GENE EXPRESSION UNIVERSITY

October 06-29

THE ULTIMATE WEBINAR SERIES IN GENE EXPRESSION STUDIES

Register here

applied biosystems
by Thermo Fisher Scientific

WILEY

Danielle de Araujo Torres ORCID iD: 0000-0002-1520-1839

Title: Reinfection of COVID-19 after 3 months with a distinct and more aggressive clinical presentation: case report

Short Running: Reinfection of COVID-19 with more aggressive clinical presentation

Author 1	**Torres, Danielle de Araujo**
Corresponding author	danitorres.orlrj@yahoo.com.br 0000-0002-1520-1839 Hospital Federal da Lagoa, Rua Jardim Botânico 501 Jardim Botânico 22470-050 Rio de Janeiro, RJ, BR
Author 2	**Ribeiro, Luciana do Carmo Bueno** lurribeiro@yahoo.com.br Hospital Universitário Gaffrée-Guinle, Rua Mariz e Barros 775, Tijuca 20270-004 Rio de Janeiro, RJ, BR
Author 3	**Riello, Anna Patrícia de Freitas Linhares** anna.riello@gmail.com Grupo Fleury, Av. Pastor Martin Luther King 126, bloco 1. 20765-971. Sao Paulo, SP, BR

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jmv.26637.

Author 4 **Horovitz, Dafne Dain Gandelman**

dafne@ceresgenetica.com.br

Instituto Fernandes Figueira/ Fiocruz, Av. Rui Barbosa, 716 – Flamengo 22.250-020

Rio de Janeiro, RJ, BR

Author 5 **Pinto, Luis Felipe Ribeiro**

lfrpinto@inca.gov.br

Instituto Nacional do Câncer,

CPq INCA- André Cavalcanti 37, Centro 20231-050

Rio de Janeiro, RJ, BR

Author 6 **Croda, Julio**

juliocroda@gmail.com

Fundação Oswaldo Cruz,

Fiocruz MS- Rua Gabriel Abrão, 92, Jardins das Nações, Campo Grande 79074-460

Campo Grande, MS, BR

To the Editor,

The COVID-19 pandemic began in December 2019 in Wuhan, China. Since then, it has rapidly spread across the globe and impacted several countries. Brazil has more than 4 million COVID-19 confirmed cases, more than 120,000 deaths and is the leader in numbers of health care professionals infected.

Most recent studies suggest that immunity can be developed after an episode of SARS-COV-2 infection. This brings a false sense of safety for professionals who have already been infected and have recovered from the disease. They return to the battlefields exposed to high viral load, often without adequate protection.

A 36-year-old female medical doctor, without comorbidities, presented on 20th March 2020 with rhinorrhea and sore throat followed by low fever, diarrhea, asthenia and mild headache until the seventh day of symptoms when RT-PCR was obtained by nasal swab. The RT-PCR collected on 27th March 2020 was positive for SARS-CoV2 with a log of 513 copies (detection limit of RT-PCR less than 100 copies).

After 11 days of initial clinical symptoms, she presented with erythematous vesicles on her right calf, along with severe musculoskeletal pain of the lower limbs with hyperesthesia.

The first serological test was performed using ELISA (Enzyme-Linked Immunosorbent Assay), 23 days after the onset of symptoms, with 0.477 IgG titers (negative: less than 1,00 S/CO). There was complete resolution of the symptoms 24 days after symptoms onset (fig1).

The patient returned to medical work at COVID-ICU in two hospitals. After returning to work she was tested twice for COVID by chemiluminescence method serologies. The results were both negatives for IgM and IgG detection, 33 days and 67 days after the acute presentation of symptoms.

Approximately 12 weeks later of the first episode of COVID-19, she presented a new clinical episode with nasal obstruction and hyaline rhinorrhea, sudden and complete anosmia and ageusia, frontal headache and asthenia.

On the tenth day of this new clinical episode, there was worsening of prostration with persistent anosmia and ageusia. She sought emergency care on the 11th day of symptoms, where she underwent a CT scan that revealed acute viral pneumonia typical of COVID-19 (fig 2a).

The ELISA serology on the 13th day of symptoms revealed positive IgA for COVID-19 with 4,240 titers (negative: less than 1,00 S/CO). Nasal swab RT-PCR on the 11th and 13th days of symptoms were negative. D-Dimer increased to 761ng/ml and DHL to 290U/L, however, serum values normalized after 48h. The neutralizing IgG titration performed by the ELISA method on the 20th day of symptoms was positive in 1,173, and after 45 days was 7,473 (immunity: titer greater than 1.00 S/CO). The pulmonary pathological changes identified on the chest CT practically disappeared on the twenty-fourth day after the onset of symptoms (fig 2b).

About 10 months after the first cases of COVID-19, there is still no consensus in literature of reinfection by SARS-CoV-2, although some reports around the world show strong evidence that it is happening. The strongest evidence of reinfection requires documentation of a new infection by a molecularly distinct form of the same virus after the elimination of the previous infection [1–3].

Human reinfection by SARS-CoV-2 was confirmed for the first time in August 2020 in Hong Kong, through genetic sequencing of two samples collected by nasal swab from the same patient with a time difference of 142 days. There was evidence that the viral genomes belong to different lineages, one of which was more incident between March and April 2020, while the other is close to strains found today [4].

As genetic difference between strains increases over time, cross-immunity between those lineages may become more difficult and different clinical pictures may occur [4]. However, it is unknown how intense the second clinical episode will be.

We raise the discussion whether the presence of a new mutation such as D614G, which replicates faster in the upper airway, could be more related to pneumonia and anosmia, to the detriment of other symptoms such as gastrointestinal manifestations [5].

Despite evidence of an effective acquired immune response after COVID-19, some studies have shown that patients with mild symptoms have developed a weaker and less lasting immune response to the virus, with a decrease in the level of antibodies after 2 -3 months of infection [6,7].

As the patient maintained intense exposure to COVID-19 in those 3 months between clinical episodes, had different symptoms and antibody detection only recently, this suggests reinfection by different lineages of SARS-CoV-2. Therefore, the hypothesis of herd immunity and duration of protection afforded by vaccines, is questioned.

Conflicts of interest

The authors declare no conflicts of interest.

Author Contribution Statement

Author 1: Conceived the presented idea and elaborated the manuscript

Author 2: Provided the clinical data and exams, and elaborated the manuscript

Authors 3, 4, 5 and 6: revised the manuscript, provided critical feedback and proposed format adjustments

REFERENCES

1. Xing Y, Mo P, Xiao Y, Zhao O, Zhang Y, Wang F. Post-discharge surveillance and positive virus detection in two medical staff recovered from coronavirus disease 2019 (COVID-19), China, January to February 2020. *Eurosurveillance*. 2020. doi:10.2807/1560-7917.ES.2020.25.10.2000191

2. Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. *J Med Virol*. 2020. doi:10.1002/jmv.25855

3. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA*. 2020. doi:10.1001/jama.2020.3204

4. To KK-W, Hung IF-N, Ip JD, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. *Clin Infect Dis*. doi:10.1093/cid/ciaa1275

5. Korber B, Fischer WM, Gnanakaran S, et al. Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus. *Cell*. 2020. doi:10.1016/j.cell.2020.06.043

6. Ni L, Ye F, Cheng M-L, et al. Detection of SARS-CoV-2-Specific Humoral and Cellular Immunity in COVID-19 Convalescent Individuals. *Immunity*. 2020. doi:10.1016/j.immuni.2020.04.023

7. Seow J, Graham C, Merrick B, et al. Longitudinal Evaluation and Decline of Antibody Responses in SARS-CoV-2 Infection. *Infectious Diseases (except HIV/AIDS)*; 2020. doi:10.1101/2020.07.09.20148429

Fig 1. Chronology of clinical and laboratory events in the reported case.

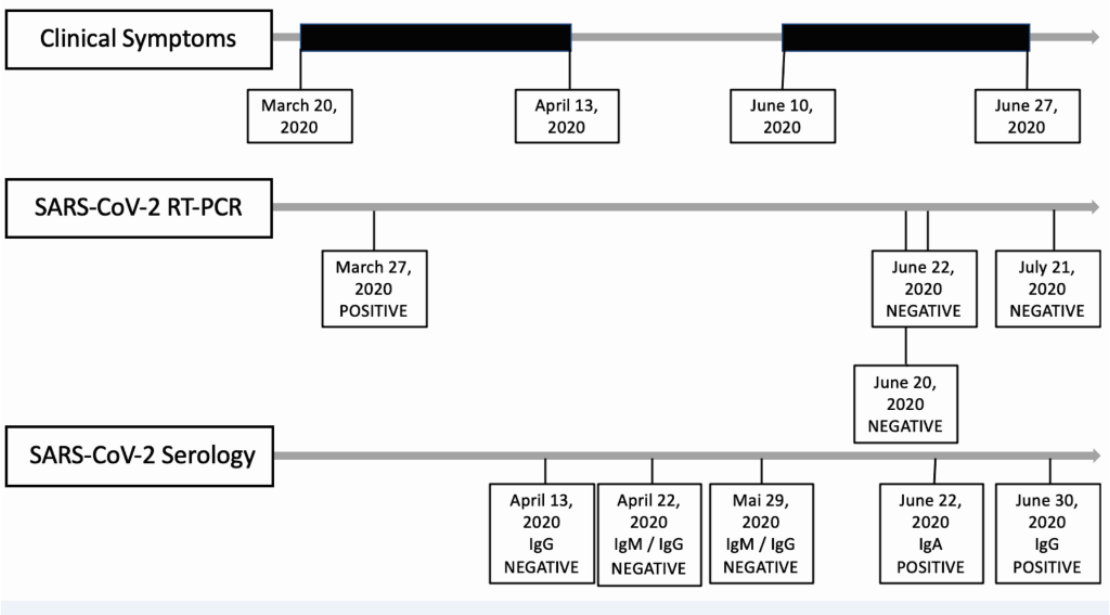

Fig 2. CT chest scans performed on the 11th day of symptoms (a, c and e) and 24th day of symptoms (b and d) of the second clinical episode. (a) and (c) Ground-glass opacities associated with bilateral and multilobar consolidation foci, predominantly peripheral, sometimes with a rounded aspect, some with areas of septal thickening, more evident in the lower right lobe. (b) and (d) Almost complete resolution of the alterations found in the previous exam, with discrete areas of attenuation in ground glass persisting. (e) Graphical demonstration with color map overlay. The areas in blue represent mild impairment, in green a little greater impairment, in yellow greater impairment and in red consolidations.