First case of concomitant cytomegalovirus (CMV) viremia in non-immunocompromised COVID 19 patient and ICU management strategy in Qatar with literature review.

Phool Iqbal[1], Suresh Menik Arachchige[2], Yousra Ali[2], Muhammad Sohaib Qamar[3], Hani Jaouni[2], and Ahmed Abdussalam [2]

[1]Hamad Medical Corporation
[2]Hamad General Hospital
[3]Ozarks Medical Center

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Abstract

COVID 19 has created one of the world's worst pandemics and is associated with various life-threatening complications, such as Cytomegalovirus (CMV) co-infection. We present a life-threatening CMV viremia co-infection in a none-immunocompromised COVID 19 patient to highlight our management approach and a comprehensive literature review.

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Author Information:

Phool Iqbal, MD, MBBS

Medical Intensive Care Department, Hamad Medical Corporation, Doha, Qatar

dr.phooliqbal89@gmail.com

Suresh Menik Arachchige, MD

Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar

nalakamenik@live.com

Yousra Ali, MBBS

Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar

yali4@hamad.qa

Muhammad Sohaib Qamar, MD

Department of Medicine, Ozarks Medical Center, West Plains, MO, USA

mu.sohaibqamar@gmail.com

Hani Walid Jaouni, MD

Senior consultant Critical Care and Pulmonology department

Hamad Medical Corporation

HJaouni@hamad.qa

Ahmed Lutfe Mohamad Abdussalam, MD

Senior Critical Care Consultant Hamad General Hospital

Assistant Professor of Clinical Medicine, Weill Cornell Medicine Qatar

Medical Intensive Care Department, Doha, Qatar

aabdussalam@hamad.qa

Key Clinical Message:

This case highlights the significance of life-threatening co-infections like CMV viremia in COVID 19 patients. It is important to be aware and to investigate patients that are deteriorating for CMV viremia.

Abstract:

COVID 19 has created one of the world's worst pandemics and is associated with various life-threatening complications, such as Cytomegalovirus (CMV) co-infection. We present a life-threatening CMV viremia co-infection in a none-immunocompromised COVID 19 patient to highlight our management approach and a comprehensive literature review.

Keywords:

COVID-19, Coinfection, SARS-CoV-2, Cytomegalovirus

Introduction:

The World Health Organization has labelled the COVID-19 as a global pandemic with over 150 million cases and more than 3.5 million recorded deaths worldwide by the end of May 2021 [1]. Most countries have faced multiple outbreaks of infection. Since the beginning of the pandemic, there have been reports of numerous short-term and long-term complications of covid-19. Of these, the most common ones include lung injury, venous/arterial thrombosis, strokes, and myocardial infarctions [2]. One of the most fatal complications include coinfection with cytomegalovirus (CMV) and is mostly seen in patients with immunosuppression as well [3,4]. There is little evidence on the management of such patients. Given the novelty of these presentations, no official guidelines have been established as of this date. In this paper, we will present such a case. We will also present a thorough literature search on the published data and present a possible clinical approach to such patients.

Case Summary:

A 50-year-old hypertensive Filipino gentleman presented to the emergency department (ED) with a one-week history of dry cough associated with high-grade fever, fatigue, and myalgias. His vital signs showed tachypnea around 22-26/min, tachycardia with a heart rate of 103-110/min, a blood pressure of around 175/112 mmHg, and desaturation requiring 10l/min non-re-breather mask (NRM) to maintain o2 saturation of around 86-88%. He was tested positive for COVID-19 PCR from a nasopharyngeal swab. His chest XR revealed bilateral infiltrates predominantly in the lower zones (Figure 1). CT pulmonary angiogram (CTPA) ruled out PE but showed bilateral ground-glass attenuation of the upper lobes, and bilateral lower lobes segmental consolidations with bronchogram. His overall clinical picture was suggestive of severe COVID-19 pneumonia leading to acute respiratory distress syndrome (ARDS). He was being treated based on local guidelines however his condition deteriorated on the 6^{th} day of hospital stay, with an increase in respiratory distress. He was having tachypnea at around 40/min and was kept on non-invasive ventilation with continuous positive airway pressure (CPAP) ventilation. He was shifted to an ICU facility. He did not improve and was intubated and mechanically ventilated on the 8^{th} day of his admission. He was spiking fever and there was a rise in his inflammatory markers concerning for a cytokine storm. Septic workup did not reveal any microorganism

growth or any source of infection. However he was started on broad-spectrum anti-microbial drugs to cover any superseded infection in severe COVID 19 patient .i.e. Meropenem, Vancomycin and anidulafungin as per the recommendations of the infectious disease (ID) specialists. His Pao2 was not improving, even after proning him multiple times and giving him inhaled nitric oxide. Therefore, the decision to commence the patient on veno-venous extracorporeal membrane oxygenation (V-V ECMO) was made on the 16^{th} day of his admission. CT thorax did not reveal any pulmonary embolism or barotrauma. However, it redemonstrated the bilateral ground-glass opacities (Figure 2). The patient's hospital course improved initially, and he was extubated on the 25^{th} day of his admission and antibiotics were ultimately stopped after the completion of their course.

On the 31^{st} day of admission, he was re-intubated due to tachypnea and abnormal paradoxical breathing pattern. Initial chest XR showed new lung infiltrates in the left upper zone. Bronchoscopy and subsequent bronchoalveolar lavage fluid cultures were negative. Blood cultures grew Enterococcus faecalis and sputum cultures grew Klebsiella pneumonia. He was given a course of antibiotics according to the sensitivities of the cultures. On the 39^{th} day of admission, the patient was tracheostomized due to a prolonged course on mechanical ventilation. The patient had fluctuations in his GCS, drowsiness, intermittent fever spikes, rise in inflammatory markers and was difficult to wean off from high oxygen settings. Septic workup was repeated including blood cultures, urine culture, TB work up, tracheal aspirate cultures, BAL fluid cultures and respiratory viruses including CMV, EBV and adenovirus PCR. His urine and BAL cultures grew Candida Albicans sensitive to Fluconazole. Furthermore, the BAL cultures and blood cultures were positive for CMV. He was started on Ganciclovir with weekly CMV PCR. His condition improved and was de-cannulated off ECMO. His GCS stabilized and he was able to open his eyes and follow simple commands. The patient was then followed with repeat CMV PCR viral counts to optimize the anti-viral therapies according to the ID specialists. The trend of CMV PCR viral load is shown in figure 3. On follow up, the patient in under physical and occupational therapists to help with critical care myopathy.

Discussion:

Since the beginning of the COVID 19 pandemic, the world is struggling to cope up with the infection and its aftermath. There are many associated complications and co-infections. Some of these include myocardial infarction, stroke, pulmonary embolism, various viruses, and fungi co-infection like CMV, EBV and currently mucormycosis (also known as black fungus) is also seen in many cases with high mortality rates [5,6,7]. CMV viremia is common in the immunocompromised state especially in solid organ transplant patients [8]. However, an immunosuppressive state due to dysregulated immunity or certain immune modulators like Tocilizumab or steroids, in COVID 19 patients, can lead to CMV viremia as seen in our case and in the literature as well [9,10,11]. We performed a literature review of articles on Google Scholar using advance search option with following keywords in title "allintitle: COVID 19 and cytomegalovirus and Pubmed search strategy with following keywords respectively ((((cytomegalovirus[Title]) OR (CMV[Title]))) AND ((((COVID 19[Title]) OR (SARS COV 2[Title])) OR (coronavirus disease[Title])))). We managed to find approximately 40 articles on CMV viremia in COVID 19 patients. Upon screening, a total of 11 articles of severe COVID 19 infection that did not have any underlying immunosuppressive state or malignancy were selected (Table 1) [12,13,14,15,16,17,18,19,20,21,22], in order to correlate with the management strategy in our patient.

DOI	Type of Study	Age (yrs)	Comorbid conditions
10.12890/2020_001911	Case Report	62	None
10.1136/ bmjgast-2020-000556	Case Report	45-65	None
10.12890/2020_001652	Case Report	92	Diabetes Mellitus and Hypertension
10.1016/j.idcr.2020.e00962	Case Report	68	Hypertension and Glaucoma
10.21203/rs.3.rs-52829/v1	Observational Study	60s	None
10.11604/pamj.2020.36.167.23922	Case Report	37	NA
10.4103/jpgm.JPGM_1168_20	Case Report	75	Hypertension
10.1016/j.idnow.2021.01.005	Retrospective Study	Median age 56	Hypertension (47%), Diabetes Mellitus (32%),

DOI	Type of Study	Age (yrs)	Comorbid conditions
10.1002/ccr3.3487	Case Report	42	None
10.1002/ccr3.3600	Case Report	71	Post Tuberculosis aspergilloma
10.1016/j.idcr.2021.e01111	Case Report	75	Diabetes Mellitus and Overweight (BMI 26.2)

The table not only highlights the risks of getting severe CMV viremia but also shows the management strategy and their outcomes. Our patient was not immunocompromised, however due to severe COVID 19 infection leading to dysregulated immunity and further management with steroids and Tocilizumab leading to immunosuppressive state might have contributed to CMV viremia. This concern needs a standard and effective management strategy. Currently, there are no recommended guidelines for initiating empiric anti-fungal therapy in CMV viremia in COVID 19 patients. From the literature, CMV viremia in covid-19 patients have being treated with predominantly IV ganciclovir, in some cases valganciclovir and in one case with foscarnet. However, the duration of the treatment is not clear. Patients have improved with days to weeks [12]. In our perspective, patient with severe COVID 19 disease that have delayed recovery, partial or no response to supportive/local management, must be investigated for superseded co-infections and reactivations of infections like CMV viremia with initiation of empiric therapy [23].

Conclusion:

Through our case, we aim to highlight the significance of a life threatening co-infections like CMV viremia in COVID 19 patients. The management strategy depends on the clinical state of the patient and availability of resources. However, prompt investigation in critically ill COVID 19 patients that do not respond to treatment, must be done to avoid fatal complications and death.

Authors' Contribution:

Drs. Suresh Menik Arachchige, Phool Iqbal and Yousra Ali were equally involved with the litreture search, writing, and editing the paper.

Drs. Ahmed Abdussalam, Hani Jaouni and Muhammad Qamar were involved with editing the paper and proving guidance.

Ethical Disclosure:

This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose. All authors have reviewed and agreed to the content present in this Article.

Consent:

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of

this journal upon request.

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