Thorac Res Pract. 2023; 24(1): 45-48 DOI: 10.5152/ThoracResPract.2023.22076

Case Report

Can Coronavirus Disease 2019 Induce Sarcoidosis: A Case Report

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Cite this article as: Racil H, Znegui T, Maazoui S, et al. Can coronavirus disease 2019 induce sarcoidosis: A case report. *Thorac Res Pract.* 2023;24(1):45-48.

Abstract

Since the emergence of coronavirus disease 2019, a large spectrum of clinical manifestations following this acute viral infection has been reported especially autoimmune manifestations and inflammatory disorders. However, a causal link has not yet been established. Herein, we reported a case of pulmonary mediastinal sarcoidosis following coronavirus disease 2019 infection. A 41-year-old woman with no clinical or radiographic symptoms or signs of sarcoidosis prior to coronavirus disease 2019 infection developed dyspnea, cough, and fatigue, a few months after discharge. A chest thoracic scan performed 3 months after hospital discharge showed regression of ground-glass opacities with the appearance of pulmonary micronodules. Clinical examination and spirometry were normal. The evolution was marked by progressive worsening of dyspnea and significant weight loss. A chest thoracic scan performed 6 months after discharge showed bilateral and symmetrical hilar and mediastinal and paratracheal lymphadenopathy. Bronchoalveolar lavage with cell count showed a lymphocytosis of 19.5% and a CD4/CD8 T cell ratio of 2.2. Endobronchial lung biopsy revealed noncaseating epithelioid granulomas. Sputum culture excluded tuberculosis. The diagnosis of pulmonary-mediastinal sarcoidosis was made. She was treated with an oral corticosteroid. The patient showed significant improvement during the 3-month follow-up period. Post-coronavirus disease sarcoidosis is very rare. Complementary studies are needed to discern the link between these diseases.

KEYWORDS: COVID-19, sarcoidosis, inflammation
Received: *July 24, 2022* ***Accepted:*** *October 19, 2022* ***Publication Date:*** *February 10, 2023*

INTRODUCTION

Since the worldwide coronavirus disease 2019 (COVID-19) pandemic began, a number of post-viral inflammatory disorders and autoimmune diseases have been reported.[1] While the occurrence post-COVID-19 infection of autoimmune diseases has been well elaborated, the development of sarcoidosis remains obscure and only a few cases in the literature have been reported. The link between these diseases is not clear, but several mechanisms of this virus have been proposed as a trigger for abnormal inflammatory response.

Herein, we report the third case of pulmonary mediastinal sarcoidosis following a COVID-19 infection diagnosed in a 41-year-old Tunisian patient.

CASE PRESENTATION

We present a 41-year-old patient with no history of any autoimmune diseases or sarcoidosis hospitalized in our department in November 2020 with complaints of fever and diarrhea for several days. Coronavirus disease 2019 infection was confirmed by reverse transcription-polymerase chain reaction. The oxygen saturation was 92%. Chest thoracic scan (Figures 1A and 1B) showed common manifestations of COVID-19 without lung architectural distortion. The extent of lung abnormalities was estimated at 25%-50%. The infection's severity was classified as moderate requiring low-flow oxygen therapy (2 L/min) and corticosteroid therapy. The length of the stay in the hospital was 5 days. The patient reported an initial improvement, followed few weeks later by the onset of persistent fatigue, cough, and exertional dyspnea. Clinical examination was normal, notably with no signs of bacterial infection. Chest thoracic scan at 3 months after discharge showed a significant regression of ground-glass opacities with the appearance of nodules in the lower lobes of both lungs. Bronchial fibroscopy and spirometry were normal. Six months later, the patient reported significant weight loss with progressively worsening dyspnea. Chest thoracic scan (Figures 2A and 2B) showed bilateral and symmetrical hilar, mediastinal and paratracheal lymphadenopathies, and bilateral lower lobe nodules. Bronchoalveolar lavage with cell count showed a lymphocytosis of 19.5% and a CD4/CD8 T-lymphocyte ratio of 2.2. Endobronchial lung biopsy revealed noncaseating epithelioid granulomas. Sputum smear and culture ruled out tuberculosis. The angiotensin-converting enzyme II (ACEII) level was high. The diagnosis of sarcoidosis was established on the basis of compatible clinical, radiologic, and histological findings. Spirometry was normal: forced expiratory volume in one second (FEV1: 2.320 L, 92% of predicted normal value), forced vital capacity (FVC: 2.670 L, 86%), and an FEV1/FVC ratio of 86%. Ophthalmology test, echocardiography,

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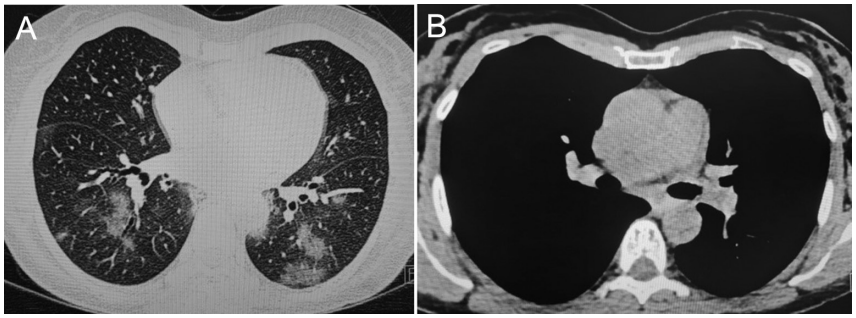

Figure 1. (A) Typical computed tomography (CT) manifestations of coronavirus disease 2019. (B) Initial CT of the mediastinum.

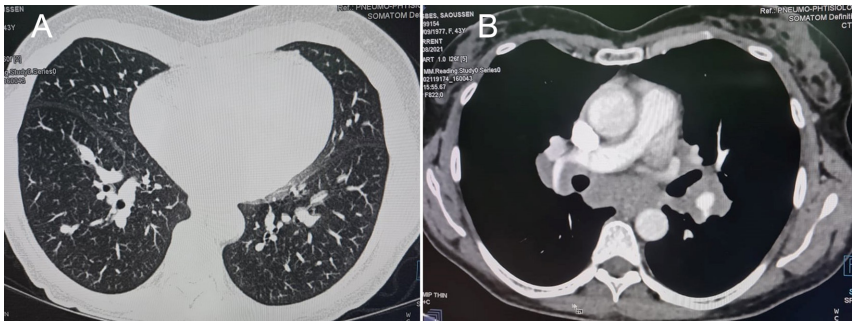

Figure 2. (A) Bilateral lung nodules. (B) Bilateral and symmetrical hilar, mediastinal lymphadenopathies.

and nervous system evaluation ruled out extrapulmonary sarcoidosis. Treatment started with prednisolone. During the 2-month follow-up period, the patient's symptoms subsided and she showed much improvement.

DISCUSSION

The occurrence post-COVID-19 infection of autoimmune diseases has been well elaborated. A systematic review of reported cases, published in October 2020, found that 33 cases of patients with COVID-19 developed an autoimmune disease after 2 to 33 days after the onset of viral illness. These autoimmune diseases included subacute thyroiditis, Kawasaki disease, coagulopathies, antiphospholipid syndrome, immune thrombocytopenic purpura, autoimmune hemolytic anemia, and Guillain–Barré syndrome.[2]

The development of sarcoidosis post-COVID-19 infection remains extremely rare. Only 6 cases were previously reported (Table 1). Recently, a case of pulmonary-mediastinal sarcoidosis following a COVID-19 infection was published on January 12, 2022. It is about a patient with a previous prostate cancer history who developed pulmonary sarcoidosis 1 year after severe COVID-19 disease. However, the patient's history of prostate cancer could be a confounding factor in attributing the development of sarcoidosis to a post-COVID-19 effect.[3] Five other case reports of sarcoidosis, including 1 case of sarcoidosis stage 1, 1 case of sarcoidosis stage 2 published on April 2021, and 3 cases of biopsy-confirmed sarcoid-like reaction, were diagnosed several weeks after COVID-19 infection.[4-6] To our knowledge, our patient was the third case of pulmonary-mediastinal sarcoidosis. He had no personal or family history of cancer or interstitial lung diseases, and he developed manifestations of sarcoidosis after 6 months of COVID-19 infection.

MAIN POINTS

- Here, we present the third case of pulmonary mediastinal sarcoidosis following a coronavirus disease 2019 (COVID-19) infection, confirmed on pathology.
- Coronavirus disease 2019 has been implicated in the development of granulomatous manifestations.
- Sarcoidosis following COVID-19 infection is very rare and the link between these diseases remains obscure.

The link between COVID-19 and sarcoidosis is not well established. It has been suggested that this virus might trigger the formation of noncaseating granulomas via the renin–angiotensin system and the innate immune system. Indeed, the S protein of this virus attaches to host cells through ACEII, allowing fusion with the cell membrane and release of viral RNA. After entry, through this host receptor (ACEII), severe acute respiratory syndrome coronavirus 2 causes an exacerbated inflammatory response and favors a "cytokine storm" that is considered central to the progression of the disease to acute respiratory distress syndrome. It activates pro-inflammatory cytokines such as interleukin (IL)-6, IL-10, interferon-gamma (IFN-γ), and tumor necrosis factor-alpha. This cytokine dysregulation is common to the pathophysiology of both COVID-19 and sarcoidosis. Research demonstrated a high percentage of Th17.1 cells in the lung lavage of sarcoidosis patients compared with control patients and that approximately 60% of these cells, which present the dominant phenotype, produced only IFN-γ.[3,4,7]

Several studies confirm the role of ACEII expression and activity in COVID-19 pathogenesis. The physiological role of ACEII is to cleave angiotensin II to angiotensin.

Table 1. Case Reports of Sarcoidosis Following COVID-19 Infection

Authors	Publication	Case Presentation	Diagnosis
Behbahani et al[5]	July 2020	• A 72-year-old woman with a medical history of asthma, hypertension, hyperlipidemia, obstructive sleep apnea, and seizure disorder • Two weeks after COVID-19 infection: violaceous nodules on the glabella, submental chin, and anterior shin	Sarcoid-like reaction
Mertz et al[4]	April 2021	• A 32-year-old woman • Possible COVID-19 diagnosed on March 2020 • Apparition of tachycardia 2 weeks after initial improvement	Lofgren syndrome with pulmonary stage 2 sarcoidosis
		• A 51-year-old woman • SARS-CoV-2 pneumonia in April 2020 • One week later: latero-cervical lymphadenopathies	Sarcoidosis stage 1
		• A 32-year-old woman • *Possible COVID-19 infection • Next month: Isolated erythema nodosum lesions of the legs	Sarcoid-like reaction
Polat Ekinci et al[6]	August 2021	• A 55-year-old woman with a history of hypertension, hyperlipidemia, and hypothyroidism • One month after COVID-19 infection: infiltrated and tender plaques over old scar sites on both knees, subcutaneous nodules on both arms, 3 subcutaneous papules on periorbital areas, and a single papule in the glabellar region	Sarcoid-like reaction
Capaccione et al[3]	January 2022	• A 61-year-old male never-smoker with a history of prostate cancer and chronic kidney disease • One year after severe COVID-19 disease: fatigue and weight loss • Chest CT: pulmonary nodules and extensive mediastinal and hilar adenopathy	Pulmonary-mediastinal sarcoidosis

COVID-19, coronavirus disease 2019; CT, computed tomography; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Angiotensin-converting enzyme II is highly expressed by lung epithelial cells, a major target of the disease, resulting in an inflammatory response in the lower airways of the lungs. Moreover, it is known that ACEII is regulated in macrophages located within the granulomatous tissue in sarcoidosis and plays an important role in granuloma formation and in the regulation of tumor necrosis factor-alpha production.[4,7]

Furthermore, recent finding reports that CD8+ mucosal-activated invariant T cells, which may be involved in the pathogenesis of sarcoidosis, might also play a role in self-sustaining inflammation in the lungs of patients with COVID-19.[8]

As with other autoimmune diseases, disruption of the immune system is likely a causative agent in the development of sarcoidosis after COVID-19 infection. Longer follow-up is needed to confirm the diagnosis or to differentiate it from transient symptoms due to the host's immune response to COVID-19.[9]

Because of the rarity of the disease, treatment and outcomes would be similar to those of people who are not infected with COVID-19.

CONCLUSION

This case report may be valuable for increasing awareness of the possibility of post-COVID sarcoidosis. The shared mechanism needs to be studied, but it requires more patients.

Informed Consent: Written informed consent was obtained from the patient for publication of this case report.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.R., S.M.; Design – S.M., A.T.; Supervision – H.R., N.C.; Materials – T.Z.; Data Collection and/or Processing – N.H., A.T., S.H.; Analysis and/or Interpretation – N.H., S.H.; Literature Review – N.C., H.R., T.Z.; Writing – T.Z., H.R.; Critical Review – N.C., H.R.

Acknowledgments: The authors would like to thank the patient who agreed to share this data.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declare that this study had received no financial support.

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