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Case Report

Case Report of SARS CoV-2 Coinfection with Varicella Zoster Virus

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Abstract

Covid-19 is a new disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and is associated with respiratory complications in adults. Varicella (chickenpox) is an acute infectious disease that usually causes no complications in children, while the most common complication in adults it causes is pneumonia. Patients with COVID-19 coinfection with Varicella can develop a severe respiratory infection. Immunocompromised patients with varicella pneumonia are at an increased risk of developing acute respiratory failure. This paper presented a 38-year-old patient with SARS-CoV-2 and Varicella Zoster virus coinfection. The patient initially had symptoms of COVID-19 infection and signs of bilateral pneumonia, as confirmed by a Polymerase Chain Reaction (PCR) test for SARS-CoV-2. On the fifteenth day of hospitalization, he developed clinical features of Varicella, which was subsequently confirmed by serology testing (Enzyme-Linked Immunosorbent Assay (ELISA) Imunoglobulin M (IgM) Varicella Zoster Virus (VZV) positive). The paper aims to establish a connection between COVID-19 and Varicella and possible modulation of the immune response to the two viral infections.

Keywords: SARS CoV-2 virus; Varicella; Acute respiratory distress syndrome

Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; PCR: Polymerase Chain Reaction; ELISA: Enzyme-Linked Immunosorbent Assay; IgM: Imunoglobulin M; VZV: Varicella Zoster Virus; ARDS: Acute Respiratory Distress Syndrome; ACE2: Angiotensin Converting Enzyme 2; CRP: C Reactive Protein; ABG: Arterial blood gas; ICU: Intensive Care Unit; NIV: Noninvasive Ventilation; MV: Mechanical Ventilation; V-V ECMO: Venovenous Extracorporeal Membrane Oxygenation; CNS: Central Nervous System; OSCI: Ordinal Scale of Clinical Improvement

Introduction

The new Coronavirus that appeared in Wuhan in 2019 was named SARS-CoV-2. The clinical presentation in adults ranges from asymptomatic, mild colds to the development of Acute Respiratory Distress Syndrome (ARDS) [1]. COVID-19 infection starts with virus penetration into target cells that have receptors for Angiotensin Converting Enzyme 2 (ACE2), which is found not only in the alveolar epithelium cells but also in the endothelium of muscle cells, brain, liver, and kidneys, making COVID-19 a multisystem disease [2]. About 20% of infected adults develop pneumonia, some of which grow into very severe conditions [3].

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Varicella is an acute childhood infection caused by the Varicella Zoster Virus (VZV) with an increasing incidence in adults. Pneumonia is the most common complication in adults, showing a more severe clinical picture in immunocompromised patients [4,5]. The mortality rate ranges from 10%-33%, and 50% of patients are on mechanical ventilation [6]. The paper presents a 38-year-old patient with SARS-CoV-2 and Varicella Zoster virus coinfection.

Case Presentation

A thirty-eight-year-old man without comorbidities was admitted on December 11, 2020, to the University Clinical Center of Vojvodina at the Clinic for Infectious Diseases, under diagnosis of bilateral pneumonia caused by SARS-CoV-2 viral infection, confirmed by a rapid antigen test for SARS CoV-2 and then by RT-PCR (real-time reverse transcriptase polymerase chain reaction) nasopharyngeal swab test. He was admitted on the sixth day after the onset of symptoms, including elevated body temperature, cough, weakness, and malaise. Objectively, at the moment of admission, the patient was febrile (38.30°C), pale, intoxicated, normotensive (130/80 mmHg), tachycardic (115/min), eupneic at rest, with SaO2 97% at room air test, 19/min respiration rate, normal findings on auscultation of lungs. Initially, signs of bilateral pneumonia were described on an X-ray of the lungs and heart on admission (Figure1).

Laboratory findings on admission showed the following values: leukopenia 3.36 × 10^9/L, lymphopenia 16.9%, platelets 160 × 10^9/L, C Reactive Protein (CRP) 26.5 mg/L, D-dimer 927 ng/ml, fibrinogen 3, 4 g/l, normal red blood cells, nitrogen compounds, and hepatogram, with hypokalemia 3.4 mmol/L, hyponatremia 129 mmol/l and hypochloremia 95 mmol/L. In the initial findings, the value of interleukin 6 (IL6) was 14 pg/ml.

Parenteral combination therapy (Ceftriaxone 2 g/12 h and Levofloxacin 500 mg/24 h for ten days), corticosteroid therapy (Dexamethason 8 mg/24 h for ten days), prophylactic anticoagulant therapy with low molecular weight heparin, gastroprotective and multivitamin therapy were introduced. Initially, upon admission,

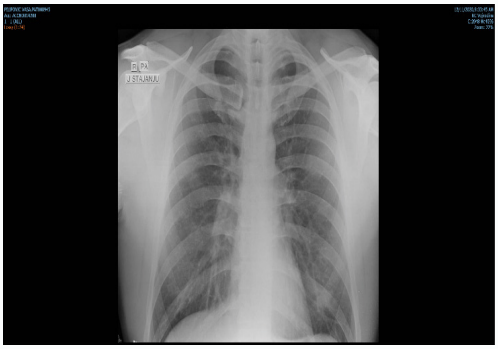

Figure 1: X-ray of the lungs on admission.

oxygen therapy was introduced using a mask delivering oxygen at a flow rate of 4 l/min. Due to maintained febrility, deterioration of X-ray findings on the lungs, and a rise in IL6 (80 pg/ml), CRP (72.7 mg/L), and fibrinogen (5.6 g/l) values, the patient was administered Tocilizumab (8 mg/kg/BW/24 h) on the fourth and fifth day of hospitalization according to the National Treatment Guidelines version 10 for COVID 19 patients. The patient became afebrile on the sixth day of hospitalization. On the seventh day of hospitalization, his respiratory function and gas exchange worsened (Arterial Blood Gas (ABG): pH 7.49, pO2 43 mmHg, pCO2 34 mmHg, HCO3 24.4 mmol/l, SaO2 83%) along with worsening X-ray findings on the lungs (Figure 2).

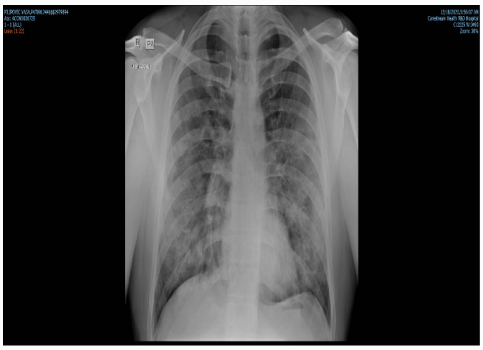

Figure 2: X-ray of the lungs on the 7th day of hospitalization.

Oxygen flow was increased to 10 l/min, establishing a satisfactory gas exchange. In the further course of hospitalization, there was a subjective improvement, the patient was afebrile, and the oxygen flow was gradually decreased so that on the 14th day of hospitalization, oxygen therapy was completely discontinued and improvement was verified on the X-ray of the lungs. On the 17th day of hospitalization, the patient became febrile and reported non-specific changes on the tongue, enanthems on the soft palate, palatal arches, and individual vesicles on the chest, scalp and face that would clinically correspond to vesicle stage varicella rash. Subsequently, the patient reported positive contact with a daughter who had Varicella. Chickenpox developed on the 21st day of incubation.

The laboratory findings showed leukocytes 4.19 × 109/L, CRP 0.8 mg/L, D-dimer 1733 ng/ml, aminotransferase elevated up to 2 times the reference value. A CT angiography of the chest was taken and showed diffuse bilateral reticular opacities as well as GGO (Ground-Glass Opacity) sparing apices, as well as bilateral posterobasal consolidations as part of Covid-19 type inflammatory changes. In addition to the above, multiple smaller inflammatory type nodules were detected, without thrombosis of the pulmonary artery and its branches. The appearance of chickenpox was accompanied by the patient's worsening general condition, respiratory function and X-ray findings on the lungs, along with the development of varicella pneumonia. Serology test confirmed acute VZV viral infection (ELISA IgM VZV positive). The patient was delivered oxygen at a flow of 15 L/min, at which he did not achieve satisfactory gas exchange (arterial blood gas analysis pH 7.36, pO2 56 mmHg, pCo2 40 mmHg, SaO2 87%). Due to the need for noninvasive ventilation, the patient was transferred to the Intensive Care Unit (ICU) of the Clinic for Infectious Diseases on the seventeenth day. Antiviral therapy (Acyclovir), corticosteroid therapy (Methylprednisolone) along with other supportive therapy was continued. The next day, the patient developed ARDS and, despite the Noninvasive Ventilation (NIV) with high oxygen fraction, unacceptable arterial gas exchange, so he was subjected to sedation and control Mechanical Ventilation (MV). The control PCR test for SARS-CoV-2 was negative. On the nineteenth day of hospitalization, Veno-Venous Extracorporeal Membrane Oxygenation (V-V ECMO) was initiated, and the patient was transferred to the Intensive Care Unit of the Institute of Pulmonary Diseases. Multiplex PCR panel of tracheal aspirate was negative. On January 12, 2021, the patient was removed from V-V ECMO and then extubated. Until January 31, he was on long-term oxygen therapy 3l/min. After removal from MV and extubation, the patient developed psychoorganic syndrome and due to suspected varicella encephalitis, he underwent lumbar puncture. Cerebrospinal fluid cytological and biochemical finding was normal, ruling out Central Nervous System (CNS) infection. The patient was discharged as recovered on January 31, 2021 for self-treatment with a home oxygen concentrator.

Discussion

The paper presented the case of a thirty-eight-year-old patient with combined SARS-CoV-2 and Varicella Zoster viral primary infection that led to ARDS. According to current knowledge and review of the available literature, few similar articles have been published to date [7-9]. The described cases of coinfection are more common in children [7,8]. Cases of VZV reactivation and the appearance of herpes zoster have been described in adults [10]. Incubation periods for COVID-19 and chickenpox are about 14 and 21 days, respectively. The attack rate in collectives is 2%-3% for SARS-CoV-2 and 70% for VZV. The clinical picture of our patient corresponds to the clinical picture of patients who developed bilateral pneumonia [3]. On SARS-CoV-2 pneumonia X-ray of the lungs, bilateral infiltrations and ground-glass opacities were described. Complementary CT angiography is used to rule out possible thromboembolism and helps with patients who have a clinical picture of COVID-19 but false negative PCR tests [11]. Roux et al. [8] showed the occurrence of pleuropneumonia in a ten-month-old child with these two viruses coinfection. Pleuropneumonia was also described in seven preschool children with COVID-19 [12]. Pleural effusions have been described in critically ill adult patients (older than 50 years) in a percentage of 10.3% [13]. The patient was hospitalized as a moderately severe clinical presentation according to the World Health Organization OSCI (Ordinal Scale of Clinical Improvement) [14]. He was treated according to the national guidelines.

Varicella is an acute usually childhood infectious disease. Varicella is diagnosed on the basis of a typical clinical picture, anamnestic data and epidemiological survey. In patients with SARS-CoV-2 infection, cutaneous manifestations can occur in as much as 20.4%, as shown by an Italian study [15]. Genovese et al. [16] presented in their study an eight-year-old boy with COVID-19 and Varicella-like skin

manifestations. Making a precise diagnosis requires a serology test and a positive epidemiological survey in terms of the patient's contact with a person who had Varicella. Complications in the form of pneumonia occur more often in adults and immunocompromised patients [17]. The incidence of varicella pneumonia is between 0.32-1.36 cases per 100,000 people per year [18,19]. Mortality rates range from 10%-33% and up to 50% of patients on MV [6]. John et al. [17] reported varicella pneumonia mortality in 29.2% of respondents. Therapeutic options for treating severe forms of varicella pneumonia are cardiorespiratory support, antiviral, corticosteroid therapy. Risks for the development of varicella pneumonia are immunocompromised conditions, smoking, pregnancy and a large number of skin lesions [20]. Although the patient in our work was initially immunocompromised, varicella pneumonia developed on the 21st day after the onset of symptoms of COVID-19. Varicella pneumonia can lead to rapid progression and fulminant respiratory failure despite cardiorespiratory support. ECMO has proven efficient in such patients. In one study of 20 patients connected to ECMO, 16 of them survived [21].

The appearance of multiple viral infections is rare, but can occur more often in patients with primary or secondary immunodeficiency [22]. In our opinion, there are three hypotheses for the development of two viral infections and severe clinical picture. The first is that the SARS-CoV-2 virus caused secondary immunodeficiency and a predisposition to severe varicella pneumonia, the second is that biological therapy (Tocilizumab) led to immunosuppression, and the third is a random coincidence of both diseases. The connection between these two viruses has not yet been explained in the literature. Certain studies indicate that the inflammatory response in COVID-19 triggers VZV reactivation and the development of herpes zoster. Immunity to a primary virus can model the immune response to a secondary infection [23,24]. Other researchers have noted that the cytokine storm that occurs in more severe forms of COVID-19 triggers VZV reactivation [25]. One of the possible explanations for reactivation could be a COVID-19 related decrease in the absolute number of lymphocytes, especially CD3 and CD8 lymphocytes [26]. In addition to activation-induced cell death, SARS-CoV-2 directly infects lymphocytes, especially T cells, causing lymphopenia and eventually weakened antiviral immune response.

Conclusion

The possible immunosuppressive effect of SARS-CoV-2 could increase the likelihood of coinfections and affect their severity in patients with COVID-19. Rapid cardiopulmonary deterioration in COVID-19 infection should raise suspicion of an accompanying infectious process. This case of an adult with SARS-CoV-2 infection and concurrent primary VZV infection highlights the importance of considering coinfection in patients with COVID-19 with unusual clinical manifestations. Our work opens a question answered so far, namely, how the immune response to SARS-CoV-2 affects the severity of the varicella clinical picture in adults.

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