

Case Reports of COVID-19 Recurrence

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Abstract

The first confirmed case of COVID-19 reinfection in the United States occurred the week of October 14, 2020 in a 25-year-old Nevada man who tested positive for the virus in April, recovered, then fell ill and tested positive again in June. In his case the second presentation was more serious and he was hospitalized and given oxygen. Genetic sequencing turned up significant differences between the virus samples taken in April and June indicating a second infection rather than the virus lingering dormant in the system after the first bout of illness. Other documented cases of patients have similarly been presented. In these infections genomic sequences were able to confirm infections as distinct isolates of SARS-CoV-2. None of the individuals had known immune deficiencies and one had pre-existing antibody (IgM) against SARS-CoV-2. In other instances, because of the wide range of serological testing platforms used, it is impossible to compare results from one assay to another and since genomic information isn't always available, it is difficult to determine if these are new infections or resurgence of dormant virus. Antibody levels are also highly dependent on the timing after exposure so even they may not assist in determining the true reinfection versus reoccurrence. PCR tests for the virus can remain positive up to three months. That too doesn't determine infectiousness. There are multiple proxies for determining infectiousness. However, most of them require biosafety level 3 facilities and are not routinely done in clinical labs.

Keywords: COVID 19, Virus, Biosafety

Accepted on Nov 19, 2020

Introduction

While reinfection rates of coronavirus have been the focus, they are rare and repeat bouts of illness, are a reality in patients who previously presented with symptoms and tested positive months earlier. For the patients and their health care providers they portend a nightmare of uncertainty for the future effectiveness of vaccines, quarantines and lockdowns [1,2]. This is distinct from "Long-haul" COVID syndromes since these patients were asymptomatic between the presentations. These cases are very challenging to determine if this is a real reinfection. More than likely it is a resurgence of symptoms connected to the original infection. The virus may set off an inflammatory response that flares up later or perhaps even a chronic low-grade infection that smolders for weeks. For clinicians and patients alike, it is important to understand these occurrences since they lead to worrying if this will lead to hospitalization, prolonged illness and long-term sequelae. How should they be treated acutely? Additionally, these patients may still transmit the virus to others and procedures to quarantine, mask are equally necessary to help protect communities. More knowledge of these presentations and their course is needed to answer these questions [3,4].

Method

A total of 600 patients who tested positive at the Miami Veterans Health System were followed during the period of 4/12/2020 to 10/21/2020. This report summarizes a group of seven veterans who presented PCR positive for COVID 19 and after at least two months re-presented with a positive PCR test Table 1.

Results

The patients re-tested were COVID19-PCR positive again an average of 94.9 days (Range 62-172 days) from their original presentation and first COVID 19-PCR positive test. In the majority of the cases, patients were asymptomatic at the time of the second presentation and would have gone undetected if not for hospital prescreening requirements for procedures/surgery. Only one patient, a young woman, had typical symptoms (fever, headache) at the time of the second presentation which resolved in less than a week. Two other patients did complain of fatigue in the month prior to subsequent positive test and one noted persistence of loss of taste and smell for the previous 2 ½ months.

We do not have laboratory evidence of reinfection however, we have each patient's acknowledgement that they had not violated social distancing, use of masks, hand washing and no recent travel or animal exposure. Additionally, they indicated that family members in the same household have tested negative for the virus. Four of the patients had tested negative by PCR between their first and second attacks and in two other cases, the patients had evidence of immuneresponse. Their ages varied widely from 27 to 72 years of age. There were two women, two African Americans and four Hispanics. Their underlying conditions were also variable. Three patients could be considered immune compromised (psoriatic arthritis, renal/liver transplant and HIV (undetectable viral load) and sarcoidosis. Two of those patients were receiving immunosuppressive therapy (Adalimumab, Tacrolimus/Sirolimus) chronically. Three patients were insulin-requiring diabetics.

Table 1. Patients who presented with recurrence of covid-19 test positive.

Age	Initial symptoms	Interim covid19 test	Subsequent presentation	#days between 1st & 2nd test	Conditions	Resolution covid retest
38	Cough, fever Loss taste/ smell	NEG.	ASX	62	MDEPRESSION, PTSD	RESOLVED-1 WEEK
60	Cough	NEG.	ASX	75	MDEPRESSION, PTSD, Hx BLADDER CA	RETEST pending
60	Acute Renal failure	NEG.	FATIGUE	72	DIABETES	POSITIVE PCR
27	Fever, "Flu-like"	Antibody +	FATIGUE, LOSS TASTE	79	PSORIATIC ARTHRITIS	RETEST pending
33	Fever, cough, Diarrhea	Antibody +	Fever, headache	172	PTSD, Allergic rhinitis	RESOLVED- 3 days
71	Fever, Pneumonia Respiratory insufficiency	NEG.	ASX	93	Renal/liver transplant HIV, CHF, DIABETES, CRD	RESOLVED- 17 days
72	Dyspnea, fatigue, headache	NEG.	FATIGUE	111	Pulmonary/ CardiacSarcoidosis	RetestPending

Their initial presentation included typical symptoms of cough, fever," flu-like" illness, loss of taste, smell, and fatigue. One patient had diarrhea; one had acute renal failure on top of chronic renal insufficiency. Only one patient was hospitalized during the initial presentation for GI bleeding and small bowel obstruction. During that hospitalization he developed respiratory failure with bilateral pneumonia and tested positive for COVID-19. He did not require intubation or surgery and recovered. He remained COVID + for two months; tested negative the third month and re-tested positive four months later as part of routine screening. Since he was asymptomatic at that time, it was determined that there was no suspicion for new acute COVID infection and that he would test positive due to his immune suppressed state. Five months later he tested negative. None of the patients received hydroxychloroquine, Remdesivir, dexamethasone at the time of their initial COVID-19 presentation. Only the patient with HIV was chronically receiving antiviral drugs-Dolutegravir and Lamivudine.

Discussion

Although a rare phenomenon (1.2%) of our population we were following, it is an important occurrence for providers to be aware of. It has been described previously by French national case series of 11 COVID-19 patients who also experienced a second clinically- and virologically-confirmed acuteCOVID-19 episode [5]. In their series, the patients presented the second time with at least one major clinical sign of COVID-19, including fever or chills, flu-like syndrome, dyspnea, anosmia or dysgeusia and a positive SARS-COV-2 RT-PCR test. Their patients showed radiographic signs of acuteCOVID-19 and averaged 10 days median duration of symptoms for their second episode. Four of their 11 patientswere health care workers who had a first mild COVID-19 episode with complete recovery, returned to work in COVID units. All of them experienced a clinical relapse requiring sick-leave but no hospitalization after a median symptom-free interval of 9 days. In contrast, none of our patients were health care workers and all but one was either asymptomatic or had recent presentation of fatigue, and loss of taste/smell.

COVID-19 recurrences are different from secondary complications, "long-haul" symptoms or persistence of traces of viral RNA that can be detected in respiratory samples up to 6 weeks after onset of symptoms in clinically-cured patients. All of our patients had tested negative by PCR tests and two had evidence of antibodies in between their initial infection and the subsequent episode. While immuno suppressive factors

such as drugs or pathological conditions could contribute to impaired viral clearance and favor viral reactivation, the three patient who met this criterion had tested negative by PCR and averaged 79, 93 and 11 days between their initial illness and second positive test.

While the patients did not have significant symptoms on second presentation, the finding of testing positive for COVID- PCR again did have significant implications for them. They all had anxiety and had to deal with the uncertainty of the meaning of the positive re- test. Additionally, it led to cancellations of necessary procedures and surgery and clinic follow-up appointments which further intensifies the impact on these patients' health. Patients were advised, based on an abundance of caution, to re-quarantine for 10 days, although there was no objective evidence of active infection. This had untoward impact on their families and their employment. The majority of the patients expressed frustration and anger at the occurrence primarily because of the impact on their scheduled procedures. Despite diagnoses of major depression and PTSD in four of the patients, there was no exacerbation of symptoms related to these diagnoses. On follow-up, to date, only two have been retested and are negative, two are pending lab results, two have not been retested and one remains positive 20 days after his second positive and 72 days from the original presentation.

Conclusion

Our case series has limitations. The limited number of observations is important. Additionally, the resolution of the initial infection was primarily clinically-defined and only 5 of the patients tested negatively for the virus by PCR and only two had antibody testing prior to the subsequent positive test. Negative, two are pending lab results, two have not been retested and one remains positive 20 days after his second positive and 72 days from the original presentation. Additionally, viral culture was not performed on any of the patients to determine if this was re-infection, smoldering viral carriage or inflammatory response. More research is needed and long-term assessment of these patients. The question of reinfection versus resurgence of the infection could have significant implications for our understanding of COVID-19 immunity and outcomes.

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