VIA MEDICA

CASE REPORT

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Clinical features of a young patient with COVID-19 presented with ARDS and severe thrombocytopenia

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ABSTRACT

Case report of a 33-year-old male SARS-CoV-2 positive patient admitted to hospital because of hemoptysis, dyspnea, fever, oxygen saturation of 60%, hypoxemia, elevated C-reactive protein (CRP). The patient was not vaccinated and it was his first infection with the virus. The symptoms started 10 days before with headache, fever, and cough. Chest radiography on hospital admission detected diffuse interstitial pneumonia in both lungs. Initial CT (Computed Tomography) presented extensive lung involvement with bilateral wide areas of consolidation with air bronchogram, the non-consolidated area showing patchy ground glass infiltration. The patient was hospitalized in ICU (Intensive Care Unit), oxygen support was started immediately with non-invasive ventilation (NIV), CPAP (Continuous Positive Airway Pressure) mode, FiO2 (Fraction of inspired Oxygen) 100%, PEEP (Positive end-expiratory pressure) 8, and the saturation started to increase. Therapy consisted of parenteral antibiotic, low-molecular weight heparin (LMWH) in prophylactic doses, pulsed dose of corticosteroid (methylprednisolone), Remdesivir, tocilizumab (Actemra), albumin, protein-pump inhibitor, antipyretics, fluids, physical therapy. Microbiology results from sputum detected MRSA (methicillin-resistant Staphylococcus aureus) and therapy with Vancomycin was started according to recommendations. After three days of vancomycin therapy, the patient manifested profuse epistaxis and tamponade was necessary. Hemostasis result was normal, but severe thrombocytopenia was noticed in the blood count. Platelets and plasma were administered and the bleeding stopped. Vancomycin was replaced with Linezolid. In the next days of follow up, the platelets increased, and the corticosteroid dose was slowly reduced. During the treatment as the health status of the patient improved, the CPAP therapy was replaced with routine oxygen support, gradually lowering the oxygen flow until saturation of 94% was achieved at ambient air. The COVID-19 pandemic is still evolving and the medical fraternity is posed with a huge challenge. COVID-19 is primary a respiratory viral infection, but the virus can affect many organs and systems, presenting various signs, symptoms and outcomes.

Key words: COVID-19, ARDS, COVID-19-associated coagulopathy, thrombocytopenia, pneumonia

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Introduction

China reported to the World Health Organization (WHO) on December 31, 2019, about the outbreak of a novel coronavirus (n-CoV) causing pneumonia in adults in the city of Wuhan in Hubei province. The identified virus is named SARS-CoV-2 and the illness caused by the virus is named corona virus disease 2019 (COVID-19) [1]. On January 30, 2020, WHO declared the outbreak a Public Health Emergency of International Concern, and later, on March 11, 2020 — a pandemic [2]. In The Republic of North Macedonia, the first case of a COVID-19 infection was detected in a woman who returned from Italy, on February 26, 2020 [3]. The symptomatology of COVID-19 patients varies from asymptomatic/mild symptoms to critical illness and mortality. The majority of the patients have a mild presentation, with complaints on the most

common respiratory symptoms; however, a significant number of patients experience serious symptoms and an unfavorable course; from severe respiratory distress, neurologic alterations, coagulation disorders to multi-organ failure disease, hyper-inflammatory syndrome and death [4]. COVID-19 can cause viral pneumonia with additional cardiovascular complications. In early studies of patients admitted with COVID-19 in China, 32–46% of patients had underlying diseases, including hypertension (15–31%), cardiovascular disease (14.5–15%), and diabetes (10–20%). Then, a meta-analysis of six COVID-19 studies reported the prevalence of hypertension, cardiac and cerebrovascular disease, and diabetes to be 17.1%, 16.4%, and 9.7%, respectively [5]. Clinical presentation may overlap and vary, and a patient's clinical status may change over time. Furthermore, factors associated with mortality in COVID-19 patients include male sex, advanced age, and presence of hypertension, diabetes mellitus, cardiovascular diseases, and cerebrovascular diseases as well as complications of acute cardiac injury, cardiomyopathy, and heart failure [6]. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as the receptor to enter the host cell. The cardiovascular disorders share an underlying renin-angiotensin system (RAS)-related pathophysiology and pharmacologic RAS inhibitors both increase ACE2 levels, which may increase the entry of SARS-CoV-2 into the lungs and heart. Thus, the infection may have a direct impact on cardiovascular diseases [7]. Prone positioning is a lifesaving non-pharmacologic strategy that should be part of the toolbox in every ICU that manages patients with ARDS. The use of prone positioning requires an understanding of indications and risks, along with appropriate health system planning through the development of protocols and procedures as well as simulation and practice to gain competence and expertise [8].

Case presentation

Case report of a 33-year-old male SARS-CoV-2 positive patient admitted to hospital because of hemoptysis, dyspnea, fever, oxygen saturation of 60%, hypoxemia with partial oxygen pressure (PaO2) of 38 mmHg, elevated C-reactive protein (CRP) of 180 mg/L. The patient was not vaccinated and it was his first infection with the virus. The symptoms started 10 days before with headache, fever, and cough. He was first examined by her family doctor and tested for SARS-CoV-2 infection, with positive PCR (Polymerase Chain Reaction) result. During first days of the beginning, he was advised to have a rest, take lots of fluids, antipyretics, and vitamins (vitamin D 4000IE, vitamin C 2000 mg per day). Because the fever persisted and cough was more often, he was referred for a check-up at the triage center of the City General Hospital "8mi Septemvri", the biggest country's COVID-19 center. A detailed physical examination was performed, lung auscultation showed diminished breathing sounds diffuse, prolonged expiration and crackles in lower and middle parts. The electrocardiogram revealed sinus rhythm, tachycardia of 120 beats/min, normal axis, no changes in morphology and conductivity, and no signs of acute cardiac presentations. Chest radiography on hospital admission detected diffuse interstitial pneumonia in both lungs (Fig. 1a), and during hospital treatment resolution was noticed (Fig. 1b — Chest X-ray on Day 15; Fig. 1c — Chest X-ray on Day 20). Initial computed tomography (CT) at hospital admission presented extensive lung involvement with bilateral wide areas of consolidation with air bronchogram, the non-consolidated area showing patchy ground glass infiltration (Fig. 2). Chest ultrasound performed the second day after hospitalization, presented small bilateral pleural effusion and subpleural consolidation areas (Fig. 3). Central line, urine output and further Intensive Care Unit (ICU) monitoring was performed, initial Sequential Organ Failure Assessment (SOFA) score was 8. The SOFA score ranges from 0 to 24 points, with a higher score indicating a worse organ function. Six organ systems are rated from 0 to 4 points based on ratio of PaO2 to fraction-inspired oxygen, Glasgow Coma Scale score, mean arterial pressure, serum creatinine level, bilirubin level, and platelet count [9].

The patient was normotensive with normal urine output. Laboratory tests and gas analysis are presented in Table 1 in chronological order during the hospitalization. The patient was hospitalized in ICU, oxygen support was started immediately with non-invasive ventilation (NIV), Continuous Positive Airway Pressure (CPAP) mode, Fraction of inspired Oxygen (FiO2) 100%, Positive end-expiratory pressure (PEEP) 8, and the saturation started to increase. Therapy consisted of parenteral antibiotic (ceftriaxone 2.0 g at the beginning), low-molecular weight heparin (LMWH) in prophylactic doses, pulsed dose of corticosteroid (methylprednisolone), Remdesivir 200 mg the first day (course of 100 mg/day the next four days), tocilizumab (Actemra) 8 mg/kg administered at Day 2, albumin, fluconazole 200 mg/day, protein-pump inhibitor, antipyretics, fluid replacement, physical therapy. After the administration of initial therapy, the fever was gone. Microbiology results from sputum detected methicillin-resistant Staphylococcus aureus (MRSA) and therapy with Vancomycin was started according to recommendations. After three days of Vancomycin therapy, the patient manifested profuse epistaxis and tamponade was necessary. Hemostasis result was normal, but severe thrombocytopenia was noticed in the blood count. Platelets and plasma were

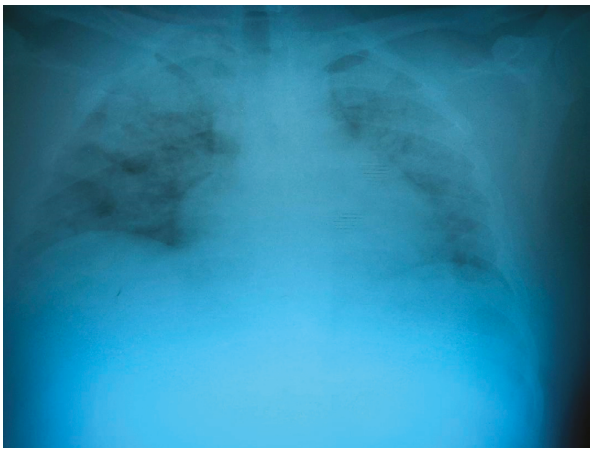

Figure 1a. Chest X-ray findings at hospital admission

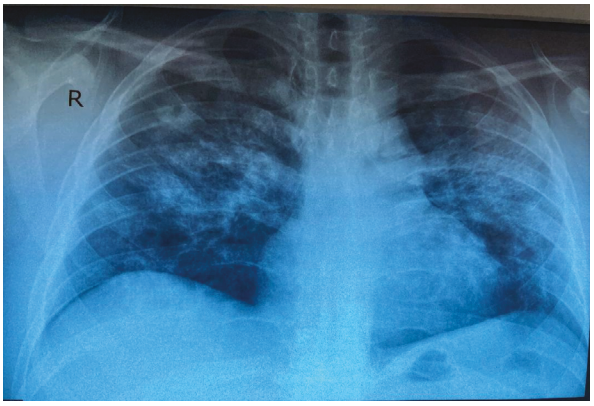

Figure 1b. Chest X-ray findings presented as the patient improved

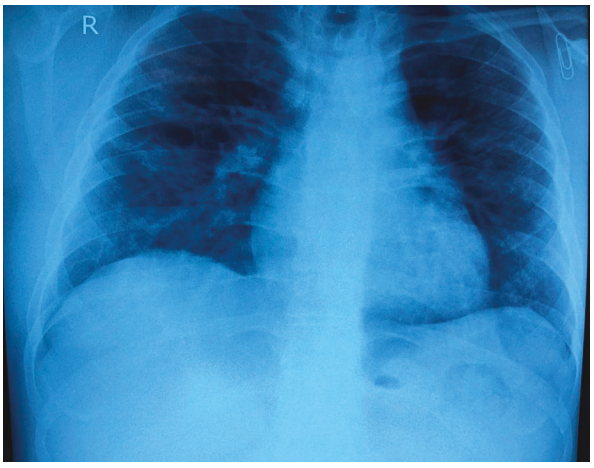

Figure 1c. Chest X-ray findings at hospital discharge

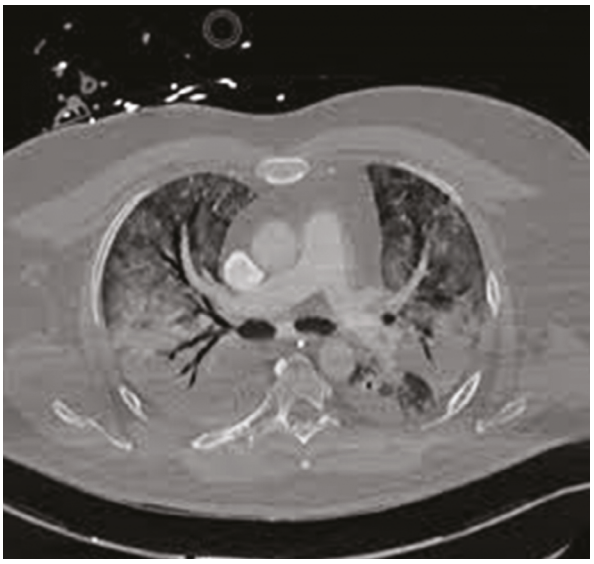

Figure 2. Initial lung CT scan presented extensive lung involvement with bilateral wide areas of consolidation with air bronchogram, the non-consolidated area showing patchy ground glass infiltration

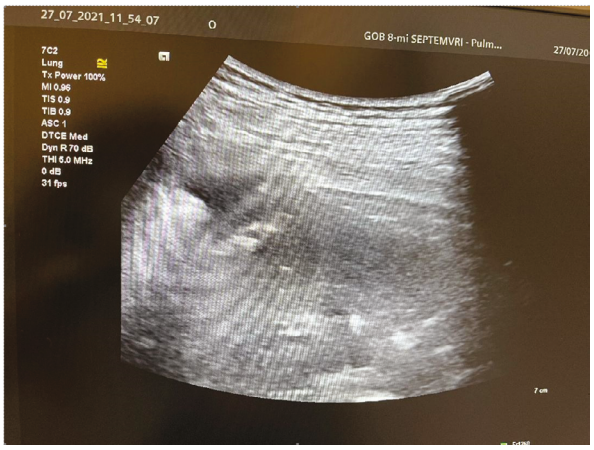

Figure 3. Chest ultrasound at hospital admission presenting small pleural effusion

administered on day 10 and 11 after hospital admission and the bleeding stopped. Vancomycin was replaced with Linezolid. Because of persistent tachycardia, with 100–120 beats/min, echocardiography was performed with heart chambers within the normal ranges, and ejection fraction of 60%, no wall motion abnormalities, no masses in the chambers, no pericardial effusion. Thyroid status was normal. Metoprolol was added to the therapy (2 x 25 mg), and the heart rate was normalized. In the next days of follow up, the platelets increased, and the corticosteroid dose was slowly reduced. Patient used the prone position with good tolerance and good results. Chest ultrasound showed improvement in subpleural consolidation areas during the hospital stay. As the health status of the patient improved, the CPAP therapy was replaced with standard oxygen support (mask with a reservoir bag at the beginning), gradually lowering the oxygen flow until saturation of 94% was achieved at room air. The patient was hospitalized for 25 days and was discharged in good health condition. In

Table 1. Laboratory findings and gas analysis at admission (Day 1) and during hospitalization

Parameter	Day 1	Day 2	Day 3	Day 5	Day 7	Day 9	Day 10	Day 11	Day 14	Day 17	Day 20	Normal range
CRP [mg/L]	180	120	110	90	85	70	55	40	25	15	6.2	< 5
Sedimentation rate (mm/h per the first hour)	62	70	45	50	35	30	37	42	30	25	20	0–22
W (white blood cells) [$\times 10^9$/L]	15.9	16.7	17.5	18.7	16,3	15.5	14.8	14.5	14.3	13.9	14.2	3.5–10
Gr (granulocyte) (%)	70	67	72	78	88	90	85	75	70	74	68	35–80
Lim (lymphocyte) (%)	5.7	6.1	6.2	6.7	7.0	7.7	8.8	10.1	12.5	14.5	18.3	15–50
Plt (platelet) [$\times 10^9$/L]	245	150	100	30	15	10	100	150	175	180	210	100–400
MPV (mean platelet volume) (femtoliters)	8.9	8.9	9.0	9.4	9.3	9.4	9.6	10.1	10.2	9.8	9.7	8–12
Er (erythrocyte) [$\times 10^{12}$/L]	3.5	3.3	3.1	2.5	2.7	2.9	3.8	4.3	4.1	4.3	3.8	3.5–5.5
Hg (hemoglobin) [g/L]	100	95	90	70	75	89	105	115	112	115	105	115–180
Hct (hematocrit) (%)	32	30	28	25	26	27	35	42	40	42	35	35–55
Na (sodium) [mmol/L]	133	135	136	137	136	140	138	141	140	139	140	136–145
K (potassium) [mmol/L]	3.3	3.2	3.4	3.6	3.8	3.9	4.0	3.9	3.7	3.8	4.0	3.5–5.1
Urea nitrogen [mmol/L]	12.4	7.4	5.6	14.0	8.5	8.0	7.7	7.0	6.5	6.2	5.0	2.8–7.2
Creatinine [μmol/L]	67	70	64	62	65	60	66	70	65	64	62	49–115
CK / CK-MB [U/L] (creatine kinase)	130	125	120	110	105	110	100	103	110	112	115	10–170
CK-MB [U/L] (creatine kinase from myocardial origin)	15	16	15	13	15	16	12	10	13	14	15	7–30
Troponin [ng/mL]	0.04	0,05	0.03	0.04	0.03	0.03	0.02	0.01	0.01	0.02	0.01	0.03––0.07
LDH (lactate dehydrogenase) [U/L]	770	760	735	684	500	420	335	278	225	210	185	81–234
Glucose [mmol/L]	6.6	6.1	5.6	5.3	5.0	5.5	5.7	5.2	5.4	4.8	4.6	4.1–5.9
Albumin [g/L]	28	25	27	28	27	30	31	30	32	34	36	35–52
Total protein [g/L]	58	55	60	62	59	61	60	64	66	65	67	60–80
AST (aspartate aminotransferase) [U/L]	35	32	28	31	26	24	23	25	27	24	30	5–37
ALT (alanine aminotransferase) [U/L]	61	64	58	55	52	45	48	50	44	40	35	10–63
Ferritin [ng/mL]	2500	2650	2300	1850	1430	1050	895	789	655	570	434	20–260
Interleukin – 6 (IL-6) [pg/mL]	284	320	360	358	220	165	120	85	35	20	8.3	2.0–5.9
Procalcitonin [ng/mL]	0.03	0.02	0.01	0.04	0.05	0.1	0.04	0.05	0.08	0.05	0.01	< 0.5
D-Dimer [ng/mL]	3100	2500	1550	1200	1050	950	800	750	650	730	800	< 500
INR (international normalized ratio)	0.8	0.8	0.9	0.9	0.9	0.9	1.0	1.0	1.0	1.1	1.0	< 1.1
aPTT (sec) (activated partial thromboplastin time)	20.5	21.5	22.0	23.1	22.8	23.3	23.6	24.5	24.3	25.2	24.6	21–35
pH (potential of hydrogen)	7.30	7.32	7.35	7.36	7.35	7.38	7.40	7.38	7.40	7.38	7.39	7.35–7.45
PaO_2 (mmHg)	38	42	47	50	55	57	60	64	67	74	77	90–100
$PaCO_2$ (mmHg) (partial pressure of carbon dioxide)	22	27	35	33	37	38	37	32	34	37	36	35–45
HCO_3 [mmol/L] (bicarbonates)	18.9	19.5	21.3	21.8	22.8	23.6	24.1	23.1	23.5	23.1	23.2	22–28
BE (base excess)	–3.8	–3.4	–2.8	–1.7	+1.1	+1.5	+2.0	+1.8	+1.4	+1.8	+1.9	–2/+2
Blood oxygen saturation (%)	60	65	70	77	82	90	94	96	95	94	94	>93

the follow-up period the X-ray was completely resolved, the patient was examined and treated multidisciplinary with a team of different specialties (pulmonologist, physical therapist, radiologist, cardiologist, mental health provider). COVID-19 is primary a respiratory viral infection, but the virus can affect many organs and systems, presenting various signs, symptoms and outcomes.

Discussion

Severe COVID-19 pneumonia has posed critical challenges for the research and medical communities. Older age, male sex, and comorbidities increase the risk for severe disease. For people hospitalized with COVID-19, 15–30% will go on to develop COVID-19 associated Acute Respiratory Distress Syndrome (ARDS). Autopsy studies of patients who died of severe SARS--CoV-2 infection reveal the presence of diffuse alveolar damage consistent with ARDS but with a higher thrombus burden in pulmonary capillaries [10]. ARDS in COVID-19 patients presents with several unique characteristics that are not regularly described in non-COVID-19 associated ARDS. Among these characteristics is the significant development of microvascular thrombosis within the lung vasculature that contributes to ventilation-perfusion mismatch and right ventricular stress. Though the cause for widespread activation of the coagulation cascade is not yet fully understood, dysregulated inflammation and direct injury to endothelial cells by SARS-CoV-2 contribute to the development of microthrombotic immunopathology [11]. Additionally, endothelial cell damage in SARS-CoV-2 infection impairs pulmonary vasoconstriction that normally occurs in response to hypoxia to restrict blood flow to poorly ventilated areas of the lung. Disruption in this physiologic adaptation in COVID-19 patients results in shunting of blood. To this end, treatment for COVID-19 related ARDS has been focused on mitigation of these drivers of disease pathophysiology through the use of antivirals, steroids, anticoagulants, and prone positioning [12]. Corticosteroids are the only therapeutic agents that have demonstrated a clear mortality benefit in the treatment of severe COVID-19. Seven Randomized Controlled Trials (RCTs) have evaluated treatment with steroids in critically ill patients and one trial in severe non-critical COVID-19 including medium and high-dose dexamethasone, hydrocortisone, and methylprednisolone. In the largest trial (n = 2104), 28 day mortality was 22.9% in the dexamethasone arm compared with 25.7% in usual care (adjusted rate ratio 0.83, confidence interval 0.75 to 0.93) [13]. Remdesivir is an antiviral drug that acts by inhibiting viral ribonucleic acid (RNA) transcription. It has in vitro activity against many RNA viruses including SARS-CoV-2. Current studies have been done on hospitalized patients with moderate or severe disease. Tocilizumab is a monoclonal antibody that blocks the IL-6 receptor and is used to treat cytokine release syndrome associated with chimeric antigen receptor (CAR) — T cell therapy. Multiple case series and observational studies were published in the early months of the pandemic that reported improved outcomes from tocilizumab [9, 14]. Patients who spent time in intensive care, especially patients with ARDS, are at high risk for Post Intensive Care Syndrome (PICS) development. Without appropriate recognition, impairments go undiagnosed and can persist for months to years and profoundly affect the quality of life. An interdisciplinary approach is essential to assist with diagnosis and management of critical illness recovery. Post-ICU recovery programs staffed by a team of providers (i.e. pulmonologists, intensivists, pharmacists, advanced practice providers, nurses, physical and occupational therapists, respiratory therapists, social workers, case managers, and mental health providers) can diagnose and treat PICS impairments [15–17].

Conclusions

The COVID-19 infection due to SARS-CoV-2 typically presents with acute onset respiratory symptoms with or without associated prodrome such as headache, lethargy, anorexia, diarrhoea and arthralgia. Presentations of COVID-19 range from asymptomatic/mild symptoms to severe illness and mortality. It is one disease with many faces, clinical presentations and outcomes.

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