with susceptibility to sarcoidosis [14].

The presence of lymphopenia in sarcoidosis has long been proven with scientific studies [15]. It is also been reported that lymphocytes' count was reduced to lower than 5% within 2 weeks after COVID-19 disease onset [16].

Lung involvement with a peripheral predominance is a presentation in COVID-19 patients and was previously seen in patients with SARS-COV and MERS-COV infections and the chest CT showed that disease progressed with ground-glass opacities, which is similar to that of SARS-CoV-2 infection [5]. Nodules in sarcoidosis also tend to be more abundant around Broncho-vascular structures and sub-pleural along the chest wall [17].

Immunological impairments such as lymphopenia in patients with sarcoidosis and their treatment by glucocorticoids and cytotoxic drugs may increase the risk

of severe bacterial and viral infections [18], so these people may be more susceptible to COVID-19 as a disease with viral source. On the other hand, many previous studies pointed to viral trigger in sarcoidosis [19] but no specific virus was mentioned.

A recent French cross sectional study on 482 patients, suggests that daily active tobacco smokers have a lower risk of developing severe or symptomatic COVID-19 as compared to nonsmokers [20]. It should be mentioned that our primary observations during the first COVID-19 outbreak (February-April 2020) on 206 COVID-19 patients admitted in intensive care units in Shahid Sadoughi hospital, Yazd, Iran, showed a possible negative association between smoking and coronavirus-2 infection. An observation that was addressed in the literature for sarcoidosis. Some previous studies mentioned that current smokers also have less probability for developing sarcoidosis [21, 22].

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Conflict of Interest

The authors declare no conflicts of interest.

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