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Case Report

Evaluating ground glass opacities (GGO) in the COVID-19 era. Do autoantibodies help?

Nina Pejic[1], Milica Stojkovic Lalosevic[1,2], Milos Stulic[1,2], Milica Culafic[1,3], Djordje Culafic[1,2]

[1] Clinic of Gastroenterology and Hepatology, University Clinical Center of Serbia, Belgrade, Serbia
[2] Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[3] Department of Pharmacokinetics and Clinical Pharmacy, Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia

Abstract

Introduction: COVID-19 is an infectious disease, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and there have been outbreaks worldwide. The presentation may include unspecific and mild symptoms, myalgia, headaches, high fever, dry cough, severe dyspnea and acute respiratory distress syndrome (ARDS).

Case study: We present a rare case of microscopic polyangiitis (MPA) with interstitial lung disease and without renal involvement misdiagnosed as COVID-19.

Conclusions: Differential diagnosis of COVID-19 is extremely important, and must be correctly identified in order to proceed with correct treatment.

Key words: COVID-19; microscopic polyangiitis; interstitial lung disease.

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Introduction

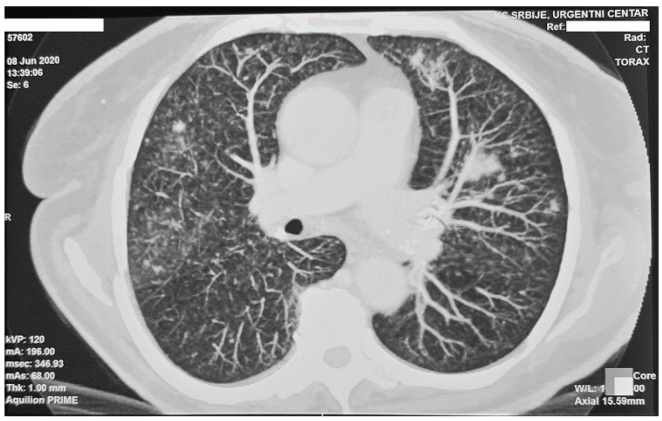
COVID-19 is an infectious disease, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that led to worldwide outbreaks, subsequently leading to declaration of pandemic by the World Health Organization (WHO). Presentation may include unspecific and mild symptoms, myalgia, headaches, high fever, dry cough, severe dyspnea and ARDS (acute respiratory distress syndrome) [1]. Several studies have suggested that the gastrointestinal tract may be affected by SARS-CoV-2, presenting with abdominal pain, diarrhea, nausea, and vomiting [2]. COVID-19 is suspected if certain clinical and epidemiological criteria are met. These clinical criteria include fever, cough, and three of the following: fatigue, headache, myalgia, sore throat, and dyspnea. Diagnosis is confirmed by positive real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) assay for COVID-19 using respiratory or blood samples, irrespective of clinical signs and symptoms. Current findings suggest that RT-PCR shows moderate sensitivity (63–78%) [2], and RT-PCR should be repeated in patients with positive imaging [3]. Differential diagnosis of COVID-19 is extremely important, and should be correctly identified in order to proceed with correct treatment. We present a rare case of microscopic polyangiitis (MPA) with interstitial lung disease misdiagnosed as COVID-19.

Case study

A 69-year-old female patient with presentation of fever, myalgia, headaches, and dry cough was admitted in the emergency department of the Clinical Center of Serbia on June 8, 2020 and was suspected to have COVID-19 infection. The patient had experienced mild dyspnea and nonproductive cough during the five days period prior to admission, with additional feeling of malaise and fatigue. The body temperature was up to 40 °C. Apart from a cryptogenic liver cirrhosis, diagnosed six months prior, all other medical history was insignificant. The following observations were made during a previous hospitalization in our institution: hepatotropic viral markers were negative, thyroid function was normal, and insulin levels, oral glucose tolerance test, cholesterol levels and alpha-1 antitrypsin levels were in the normal range. Wilson disease was excluded based on laboratory findings, neurological examination, and genetic testing. Immunology tests at

that time were in reference range. Imaging methods showed no evidence of primary sclerosing cholangitis. Percutaneous liver biopsy demonstrated presence of regenerative nodules, fibrosis of multiple portal tracts, and mild loss of hepatocytes with centrilobular necrosis at some points, therefore, the diagnosis of cryptogenic cirrhosis was made. Physical examination during this hospitalization was unremarkable. Laboratory findings showed marked inflammation, C-reactive protein (CRP) of 45 mg/L with procalcitonin of 0.1 ng/mL, erythrocyte sedimentation rate of 90 and Interleukin-6 of 100 pg/mL. During complete blood count, mild lymphopenia (0.96×10^9/L, reference 1.2-3.4 10^9/L), normochromic, normocytic anemia (haemoglobin 10^9 g/L, MCV 89 fL), as well as thrombocytopenia (platelets 110×10^9/L, reference 150-450 10^9/L) were observed, with leukocytes within the normal range. There were also signs of mild hepatocellular necrosis (AST 55 U/L, ALT 62 U/L, reference range up to 41 U/L), without cholestasis, hypoalbuminemia (albumins 30 g/L, reference range 35-53 g/L) and elevated INR (INR 1.5, with reference 0.8-1.2) other unremarkable parameters including kidney function tests were consistent with her previous medical history. SARS-CoV-2 RT-PCR from a nasopharyngeal swab was negative two times a in row. Chest computed tomography (CT) revealed bilateral micronodular infiltrates with ground glass opacities (GGO) (Figure 1). Considering the limited sensitivity of RT-PCR, we treated the patient according to the national COVID-19 guidelines for 10 days, which at that time included antiviral therapy; however clinical and laboratory response was not observed. Taking into account that the patient's condition failed to improve, differential diagnosis of tuberculosis and sarcoidosis were investigated, and ruled out, and immunological tests were repeated because of CT findings. ANA HEp-2 was in high titer 1:320, as well as p-ANCA (anti-neutrophil cytoplasmic antibody) 1:160, with levels of anti-MPO-ANCA of 65 U/mL. According to clinical presentation, immunology, and chest CT, microscopic polyangiitis without renal involvement was diagnosed. Pulmonary function test indicated mixed restrictive or obstructive pattern with FVC 87% and FEV1 72% and bronchoscopy revealed interstitial pneumonia with fibrosis and honeycomb changes. After initiation of corticosteroid therapy with a dose of 1 mg/kg/day and cyclophosphamide with a dose of 1.5 mg/kg/day, complete clinical and laboratory improvement was achieved. Corticosteroids were tapered and cyclophosphamide was replaced with azahioprine with dosage 2mg/kg/day during maintenance therapy.

Figure 1. Chest computed tomography findings of bilateral micronodular infiltrates with a ground glass opacity.



Discussion and conclusions

MPA is a systemic condition and ANCA associated vasculitis affect small blood vessels, primarily of kidneys and lungs, where the major auto-antigen target is myeloperoxidase (MPO-ANCA) [4]. The average annual incidence is about 5.9 in 1,000,000, making the MPA an uncommon disease. In everyday clinical practice it is difficult to establish the diagnosis of MPA, due to its overlap with other vasculitides, especially granulomatosis with polyangiitis. Screening for specific anti-MPO immunoassay, should be included in the workup towards a diagnosis of MPA. Renal involvement is the most common clinical feature of MPA, characterized by rapidly progressive glomerulonephritis, which occurs in more than 80% of the patients. The patient's kidney remains unaffected in a small number cases, which was in the case of our patient. The most frequent manifestation of lung disease is diffuse alveolar hemorrhage (DAH), caused by pulmonary capillaritis, whereas interstitial lung disease (ILD) is additionally uncommon, presenting with interstitial pneumonia and/or fibrosis. ILD is usually detected in patients older than 65 years and is usually seen before complete vasculitis syndrome. The major CT feature of ILD associated with MPA include usually bilateral ground glass opacities (GGO) and consolidations, with predominantly peripheral distribution [5]. The treatment for MPA consists of immunosuppressive (corticosteroid) and immunomodulatory (cyclophosphamide or methotrexate) therapy. Initial therapy should be combination of immunosuppressive and immunomodulatory therapy, whereas maintenance of remission should be achieved through immunomodulatory therapy. Azathioprine or methotrexate are preferred over cyclophosphamide due

to its side-effects. Prognosis of these patients is generally good, with 90% of patients responding to therapy, and 75% achieving complete remission, which was the case of our patient.

In the era of COVID-19 pandemic, we need to emphasize that in patients presenting with fever and CT findings of GGO and negative RT-PCR for SARS-CoV-2 from a nasopharyngeal swab, differential diagnosis should be made before initiation of treatment. It should be noted that ILD with GGO, although rare, may be the first manifestation of MPA. ANCA testing should be included in the diagnostic workup of interstitial pneumonia.

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Authors' Contributions

Conception and design: Pejic N, Stojkovic Lalosevic M; administrative support: Culafic Dj, Stulic M, Culafic M; provision of patients: Stojkovic Lalosevic M; data analysis and interpretation: all. All authors have written, read and agreed to the last version of the manuscript.

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Corresponding author

Milica Stojkovic Lalosevic, MD, PhD
Assistant Professor, Clinic of Gastroenterology and Hepatology, Clinical Center of Serbia, University of Belgrade, 11000 Belgrade, Serbia
Tel: +381 11 3663727
Email: drmilicastojkovic@gmail.com

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