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VIA MEDICA

Bartłomiej Wnuk, Zbigniew Heleniak, Barbara Piontecka-Bułło, Tomasz Liberek, Alicja Dębska-Ślizień

Department of Nephrology, Transplantology and Internal Medicine, Medical Faculty, Medical University of Gdansk

COVID-19 and ANCA-associated vasculitis case report and literature review

Abstract

ANCA-associated vasculitis (AAV) related to SARS-CoV-2 infection is uncommon in clinical practice. Differential diagnosis could be challenging due to potentially similar clinical symptoms in both diseases, especially when lung involvement is observed. We present a case of a 65-year-old woman with SARS-CoV-2 infection and *de novo* presentation of ANCA-associated vasculitis. She was admitted to the hospital for dyspnea and fatigue. In addition, the antigen test for SARS-CoV-2 infection was positive. Laboratory tests revealed acute kidney injury and anemia. This article describes the clinical course, laboratory and radiographic features, and treatment of this rare condition. We also have performed a literature review of autoimmune diseases triggered by SARS-CoV-2 infection.

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Key words: acute kidney injury; ANCA-associated vasculitis; COVID-19

INTRODUCTION

It has been shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may trigger the presentation or exacerbation of autoimmune diseases such as systemic lupus erythematosus (SLE), vasculitis, myositis, arthritis, and crescentic glomerulonephritis [1] (Tab. 1). Concerning SLE patients, those suffering from SARS-CoV-2 infection appeared to develop more severe manifestations, with higher rates of hospitalization, invasive ventilation requirement, or death [2]. Gianfrancesco et al. described the demographic and clinical characteristics of the first 600 patients submitted to the COVID-19 Global Rheumatology Alliance and showed the differences in their hospitalization status. In the hospitalized patients, there were more patients with SLE and vasculitis as compared to the group without these diseases (17% *vs.* 9%, 11% *vs.* 5%, respectively) [3]. Kant et al. analyzed the impact of COVID-19 on patients with anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) and concluded that the incidence of COVID-19 in this group of patients appears to be similar to that of the general population [4].

De novo presentation of AAV during COVID-19 and after vaccination against COVID-19 has been recently reported in a few cases [5, 6] (Tab. 1). Distinguishing between SARS-CoV-2 infection and its coincidence with AAV may be difficult since COVID-19 alone may exhibit coexisting pneumonia and acute kidney injury (AKI), thus mimicking pulmonary-renal syndrome.

The article aimed to present a patient with typical features of AAV with AKI and pulmonary involvement during SARS-CoV-2 infection.

CASE STUDY

A 65-year-old woman with a history of arterial hypertension, postoperative hypothyroidism, and pernicious anemia was admitted to the department of nephrology for dyspnea, fatigue, and weight loss persisting for the last month before hospitalization.

Laboratory tests revealed anemia with a hemoglobin level of 7.2 g/dL (reference range 12–16 g/dL), elevated inflammatory markers with C-reactive protein (CRP) 92.71 mg/l (reference range 0.08–3.1 mg/L), and AKI with a serum creatinine (sCr) level of 11.24 mg/dL (reference range 0.6–1.3 mg/dL). Erythrocyturia and proteinuria were observed in urinalysis. The antigen test from a nasopharynx swab sample confirmed COVID-19, which was con-

Address for correspondence:
Bartłomiej Wnuk
Department of Nephrology, Transplantology and Internal Medicine, Medical Faculty, Medical University of Gdansk,
ul. Dębinki 7, 80–211 Gdańsk
e-mail: bwnuk@uck.gda.pl

Table 1. Autoimmune disease triggered by Sars-CoV-2 infection, literature search [1, 10–13]

Bibliography	Type of autoimmune disease diagnostic confirmation	Treatment and outcome
I [1]	**Crescentic glomerulonephritis** anti-myeloperoxidase antibody was at a level of 80.6 U/mL, kidney biopsy — necrotizing glomerulonephritis with cellular crescents	Methylprednisolone (1000 mg intravenous (IV)) for three consecutive days) cyclophosphamide (500 mg IV two doses at 15-day intervals) and plasma exchange (10 times)
II [10]	Systemic Lupus Erythematosus anti-La/SSB antibodies, anti-SSA/Ro, anti-cyclic citrullinated peptides (anti-CCP) antibodies, anti-double-stranded deoxyribonucleic acid antibody (anti-dsDNA), kidney biopsy (lupus nephritis class I)	Methylprednisolone pulse (1000 mg for three consecutive days), gabapentin, and vitamin B (300 mg daily) reduced symptoms
III [11]	**Cutaneous Vasculitis** skin biopsy demonstrated small- and medium-sized vessel vasculitis with neutrophils, some eosinophils, and histiocytes	Prednisolone at 0.5 mg per kilogram. Within 3 days, the vasculitis skin manifestations and general condition improved
IV [12]	**Myositis** ANA positive with cytoplasmic pattern (1:320) granular type, Anti-Ku, and anti-MI 2b positivity	Lopinavir/ritonavir and hydroxychloroquine antibiotic therapy (doxycycline and ceftriaxone) prednisolone at 1 mg per kilogram a progressive improvement in the next few days
V [13]	**Arthritis** Synovial fluid was applied to a nasopharyngeal swab and sent for SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR), which was positive	A 7-day course of a non-steroidal anti-inflammatory medication, naproxen-sodium full resolution of both pain and swelling after 4 days of therapy

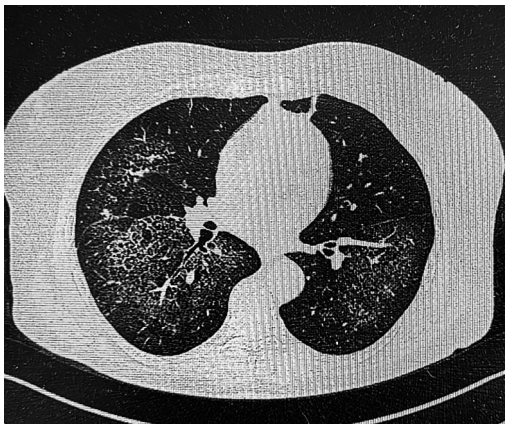

Figure 1. Thoracic computed tomography image of bilateral crazy paving mainly in the middle lobe

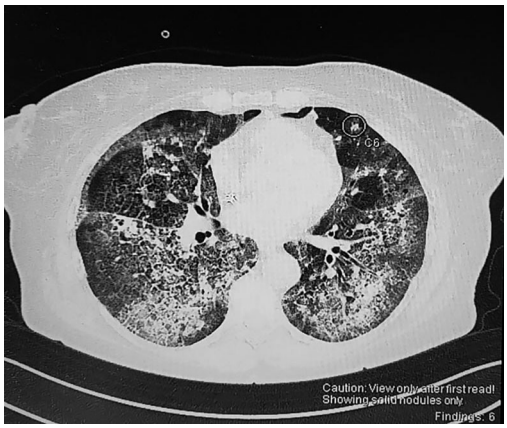

Figure 2. Thoracic computed tomography image of advanced interstitial lesions with diffuse alveolar hemorrhage

sistent with chest computed tomography (CT) showing bilateral crazy paving mainly in the middle lobes (Fig. 1a).The oxygen saturation was 94% in room air. The physical examination demonstrated paleness and no auscultatory changes.

Initially, conservative treatment was administered, which included forced diuresis and managing electrolyte imbalance; however, kidney function markers remained at high levels with sCr at 11 mg/dl despite efficient diuresis with 2–2.5l urine per day. Therefore, the patient was qualified for renal replacement therapy (RRT) (hemodialysis) and a tunneled catheter was implanted.

In the course of hospitalization, 6 units of packed red cells were transfused due to anemia; however, no signs of bleeding were observed.

The differential diagnosis of AKI included tests for multiple myeloma including serum protein electrophoresis and free light chain

Table 2. Clinical course of SARS-CoV 2 infection in the presented patient

Date	Symptoms and diagnostic tests	Treatment	Outcome
30.03.2022	Clinical condition: COVID-19 and kidney injury confirmation — dyspnea and fatigue, weight loss Laboratory results: positive antigen test for SARS-CoV-2, sCr 11.24 mg/dL (reference range 0.6–1.3 mg/dL), Hb 7.2 g/dL (reference range 12–16 g/dL), CRP 92.71 mg/l (reference range 0.08–3.1 mg/L) CT scan — bilateral crazy paving mainly in the middle lobes (Fig. 1)	Bicarbonates supplementation, forced diuresis and managing electrolytes imbalance, nasal oxygen therapy 2–4 L/min,	Improvement after oxygen therapy, efficient diuresis with 2.5 L urine per day
31.03–06.04.2022	Clinical condition: anemia — skin paleness, fatigue, dyspnea, BP 124/72 mmHg, oxygen saturation 94%, diuresis 2000–2500 mL daily Laboratory results: Hb 6.1–8.5 g/dL, sCr 11.63 mg/dL, urea 241–160 mg/dL (reference range 21–43 mg/dL), CRP 66.5–48–119 mg/L	Transfusion of packed red cells, bicarbonates supplementation, nasal oxygen therapy 3 L/min, antimicrobial therapy with ceftriaxone HD since 01.04.2022	Anemia, required repeated transfusions, significant improvement after transfusions and HD
7.04.2022	Clinical condition: pneumonia — exacerbation of dyspnea, oxygen saturation 78% in room air, Laboratory results: CRP increase at 129 mg/L	Increased nasal oxygen therapy 7–10 L/min, additional diuretics, and HD	Temporary improvement after additional HD
8.04.2022	Clinical condition: further worsening of respiratory insufficiency, diuresis reduction, anemia Laboratory results: Hb 5.8 g/dL, ANCA antibodies level at 1:1280 with MPO titer at 196.55 RU/mL CT scan — significant progression of interstitial lesions with crazy paving (Fig. 2)	HFNOT, methylprednisolone 1 g IV, TPE	Cardiac arrest, unsuccessful resuscitation Autopsy: diffuse alveolar hemorrhage

ANCA — anti-neutrophil cytoplasmic antibodies; BP — blood pressure; CRP — C-reactive protein; CT — computed tomography; Hb — hemoglobin; HD — hemodialysis; HFNOT — high flow nasal oxygen therapy; IV — intravenous; MPO — myeloperoxidase; sCr — serum creatinine; TPE — therapeutic plasma exchange

tier, which were negative. Additional tests for systemic disease revealed an increased level of ANA-HEP-2 antibodies at 1:2560 (reference range 1:80).

After eight days of isolation, the patient's control test for SARS-CoV-2 infection was negative. On the ninth day of hospitalization, the patient's condition worsened and resulted in dyspnea, respiratory failure, and diuresis reduction.

An additional CT scan revealed a significant progression of interstitial lesions with crazy paving (Fig. 1b). Also, on that day, serologies revealed a high ANCA antibody level at 1:1280 (reference range < 1:40) with myeloperoxidase (MPO) titer at 196.55 RU/mL (reference range < 20 RU/mL).

Based on the clinical and laboratory data, a diagnosis of pANCA-vasculitis was made. Therapeutic plasma exchange (TPE) was initiated, and pulse methylprednisolone therapy (1 g intravenous) was administered. The patient also was qualified for high-flow nasal oxygen therapy (HFNOT) because of respiratory insufficiency. After the TPE, the clinical condition continued to worsen and led to cardiac arrest. During resuscitation, significant bleeding from the airways was observed. After almost an hour of resuscitation, an anesthesiologist determined death. The autopsy revealed diffuse alveolar hemorrhage which confirmed the diagnosis (Tab. 2).

DISCUSSION

The presented report suggests that SARS-CoV-2 infection can be a trigger factor for vasculitis, and COVID-19 symptoms may occur simultaneously, or they can mimic AAV-like symptoms. Therefore, serological

tests against SARS-CoV-2 infection should be standard during diagnostic procedures. On the other hand, simultaneous immunological tests for AAV should be performed, especially in the case of AKI.

Izci Duran et al. described a total of six cases of AAV with AKI in COVID-19 patients in their review. All of these cases of vasculitis were diagnosed *de novo*, which suggests that SARS-CoV-2 infection may trigger autoimmunity and autoimmune diseases [1]. However, symptoms such as skin pathologies e.g. circinate erythema, coagulopathy, and general symptoms such as generalized muscle pain, nausea, vomiting, and/or diarrhea were observed in patients with already diagnosed AAV during SARS-CoV-2 infection [7, 8]. The presented patient was admitted to the hospital because of dyspnea and fatigue which are often observed in most patients with a severe clinical course of COVID-19.

Differential diagnosis was similar in other clinical studies, case reports, and case series and included serological tests such as pANCA and cANCA titer, imaging studies, and additionally, a renal biopsy was performed in all 6 described cases [1]. Camprodon Gómez M. et al also performed a skin biopsy in the search for leukocytoclastic vasculitis in a COVID-19 patient [9].

In the literature, some authors administered treatment for COVID-19 including favipiravir, tocilizumab convalescent plasma, and hydroxychloroquine [1]. On the other hand, AAV patients were treated with glucocorticoids, cyclophosphamide, rituximab, and TPE [1]. RRT was administered in patients with severe kidney failure, and respiratory support also was required in the majority of this population. The clinical course of the presented case resulted in the usage of glucocorticoids, RRT, TPE, and non-invasive ventilation. However, the clinical course in our case was fatal.

In summary, it would be reasonable to recommend performing precise differential diagnosis in patients with a positive SARS-CoV-2 test and serious pulmonary and renal involvement since SARS-CoV-2 infection can be a trigger factor for vasculitis and COVID-19 symptoms may occur simultaneously or mimic vasculitis presenting AAV-like symptoms. Therefore, in SARS-CoV-2 positive patients, especially in the case of AKI, immunological tests for AAV should be performed.

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