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CASE REPORT

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Sarcoidosis developing after COVID-19: A case report

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Abstract

COVID-19 has been implicated in the development of a range of autoimmune diseases and medical consequences. Sarcoidosis is an inflammatory disease with sustained granulomatous inflammation. The possible main pathogenesis of sarcoidosis is a dysregulation between immune response and certain environmental antigens. We present a case of sarcoidosis as an interesting sequela of COVID-19. The patient was hospitalized due to SARS-CoV-2 without complication. Ten weeks after the illness, his chest computed tomography (CT) showed bilateral hilar, paratracheal and subcarinal lymph node enlargement. Endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) was performed; pathologic findings were that of well-formed non-necrotizing granulomas. Complete eye examination reported panuveitis and papillitis in both eyes. On the basis of these findings, sarcoidosis was diagnosed. Therefore, sarcoidosis developing after COVID-19 was suggested as a possible link between the viral infection and dysregulation of the inflammation process. However, further studies are needed to confirm this association.

KEYWORDS

COVID-19, granulomatous, sarcoidosis, uveitis

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral disease induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has been implicated in the development of a range of autoimmune diseases including Guillain-Barré syndrome, systemic lupus erythematosus, autoimmune hemolytic anaemia, immune thrombocytopenic purpura, autoimmune thyroid diseases and Kawasaki disease.[1–4] Sarcoidosis is an inflammatory disease with sustained granulomatous inflammation. The possible main pathogenesis of sarcoidosis is a dysregulation between immune response and certain environmental antigens.[5,6] We present a case of sarcoidosis as an interesting sequela of COVID-19.

CASE REPORT

A 35-year-old Thai man, previously healthy with no history of medication use, was hospitalized due to SARS-CoV-2 detection on reverse transcription polymerase chain reaction (RT-PCR) testing. (At the time he was admitted, it was public health policy to admit anyone testing positive.) He had low grade fever and sore throat for 3 days. He received only symptomatic treatments including hydration, cough suppressants and antipyretics without any antiviral medications. During the admission, no complication was found, including normal chest radiography. He was discharged within 7 days without any residual symptoms. Ten weeks after the illness, he visited the 'post-COVID-19 outpatient clinic' with a 14-day history of low-grade fever, malaise, non-productive cough and exertional dyspnea. His chest radiography illustrated new abnormal findings of enlarged bilateral hilar area (Figure 1A,B). Chest computed tomography (CT) showed bilateral hilar, paratracheal and subcarinal lymph node enlargement up to 36 mm in diameter (Figure 1C,D), consistent with stage I pulmonary sarcoidosis. RT-PCR for SARS-CoV-2 result, performed for excluding the viral re-infection, in this visit was negative. Other physical

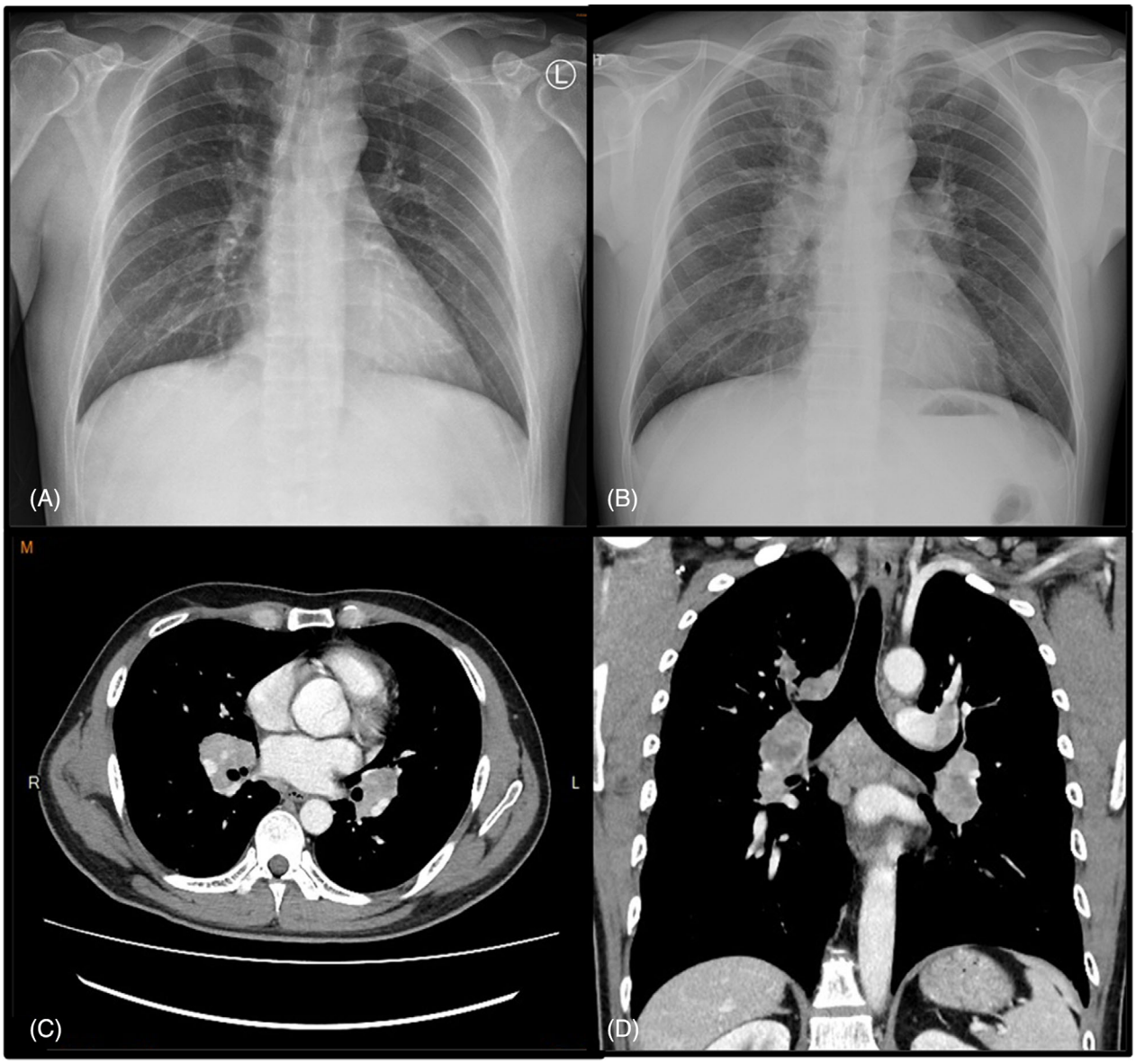

FIGURE 1 (A)) Chest X-ray at first day of SARS-CoV-2 positive shows normal finding without active pulmonary disease. (B) Chest X-ray at 10 weeks after the illness, the image illustrates bilateral enlargement of hilar and paratracheal lymph nodes. CT chest with contrast is shown in C (axial view) and D (coronal view), revealing bilateral hilar, and subcarinal lymph nodes enlargement.

examinations were normal. Neither palpable lymph nodes nor an enlarged spleen was found. Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) was taken from the mediastinal lymph nodes. Tuberculosis and fungal infection were excluded with GeneXpert MTB/RIF, fungal culture and tuberculosis culture from both bronchoalveolar lavage (BAL) and lymph node aspiration. The pathologic findings were well-formed non-necrotizing granulomas characterized by epithelioid histiocytes accompanied by lymphocytes (Figure 2).

Biochemical laboratory results showed normal values for complete blood count, liver and kidney function, as well as electrolytes and calcium level. Serum angiotensin converting enzyme (ACE) level was 20.3 U/L (8.3–21.4 U/L).

The patient later complained that he also saw floaters in his vision without ocular pain 1 week before this presentation. Complete eye examination by an ophthalmologist revealed a visual acuity of 20/25 in the right eye and 20/30 in the left eye. Anterior segment examination revealed fine keratic precipitates in both eyes. Fundus examination showed vitritis and optic disc edema in both eyes, and peripheral vascular sheathing in the right eye. Fluorescein angiography confirmed leakage at both optic disc and peripheral retinal vein in the right eye (Figure 3). He received a diagnosis of panuveitis, papillitis and retinal vasculitis in both eyes.

To screen for cardiac sarcoidosis, 12-lead electrocardiograms and cardiac magnetic resonance imaging (MRI) were

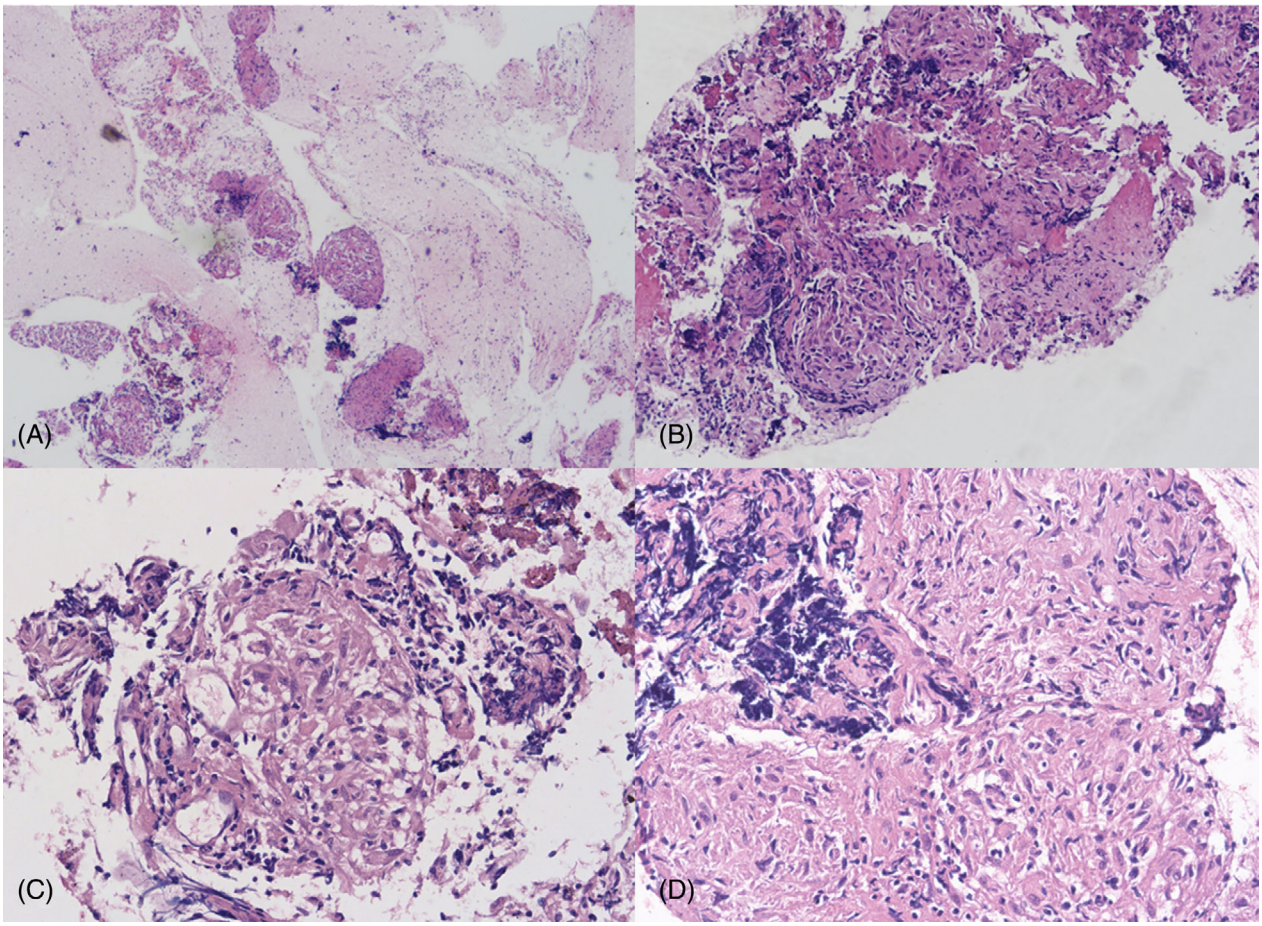

FIGURE 2 (A) At low magnification, the lesion shows tightly and well-formed non-necrotizing granulomas. (B–D) The granulomas are characterized by epithelioid histiocytes accompanied by lymphocytes.

performed with normal results. On the basis of these findings, pulmonary and ocular sarcoidosis was diagnosed. His treatment was initially started with 60 mg of prednisolone daily and gradually tapered to 20 mg over 1 month and maintained at this dose afterwards.

Two months after receiving steroid, the patient's low-grade fever and non-productive cough resolved. His chest radiography and CT showed slightly decreased mediastinal lymph node size (Figure 4). Moreover, the patient remarked his vision had much improved. The visual acuity was 20/20 in right eye and 20/25 in the left eye. Vitreous inflammation disappeared and optics disc showed less hyperemia in both eyes.

DISCUSSION

Sarcoidosis is an inflammatory, multisystemic disease with a wide range of clinical manifestations. The disease can affect any organ in the body, predominantly in the lungs, lymphatic system, skin, eyes or a combination of these sites.[5,6] Sarcoidosis is characterized by the histopathology findings of non-caseating granulomas. It has been proposed that the pathogenesis of sarcoidosis involves both genetic predisposition and environmental exposures.[5,6] A dysregulated immune response against one or more disease-promoting antigens results in an inflammatory process to eliminate the antigen. Many infections have been identified as possible precipitating factors in the development of sarcoidosis, particularly by dysregulating antigen presenting cells, alveolar macrophages and T-cells. These infections include *Mycobacterium* spp., *Cutibacterium acnes* and several viruses, notably herpes virus.[7]

SARS-CoV-2 has been reported to trigger a myriad of autoimmune and rheumatic manifestations.[2] Similarly, Mihalov et al. reported Lofgren syndrome, a clinically distinct phenotype of sarcoidosis, developing in close temporal association with COVID-19. The patient presented with bilateral pulmonary hilar lymphadenopathy with histological findings of non-caseating granuloma, erythema nodosum and polyarthritis. After Lofgren syndrome was diagnosed, the symptoms resolved after steroid therapy.[8] In addition, some cases of sarcoid-like skin reactions were reported among patients recovering from COVID-19.[9,10] Several studies have demonstrated that COVID-19 might share common features with sarcoidosis involving common mechanistic cellular pathways around the regulation of autophagy and mitophagy.[11,12]

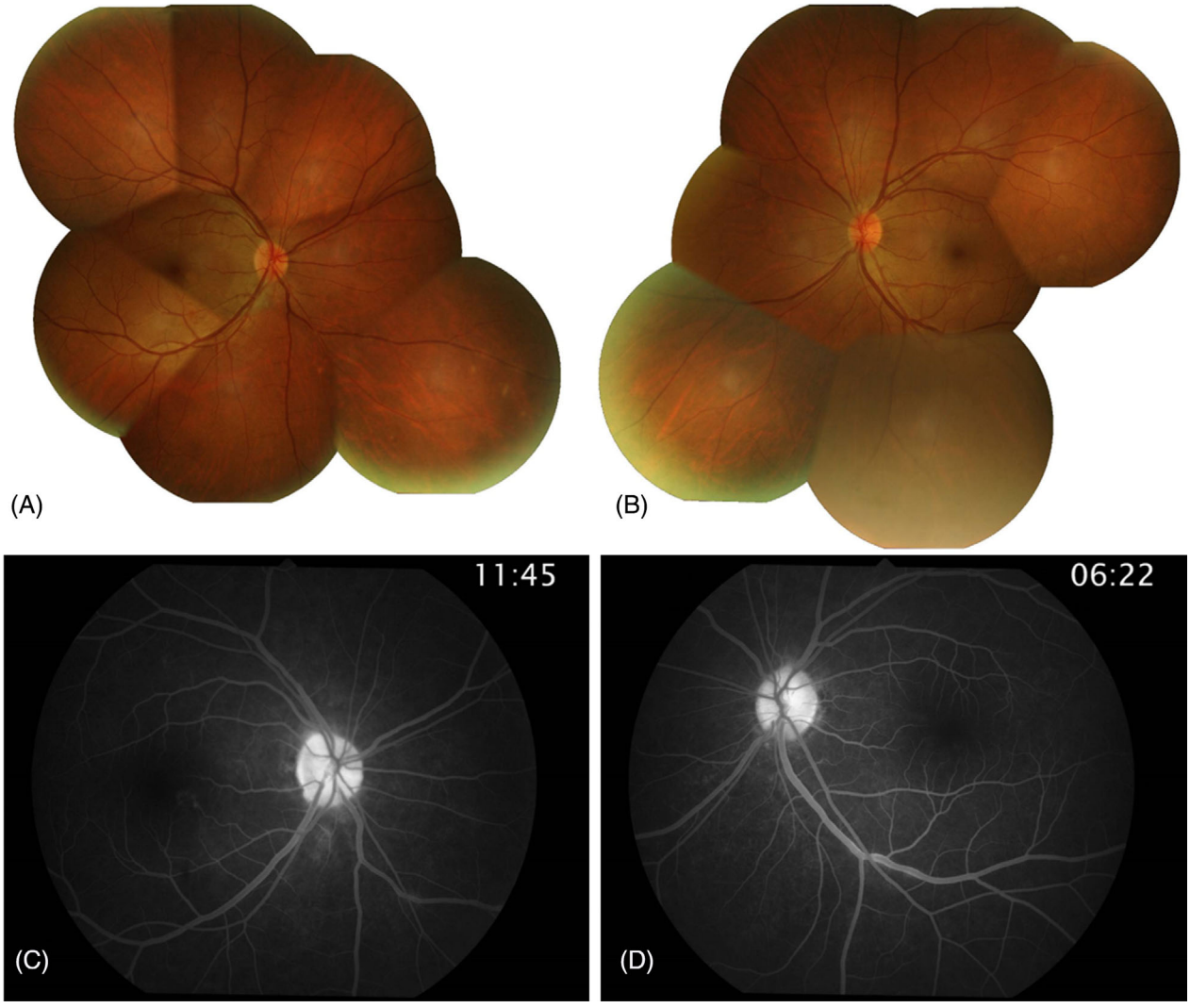

FIGURE 3 Fundus examination showed (A) optic disc edema and peripheral vascular sheathing in the right eye, (B) optic disc edema in the left eye. Fluorescein angiography confirmed (C) leakage at optic disc in the right eye (D) leakage at the optic disc in the left eye.

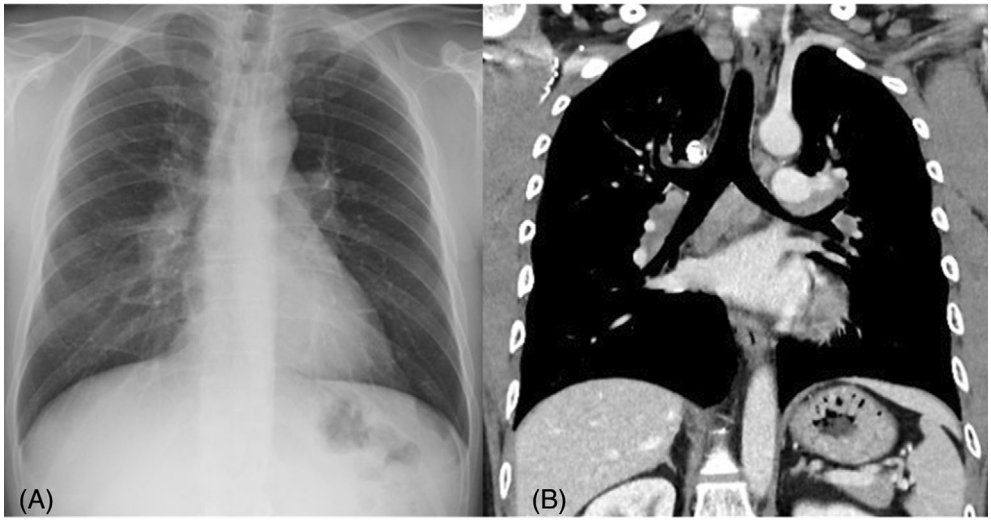

FIGURE 4 Chest radiographs, performed after receiving treatment, show multiple mediastinal lymphadenopathies which slightly decreased in size.

Our patient presented with bilateral hilar lymphadenopathy and had granulomatous formation confirmed on histology. Other causes of granulomas, such as tuberculosis and fungal infection, were also excluded with special stains from tissues, GeneXpert and culture from both BAL and lymph node aspiration. His serum ACE level was 20.3 U/L. Although within normal limits, it was considered an upper normal limit for serum ACE level.[13] Fundoscopy showed panuveitis, papillitis and retinal phlebitis which are compatible with sarcoidosis. Moreover, two chest radiographies were available for comparison. The first one was performed when SARS-CoV-2 was detected and, the later one was performed after recovery from COVID-19 when the virus was undetected. On the basis of his symptoms and new radiographic findings, we proposed sarcoidosis as a later complication of COVID-19.

In conclusion, the development of sarcoidosis after COVID-19 suggests that there might be a link between viral infection and dysregulation of the inflammatory process. Further studies are needed to confirm this association.

AUTHOR CONTRIBUTION

Dujrath Somboonviboon primarily collected the data, drafted the manuscript and arranged the figures. Anan Wattanathum performed bronchoscopy and was a major contributor in writing and reviewing the manuscript. Narumon Keorochana performed the complete eye examination. Kittisak Wongchansom interpreted the pathologic findings. All authors have read and approved the manuscript.

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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