

COVID-19 Recurrence Without Seroconversion in a Patient With Mannose-Binding Lectin Deficiency

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Abstract

Introduction: The SARS-CoV-2 virus has infected more than 63,000,000 people worldwide after emerging from Wuhan, China in December 2019. This outbreak was declared a Public Health Emergency in January 2020, and a pandemic in March. While rare, reinfection with the virus has been reported on multiple occasions.

Case Presentation: We present a case report of an individual with mannose binding lectin deficiency who tested positive on two separate occasions, months apart, and did not develop IgG antibodies to SARS-CoV-2. This patient is a 30-year-old female healthcare worker with a past medical history of ITP, pancreatitis, GERD, anxiety and recurrent pneumonia. She presented in March 2020 with fever, nasal congestion, and dry cough. She was diagnosed with COVID-19 in March 2020, via PCR through employee health. She was treated with a course azithromycin and hydroxychloroquine. Symptoms resolved, however in June 2020, SARS-CoV-2 IgG antibodies were negative. Seven months later in October, she once again developed symptoms which were milder. She was found to have a decreased level of mannose binding lectin, normal immunoglobulin levels, and normal streptococcus pneumonia IgG antibodies. On immune work-up after recovery, she was found to have a decreased level of mannose binding lectin (<50 ng/mL), normal immunoglobulin levels, and protective Streptococcus pneumoniae IgG antibodies with appropriate vaccine response. Her SARS-CoV-2 IgG returned back as positive 8 weeks after her second infection.

Discussion: This case illustrates that patients with mannose binding lectin deficiency may be at greater risk of re-infection than the general population.

Keywords

immune deficiency, mannose-binding lectin, MBL deficiency, SARS-COV2, COVID-19

The SARS-CoV-2 is the virus that is responsible for causing COVID-19 was declared a Public Health Emergency in January 2020, and a pandemic in March of 2020.¹ While rare, reinfection with the virus has been reported on multiple occasions.² Mannose binding lectin (MBL) is a component of innate immunity. Individuals with mannose binding lectin deficiency have been shown to be susceptible to severe respiratory infections especially in those with additional risk factors.³ Mannose binding lectin is indirectly associated with the adaptive immune system and routine reasons for failure to seroconvert. We present a case of an individual with mannose binding lectin deficiency who was infected with SARS-CoV-2 twice and had delayed seroconversion.

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The patient is a 30-year-old female healthcare worker with idiopathic thrombocytopenic purpura, pancreatitis, reflux and recurrent pneumonia. Her home medications included mirtazapine, quetiapine, dicycloverine, pantoprazole, and pancreatic enzyme replacement. She presented in March 2020 with fever, fatigue, sore throat, cervical lymphadenopathy, nasal congestion, chest tightness and dry cough. She was diagnosed with COVID-19 by PCR and was treated with a course of azithromycin and hydroxychloroquine. After full recovery, nasal PCR swab was negative twice prior to returning to work. Her SARS-CoV-2 IgG nucleocapsid protein (N-protein) antibodies were negative 8 weeks after her initial infection. Six months later in October 2020, she once again developed upper respiratory symptoms which included headaches, fever, and sinus congestion. She again tested positive for COVID-19 by PCR. The symptoms felt milder with the second infection with less chest tightness. On immune work-up after recovery, she was found to have a decreased level of mannose binding lectin (<50ng/mL), normal immunoglobulin levels, and protective *Streptococcus pneumoniae* IgG antibodies for 18 of the 23 serotypes with appropriate vaccine response. Her SARS-CoV-2 IgG N- protein returned as positive 8 weeks after her second infection. With both infections, hospitalization was never required, and her symptoms remained mild overall.

Antibodies against COVID-19 are typically found in most patients within 2 weeks of infection. However, it is not known to what degree this provides immunity to COVID-19.⁴ Some studies revealed severe cases of COVID-19 tend to have a greater IgG response than milder cases, and in some mild cases, the immune system does not produce adequate IgG antibodies.⁵ Given the novelty of the virus and unclear long-term immune response to the virus, it is difficult to know for sure exactly how long these IgG antibodies last. One study on health care workers in Germany found that 22% percent of COVID-19 positive workers did not develop IgG after an 8-12-week period.⁶ Findings from a study in 2005 of SARS-CoV infection demonstrated that MBL-deficient individuals are more susceptible to SARS, however the paper did not comment on recurrent coronavirus infection rates.⁷

MBL has been shown to cause microvascular injury in COVID-19 viral infections. In a study of critically ill COVID-19 patients, extensive deposits of the terminal complement complex C5b-9 as well as C4d and MASP2 were found in the lungs on histology.⁸ These findings are consistent with sustained systemic activation of the complement pathway.⁸ Studies with influenza H1N1 revealed that MBL knockout mice developed mild disease as evidenced by lower cytokine and chemokine production.⁹ This suggests that MBL could increase inflammatory responses and worsen tissue damage.⁹

Perhaps in the case of our patient, her mannose-binding lectin deficiency prevented her from developing a severe case of COVID-19. Her failure to seroconvert after her first infection may be indirectly related to her MBL deficiency by means of her milder case.⁵ This however remains hypothetical.

Reported cases of COVID-19 reinfection have been rare. A study from Hong Kong revealed that a patient tested positive on two separate occasions months apart. Genomic analysis was performed, and two different strains of the virus were found. In this study, the individuals were asymptomatic during the recurrence despite the different strains.¹⁰ This is in contrast to the individual in this case who did not seroconvert after the first exposure to the virus has had two negative SARS-CoV-2 PCR test in the interim. She was symptomatic with both infections. In a recent study from Denmark, it was found that individuals ages 65 and over were more susceptible to reinfection, in contrast to this case.¹¹

This case presents details of a patient with mannose binding lectin deficiency who developed reinfection with COVID-19 after seroconversion failure with initial infection. To the best of our knowledge, this is the first report regarding recurrent COVID-19 infection in a patient mannose binding lectin deficiency and delayed seroconversion. Additional studies would be required to determine if those with MBL deficiency are at greater risk of reinfection than the general population or failure to seroconvert.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Declaration of Conflicting Interests

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Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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References

1. Coronavirus disease (COVID-19) – World Health Organization. Who.int. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed April 25, 2021.
2. Selvaraj V, Herman K, Dapaah-Afriyie K. Severe, symptomatic reinfection in a patient with COVID-19. *R I Med J (2013)*. 2020;103(10):24–26.
3. Eisen DP. Mannose-binding lectin deficiency and respiratory tract infection. *J Innate Immun*. 2010;2(2):114–122.
4. Mathur G, Mathur S. Antibody testing for COVID-19. *Am J Clin Pathol*. 2020;154(1):1–3.
5. Liu X, Wang J, Xu X, Liao G, Chen Y, Hu C-H. Patterns of IgG and IgM antibody response in COVID-19 patients. *Emerg Microbes Infect*. 2020;9(1):1269–1274.
6. Malfertheiner S, Brandstetter S, Roth S, et al. Immune response to SARS-CoV-2 in health care workers following a COVID-19 outbreak: a prospective longitudinal study. *J Clin Virol*. 2020;130:104575.
7. Ip WKE, Chan KH, Law HKW, et al. Mannose-binding lectin in severe acute respiratory syndrome coronavirus infection. *J Infect Dis*. 2005;191(10):1697–1704.
8. Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. *Transl Res*. 2020;220:1–13.
9. Ling MT, Tu W, Han Y, et al. Mannose-binding lectin contributes to deleterious inflammatory response in pandemic H1N1 and avian H9N2 infection. *J Infect Dis*. 2012;205(1):44–53.
10. To KK-W, Hung IF-N, Ip JD, et al. COVID-19 reinfection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing [published online ahead of print 2020]. *Clin Infect Dis*. doi:10.1093/cid/ciaa1275
11. Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. *Lancet*. 2021;397(10280):1204–1212.