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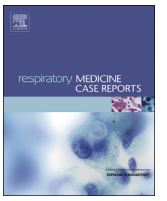

Case Report

A case of Hemophagocytic syndrome due to reactivation of Epstein-Barr virus after novel coronavirus infection

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ABSTRACT

Background: Reactivation of EBV after novel coronavirus infection is common, and co-infection with EBV in patients with novel coronavirus pneumonia may lead to more severe clinical manifestations, prolong the duration of the underlying disease, or precipitate the progression of post novel coronavirus syndrome. EBV-induced hemophagocytic syndrome is a rare and life-threatening condition, and there are no reports of EBV reactivation leading to hemophagocytic syndrome after novel coronavirus infection.

Case presentation: Here, we report a case of a 73-year-old man with EBV reactivation after novel coronavirus infection, who was diagnosed with hemophagocytic syndrome after bone marrow aspiration and died after being treated with acyclovir, dexamethasone.

Conclusions: the aim of this report is to increase clinical awareness of this type of disease for early recognition and treatment.

1. Introduction

Hemophagocytic syndrome, also called hemophagocytic lymphohistiocytosis (HLH), is an inherited or acquired immunoregulatory abnormality that causes an excessive inflammatory response by causing lymphocytes, monocytes, and macrophages to abnormally activate, proliferate, and secrete large amounts of inflammatory cytokines. Primary and secondary HLH are separated by distinct pathophysiology and initiating factors in HLH. Secondary HLH appears as a result of many illnesses such as infections, malignant tumors, rheumatic diseases, and autoimmune diseases. Primary HLH has a clear familial inheritance or genetic abnormalities. EBV-HLH is the most prevalent infection-associated HLH in China and Japan [1]. Reduced immunity is present in NCP patients, which influences the reactivation of long-term infections brought on by intracellular pathogens. Herpesvirus infections, especially those caused by the Epstein-Barr virus (EBV), are the most common kind of infections [2]. In this paper, we report a case of phagocytosis syndrome due to EBV reactivation after a novel coronavirus infection.

2. Case report

A 73-year-old man was admitted to the hospital with “cough and sputum for 20 days, accompanied by malaise and fatigue for 14 days". He was admitted to the hospital on November 17, 2019 for “erythema and blisters on the left chest and back and the left upper extremity with pain ". On examination, scattered erythema of varying sizes could be seen on the left anterior chest, back, and the medial side of the left upper extremity, which was bright red, and clusters of pinpoint-to fava bean-sized blisters could be seen on them, and herpes viruses were considered to be infected, and it was treated with ganciclovir, then he improved. This time, he was sent to the

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hospital due to his primary symptoms, which included a cough that began 20 days prior to admission, no discernible reason for the cough, yellow-green mucus phlegm, tightness in his chest, chills, and temperature swings between 37.6 and 38.2 ˚C. He utilized azolfidine since the nucleic acid test for a novel coronavirus was positive. He recovered from those therapies, and the results of the nucleic acid test were negative. He began feeling weak and not consuming enough food fourteen days ago. Following a gastroscopy, he was found to have a stage I duodenal bulb ulcer and hemorrhagic erosive gastritis. He was transferred to our hospital because he was getting worse despite treatment. On arrival to our ICU, his examination was consistent with pancytopenic; hemoglobin (Hb) was 11.2 g/dl; white blood cell count (WBC) was 2810/μL with 75.1 % neutrophils and 16 % lymphocytes and a platelets count of 93 000/μL. Direct bilirubin was 6.3 μmmol/L, alanine aminotransferase (ALT) 93 IU/l, aspartate aminotransferase (AST) 82 IU/l, lactate dehydrogenase 561 IU/l; Urea nitrogen 22.8mmol/L; Creatinine 371.9umol/L. He was Considered long COVID. His initial treatment regimen consisted of symptomatic supportive therapy such as hepatoprotective drugs. However, over the next 12 hours, his systemic inflammatory-response syndrome worsened, as reflected by the need for continuous venovenous hemofiltration therapy for renal failure, increased bloodproduct replacement for hematologic failure. He had hypofibrinogenemia (0.95g/L), a severe case of pancytopenia (WBC:1970/μL, Hb:10.2g/dl, PLT:76000/μL), and significant worsening of liver function (ALT:121U/L, AST:130U/L). Heterogeneous echogenic alterations in the liver parenchyma and splenomegaly were indicated by an abdominal ultrasonography. He was evaluated for a hemophagocytic syndrome diagnosis based on combined appeals testing. Thus, we gave him a battery of further tests. Perfect ferritin >1650ng/ml and triglycerides 2.58 mmol/L were the results. A bone marrow aspiration was finished. The picture revealed that there was hemophagy (1 % of reticulocytes), thrombocytopenia, and hypoproliferative granulopoiesis; natural killer cell activity was 12.57 % (normal: ≥15.11 %). The human herpesvirus type 4 with sequence number 11006 may be discovered through the next generation of bone marrow sequencing. Both the IgG and IgA antibodies against the EBV capsid antigen and nuclear antigen were positive. The quantification of EBV-DNA was 1.1E+06 copies/ml. For HLH, we administered acyclovir, dexamethasone, and etoposide in combination, but he ultimately passed away from multiple organ failure.

3. Discussion

Numerous earlier investigations have demonstrated that severe COVID-19 may result in the development of long COVID-19 and reactivated herpesvirus infections, mainly EBV infections [3–6]. Herpesvirus reactivation-affected extended COVID is associated with significant functional abnormalities, psychoneurologic symptoms, and laboratory results that point to a protracted inflammatory process and the potential emergence of a systemic autoimmune disease [7]. In fact, Jeffrey E. Gold et al. found a 30.3 % (56/185) prevalence of long-term COVID-19 symptoms in a study of 185 COVID-19 patients, including 4 asymptomatic patients with COVID-19. EBV reactivation was detected in 66.7 % of patients with long COVID-19 at presentation. The researchers concluded that most of the symptoms of long-term COVID-19 may not be a direct result of the SARS-CoV-2 virus, but may instead be the development of EBV reactivation caused by COVID-19 inflammation [8]. The study, published in Cell by James R. Heath's team, found four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis: type 2 diabetes, SARS-CoV-2 RNAemia, Epstein-Barr virus viremia [9]. According to all of these, immunosuppression brought on by a novel coronavirus infection raises the likelihood that EBV will reactivate, which in turn causes more severe clinical manifestations in patients with long COVID. These include a range of inexplicable symptoms, including fever, gastrointestinal disturbances, fatigue, headaches, sleep disturbances, and even HLH, which may have EBV origins.

4. Conclusion

The prognosis of patients has improved due to the high occurrence of EBV reactivation caused by COVID-19, which frequently results in more severe clinical symptoms and even hemophagocytic syndromes. As a result, early detection, diagnosis, and treatment are crucial.

Ethical approval and consent to participate

The release of medical record reports has been approved by the patient's family members.

Consent for publication

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

Availability of supporting data

All data generated or analysed during this study are included in this published article.

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CRediT authorship contribution statement

Yingmei Xiao: Writing – original draft. **Maojuan Wang:** Supervision.

Declaration of competing interest

No conflict of interest.

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References

[1] S. Imashuku, Clinical features and treatment strategies of Epstein–Barr virus-associated hemophagocytic lymphohistiocytosis 44 (3) (2002) 259–272, https://doi.org/10.1016/s1040-8428(02)00117-8.
[2] Simonnet A, Engelmann I, Moreau A S,et al. High Incidence of Epstein–Barr Virus, Cytomegalovirus, and Human-Herpes Virus-6 Reactivations in Critically Ill Patients with COVID-19[J].[2023-10-26].DOI:10.1016/j.idnow.2021.01.005.
[3] Chen T , Song J , Liu H ,et al. Positive Epstein–Barr virus detection in coronavirus disease 2019 (COVID-19) patients[J].Sci. Rep.[2023-10-26].DOI:10.1038/s41598-021-90351-y.
[4] H. He, Y. Wang, M. Wu, Sun, Positive Epstein-Barr virus detection and mortality in respiratory failure patients admitted to the intensive care unit, Clinical Respiratory Journal (2015), https://doi.org/10.1111/crj.12433.
[5] Z. Xu, L. Shi, Y. Wang, et al., Pathological findings of COVID-19 associated with acute respiratory distress syndrome, Lancet Respir. Med. 8 (4) (2020) 420–422, https://doi.org/10.1016/S2213-2600(20)30076-X.
[6] G.F. Lehner, S.J. Klein, H. Zoller, et al., Correlation of interleukin-6 with Epstein–Barr virus levels in COVID-19, Crit. Care 24 (1) (2020), https://doi.org/10.1186/s13054-020-03384-6.
[7] Zubchenko Svitlana, Kril Iryna, Nadizhko Olena, Matsyura Oksana, Chopyak Valentyna, Herpesvirus infections and post covid 19 manifestations a pi1ot observationa1 study, Rheumatol. Int. 42 (9) (2022) 1523–1530, https://doi.org/10.1007/s00296-022-05146-9.
[8] Gold J E , Okyay R A , Licht W E ,et al. Investigation of long COVID prevalence and its relationship to epstein-barr virus reactivation[J].Pathogens, 10(6):763 [2023-10-26].DOI:10.3390/pathogens10060763.
[9] Y. Su, D. Yuan, D.G. Chen, et al., Multiple early factors anticipate post-acute COVID-19 sequelae, Cell (5) (2022) 185, https://doi.org/10.1016/j.cell.2022.01.014.