Case report

Symptomatic reinfection with COVID-19: A case-report study in Iran

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Abstract

Coronavirus disease 2019 (COVID-19) resulted in a worldwide concern. The role of the immunity system and memory cells in this disease and their ability in preventing a secondary infection is a controversial issue. Here we presented a case of reinfection with this virus eight months after the first episode. A twenty-one-year-old man was referred to our local hospital on 19 February 2020 with symptoms of viral infection. COVID-19 infection was confirmed by RT-PCR. He got hospitalized for 5 days. Eight months later on 4 October 2020, he was again referred with symptoms of viral infection and para-clinical tests confirmed COVID-19 infection. He got hospitalized for 6 days in the second episode. Although the immunity system plays important role in COVID-19 infection through the presence of memory cells it doesn't guarantee permanent immunity to this virus. Reinfection with COVID-19 is possible and has been reported in some other studies.

Keywords: COVID-19, Immunity system, SARS-CoV2, Reinfection, Secondary infection

1. Introduction

According to World Health Organization (WHO), by October 23, 2021 more than 243 million people got infected by severe acute respiratory syndrome coronavirus 2virus (SARS-CoV-2) in the world and more than 4.9 million people died since its emergence in Wuhan, Hubei Province, China [1, 2].

An important issue in the course of the coronavirus disease 2019 (COVID-19) pandemic which is caused by SARS-CoV-2 is the role of the immune system and how much the immune system is capable of preventing a secondary infection [3, 4]. Infection with SARS-CoV-2 leads to immune system response with specific memory T cells and B cells and

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Received: October, 23, 2021 Accepted: May, 01, 2022 SARS-CoV-2-specific immunoglobulin G antibody (IgG) which appear in the plasma of infected individuals [5-7]. Although the persistence of neutralizing antibodies (immunoglobulin M and immunoglobulin G) in SARS-CoV-2 infection lasts about 40 days, the persistence of these antibodies in other respiratory viruses last for several months [8]. Though the presence of memory cells has been seen reinfection with SARS-CoV-2 is still a controversial issue [9].

Some studies believe that reinfection with coronavirus is unlikely [10], while some other studies reported reinfection with coronavirus [5, 11, 12]. Losing immunity to other types of coronavirus family

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within one to three years has been reported in some studies [13-17]. Here we present a case who was reinfected with the coronavirus in the North of Iran where the infection rate was one of the highest in the world.

2. Case presentation

A twenty-one-year-old man with a history of smoking cigarettes and hookah and without any other underlying diseases and resident of Rostamabad (Guilan province, North of Iran) was referred to Razi hospital (Rasht, Guilan province, North of Iran) at 9.00 post meridiem (PM) on 19 February, 2020 with symptoms of viral infection.

He was conscious with a Glasgow coma scale (GCS) of 15/15 and his symptoms were started 5 days before his referral. His symptoms included: fever and chills, fatigue, headache, myalgia, and purulent cough. His sense of smell and sense of taste were normal but he reported that he had lost his appetite. He showed no signs of respiratory distress syndrome (including color changes, grunting, retractions, and wheezing), and his O2 saturation, respiratory rate, and pulse rate were normal (Supplementary Table1).

Because the place where he lived was one of the regions with a high prevalence of COVID-19 infection at that time, for confirming the diagnosis, a nasopharyngeal swab test for detecting SARS-CoV-2 with real-time polymerase chain reaction (RT-PCR) was done for him and the test result was positive. Also, a chest x-ray (CXR) (Figure 1), and a computed tomography scan (CT scan) were done for him. He got hospitalized in the ward for 5 days and a blood examination was done for him based on the hospital protocols (Supplementary Table 2). During his hospitalization, he admired one ampule of Apotel (500 milligrams/q 4 hours) for controlling his fever, tablets of Azithromycin (500 milligrams/ twice daily), Ceftriaxone (500 milligrams/one injected ampule), Chloroquine (200 milligrams/once daily), and Oseltamivir (75 milligrams/once daily). Most of the symptoms lasted for 3 days or less since he got hospitalized except for the loss of appetite which lasted for 4 days (Supplementary Table 1). When he got discharged, another blood sample was done for him (Supplementary Table 2).

Eight months later on 4 October 2020, he was admitted again to the hospital at 2 PM with symptoms of lethargy, headache, myalgia, purulent cough, and the loss of appetite. The patient felt the symptoms less severe than the first time. He showed no signs of respiratory distress syndrome and his O2 saturation was normal. He was conscious with a GCS of 15/15 (Supplementary Table1).

The second time, he was referred to our hospital 3 days after the onset of symptoms. He said he was in a hookah house for the past two weeks. Α nasopharyngeal swab test for detecting SARS-CoV-2 RT-PCR was done for him and the test result was positive. A CT scan was done for him as well. He got hospitalized in the ward for 6 days and a blood examination was done for him based on the hospital protocols (Supplementary Table 2). During his hospitalization for the second time, he admired one ampule of Apotel (500 milligrams/q 4 hours) for controlling his fever, tablets of Azithromycin (500 daily), milligrams/twice Ceftriaxone (500 milligrams/one injected ampule), and one ampule of Dexamethasone (8 milligrams). Most of the symptoms of the patient lasted for 2 days or less since he got hospitalized except for the loss of appetite which lasted for 3 days (Supplementary Table1). When he got discharged, another blood sample was done for him (Supplementary Table 2).



Figure 1. Chest x-rays (CXR) in the first time infection

3. Discussion

Iran is one of the countries with a high prevalence of COVID-19 with more than 5 million confirmed cases and more than 112 thousand deaths [2]. Reinfection with the SARS-CoV-2 virus is not well understood and only a few case reports of reinfection with the SARS-CoV-2 virus have been reported in Belgium [18], the USA [19], Ecuador [12], and some other countries [11].

Although the number of reinfected case reports in comparison to the number of all COVID-19 cases is so small but we cannot conclude whether reinfection with this virus is rare or not. It is important to know that we survey only symptomatic patients who are admitted to hospitals and because we don't have a broad testing and general supervision of the society, we can't judge the frequency of asymptomatic reinfection in people who recovered from their first episode of the disease [20].

An interesting point of our patient is that he said he felt the symptoms more severe in the first episode whereas the cases reported from the USA [19] and Ecuador [12] showed the symptoms much more severe in the second episode of infection. The studies from Hong Kong and Belgium did not show a significant difference between the first and second episode symptoms [18]. Moreover, a chest CT scan also showed less severe lungs involvement in the second episode.

Some mechanisms can explain reinfection with SARS-CoV-2. Our patient was a smoker and smoking is an independent factor in the transmission of the virus [20]. It is also important that our patient told us about his attendance in a hookah house within two weeks before his second referral and because of his attendance in such a public place without strong hygiene protocols; he might have got reinfected in that place [21].

The duration of symptoms was longer the first time. One mechanism that can explain the less severity and duration of symptoms in the second event is the presence of immune memory cells which are made during the first exposure of the patient to the virus [5, 6]. As we know human body's immune system consists of innate and adaptive immunity. Adaptive immunity includes cell-mediated (T cells) and humoral immunity (B cells and antibodies) [22]. In the first exposure to a pathogen, memory cells are made and these memory cells cause a faster response in the following exposures [23]. Another mechanism may be a higher dose of infection with the virus during the first exposure [24]. It is also probable that the infection with the SARS-CoV-2 for the first time was with a stronger virulent type of virus [25]. Unfortunately, we didn't do genome sequencing for identifying the gene content of the virus in the first and second exposure to understand whether the reinfection was with the same type of virus or a different type.

In the para clinic exam, we see a higher lymphocytosis the second time which confirms the less severity of the disease. Previous studies showed the relationship between lymphopenia and the severity of COVID-19 infection [26, 27]. Tan et al. showed low lymphocyte percentage can be used as a prognostic factor in the disease progression and he explained how this virus can target lymphocytes [27]. We think that the severe lymphocytosis in the second exposure is due to some mechanism. First, there is a faster and stronger response in the second exposure to the virus due to memory cells generation [23], note that our patient was not immunocompromised and had not any underlying disease. Second, genetics play an important role in the function of the immune system [28, 29]. The relationship between genetics and COVID-19 infection has been studied before [30]. We think that the stronger response the second time can also be related to the genetic response of our patient. Third environmental factors can also affect the immune system response [30, 31]. Forth, the time of referral to the hospital can be an important issue. For the first time, our patient was referred to our hospital for 5 days and the second time 3 days after the onset of symptoms. We started medication and antibiotic therapy sooner the second time and this action could lead to better immune response the second time.

In conclusion, COVID-19 is a viral disease with high prevalence worldwide. Identifying the pattern of virus infection can lead us to a better understanding and management of the disease. This case presentation showed us one episode of infection with COVID-19 doesn't guarantee the individuals to be protected against the virus. However, this doesn't deny the necessity of vaccination but reflects that even vaccinated people and people with a previous infection should take care and obey the quarantine protocols.

Supplementary files

Supplementary file 1.

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Authors' contributions

All Authors contributed equally and approved the final version of manuscript.

Conflict of interests

The authors declare no competing interests.

Ethical declarations

The present study was approved by the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1400.065).

Consent for publication

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

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020; 382(8):727-33.

2. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int/

3. Iwasaki A. What reinfections mean for COVID-19. Lancet Infect Dis. 2021; 21(1):3-5.

4. Chowdhury MA, Hossain N, Kashem MA, Shahid MA, Alam A. Immune response in COVID-19: A review. J Infect Public Health. 2020; 13(11):1619-29.

5. Rodda LB, Netland J, Shehata L, Pruner KB, Morawski PA, Thouvenel CD, et al. Functional SARS-CoV-2-Specific Immune Memory Persists after Mild COVID-19. Cell. 2021; 184(1):169-83.e17.

6. Cañete PF, Vinuesa CG. COVID-19 Makes B Cells Forget, but T Cells Remember. Cell. 2020; 183(1):13-5.

7. Cox RJ, Brokstad KA. Not just antibodies: B cells and T cells mediate immunity to COVID-19. Nat Rev Immunol. 2020; 20(10):581-2.

8. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and Postinfection Immunity: Limited Evidence, Many Remaining Questions. Jama. 2020; 323(22):2245-6.

9. World Health Organization. "Immunity passports" in the context of COVID-19. Available from: https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19?gclid=EAIaIQobChMI9-PP1-

HF6wIVdIBQBh2CywoEEAAYASAAEgJz2_D_BwE.

10. Roy S. COVID-19 Reinfection: Myth or Truth? SN Compr Clin Med. 2020; 2(6):710-3.

11. Selvaraj V, Herman K, Dapaah-Afriyie K. Severe, Symptomatic Reinfection in a Patient with COVID-19. R I Med J (2013). 2020; 103(10):24-6.

12. Prado-Vivar B, Becerra-Wong M, Guadalupe JJ, Márquez S, Gutierrez B, Rojas-Silva P, et al. A case of SARS-CoV-2 reinfection in Ecuador. Lancet Infect Dis. 2021; 21(6):e142.

13. Callow KA, Parry HF, Sergeant M, Tyrrell DA. The time course of the immune response to experimental coronavirus infection of man. Epidemiol Infect. 1990; 105(2):435-46.

14. Chang SC, Wang JT, Huang LM, Chen YC, Fang CT, Sheng WH, et al. Longitudinal analysis of Severe Acute Respiratory Syndrome (SARS) coronavirus-specific antibody in SARS patients. Clin Diagn Lab Immunol. 2005; 12(12):1455-7.

15. Huang AT, Garcia-Carreras B, Hitchings MDT, Yang B. A systematic review of antibody mediated immunity to coronaviruses: kinetics, correlates of protection, and association with severity. Nat Commun. 2020; 11(1):4704.

16. Mo H, Zeng G, Ren X, Li H, Ke C, Tan Y, et al. Longitudinal profile of antibodies against SARS-coronavirus in SARS patients and their clinical significance. Respirology. 2006; 11(1):49-53.

17. Wu LP, Wang NC, Chang YH, Tian XY, Na DY, Zhang LY, et al. Duration of antibody responses after severe acute respiratory syndrome. Emerg Infect Dis. 2007; 13(10):1562-4.

18. Van Elslande J, Vermeersch P, Vandervoort K, Wawina-Bokalanga T, Vanmechelen B, Wollants E, et al. Symptomatic Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Reinfection by a Phylogenetically Distinct Strain. Clin Infect Dis. 2021; 73(2):354-6.

19. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzalski A, et al. Genomic evidence for reinfection with SARS-CoV-2: a case study. Lancet Infect Dis. 2021; 21(1):52-8.

20. Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020; 133(9):1032-8.

21. Shekhar S, Hannah-Shmouni F. Hookah smoking and COVID-19: call for action. Cmaj. 2020; 192(17):E462.

22. Marshall JS, Warrington R, Watson W, Kim HL. An introduction to immunology and immunopathology. Allergy Asthma Clin Immunol. 2018; 14(Suppl 2):49.

23. Ratajczak W, Niedźwiedzka-Rystwej P, Tokarz-Deptuła B, Deptuła W. Immunological memory cells. Cent Eur J Immunol. 2018; 43(2):194-203.

24. Guallar MP, Meiriño R, Donat-Vargas C, Corral O, Jouvé N, Soriano V. Inoculum at the time of SARS-CoV-2 exposure and risk of disease severity. Int J Infect Dis. 2020; 97:290-2.

25. Kumar A, Prasoon P. SARS-CoV-2-specific virulence factors in COVID-19. J Med Virol. 2021; 93(3):1343-50.

26. Tavakolpour S, Rakhshandehroo T, Wei EX, Rashidian M. Lymphopenia during the COVID-19 infection: What it shows and what can be learned. Immunol Lett. 2020; 225:31-2.

27. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther. 2020; 5(1):33. 28. Knight JC. Genomic modulators of the immune response. Trends Genet. 2013; 29(2):74-83.

29. Aguirre-Gamboa R, Joosten I, Urbano PCM, van der Molen RG, van Rijssen E, van Cranenbroek B, et al. Differential Effects of Environmental and Genetic Factors on T and B Cell Immune Traits. Cell Rep. 2016; 17(9):2474-87.

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30. Ellinghaus D, Degenhardt F, Bujanda L, Buti M, Albillos A, Invernizzi P, et al. Genomewide Association Study of Severe Covid-19 with Respiratory Failure. N Engl J Med. 2020; 383(16):1522-34. 31. Dietert RR, Golemboski KA, Austic RE. Environment-immune interactions. Poult Sci. 1994; 73(7):1062-76.