

Case Series

Dilemma and implication of COVID-19 recurrences among healthcare workers

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ABSTRACT

Reports of second infections with COVID-19 have intrigued researchers around the globe. They increase the burden on the already surging infected cases and add to the existing stigma around COVID. Moreover, it is mentally and physically taxing for the individual to go through the same stress for the second time. We aim to describe three cases of Re-Detected Positives (RDP) among healthcare workers in a tertiary care institute. The case histories were taken in detail over the telephone comparing the course, clinical history, contact history, and lab investigations of a first and second infection in each of them. A standard format developed for contact tracing in the institute was used for this. The period observed between two infections in these cases were 2-3 months and all the cases had tested negative by RTPCR before re-testing positive. Case 1: RDP by RTPCR 2.5 months after the first episode. He was asymptomatic, anti-bodies to SARS-Co-V 2 were also present in serum. Case 2 and 3: RDP by RTPCR and rapid antigen around 2.5 months after the first episode. They were symptomatic, antibodies absent and the contacts subsequently turned positive. Prolonged shedding of virus, reactivation, reinfection, dead viral shedding, false test results is the possible causes scientifically discussed. Second infections can be seen in COVID-19. It is expected to present with more severe signs and symptoms. Hence, general precautions should be taken even after recovery from the disease, especially in the case of HCWs who are constantly exposed.

Keywords: COVID-19, Reinfection, Reactivation

INTRODUCTION

It's been seven months since the declaration of COVID-19 pandemic by WHO and there has been a continuous surge in cases. Since then the Health Care Workers (HCWs) have been involved actively at various fronts in the care of COVID-19 patients. A huge number of HCWs are already infected with COVID-19, recovered, and joined back to work again in COVID settings. HCWs are at 3.4% more risk of being infected with COVID-19.¹ Thus, these HCWs are re-exposed to the virus making them more susceptible to recurrence of infection. There have been few reported cases where the post-discharge

patients retested positive.^{2,3} Recently, print media has reported such cases of HCWs from various hospitals who were re-tested positive for COVID-19 after recovery of the previous COVID-19 infection. Three previous studies, one in Hongkong, in the USA and one amongst Health care workers in Mumbai have shown proven cases of reinfection by the genomic study.⁴⁻⁶ As important as it is to decrease the transmission rate at this point and flatten the curve, it is also important to be prepared with strategies and guidelines predicting the resurgence of COVID-19 cases which might be due to re-detected positives.

CASE SERIES

Here we present three case scenarios of recurrence of COVID-19 among health care workers (Figure 1). The

data has been obtained from contact tracing records maintained by the Department of Community Medicine for all health care workers during the COVID-19 pandemic.

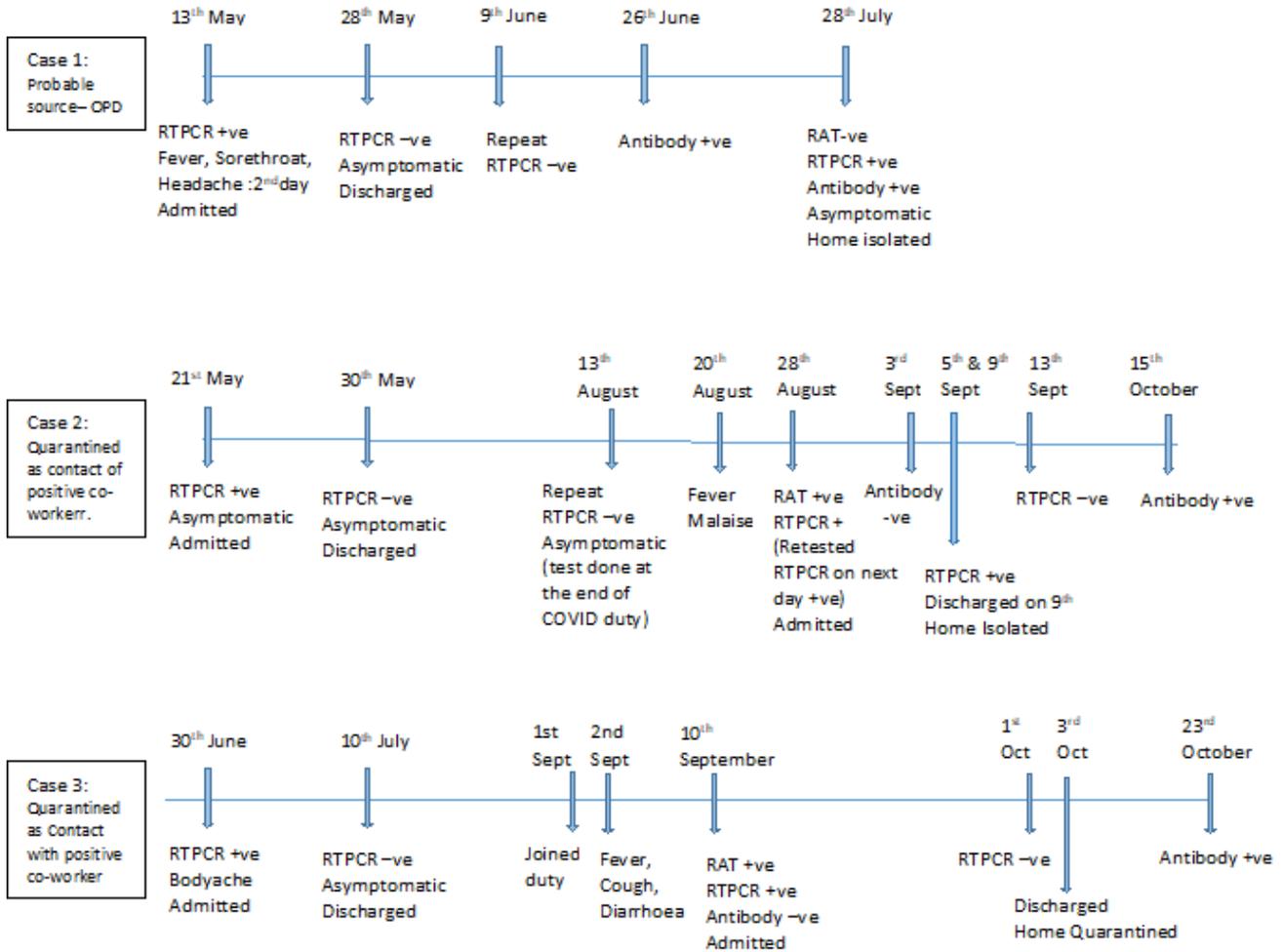


Figure 1: Timeline of the cases of recurrences of COVID-19.

The first case is a 30 years old male HCW who tested positive by RTPCR for COVID-19 for the first time on 13th May 2020. During this episode, he presented with complaints of fever, sore throat, and headache for two days. The probable source of infection during this episode could be an outpatient. Also, at this time, the case was residing in an area declared as a containment zone. He had no comorbidities and had not taken any prophylaxis. No abnormality was detected on Chest Radiograph. He was then isolated as per protocol. No contacts were identified at the workplace or residence. Subsequently, he tested negative on 28th May 2020 and was discharged symptom-free. A repeat swab on 9th June 2020 also tested negative for SARS CoV-2 by RTPCR. The case had tested for antibodies to COVID-19 by Rapid antibody kit on 26th June 2020 from a private lab and the result showed the presence of antibodies. However, there is no record of the titer. On 28th July 2020, he re-tested positive by RTPCR for COVID-19. He was asymptomatic and was working in an isolation ward for

COVID-19 with full personal protective gear and no breach in PPE was reported. Hence, no definite exposure could be identified. There were no contacts this time too either at the workplace or residence. The Rapid Antigen Test (RAT- Ag- SD Biosensor Standard Q COVID-19 Ag detection Kit) on 29th July 2020 showed a negative result. Repeat antibody titer on 29th July 2020 was also reactive to ANTI-SARS-COV-2. The case was however re-isolated as per protocol. No repeat testing was performed at the end of the isolation period.

The second case is a 32-year-old female HCW who tested positive by RTPCR for COVID-19 for the first time on 21st May 2020. She had been exposed to her co-worker who tested positive. As per protocol she was tested at the end of the quarantine period and the result turned out to be positive. She was asymptomatic throughout the isolation period. Her husband and daughter were quarantined and tested negative at the end of quarantine. She tested negative by RTPCR on the 30th of May and

was discharged from the hospital. She was asymptomatic but tested herself again on 13th August after COVID ward duty which was negative (RT-PCR). She was normal until she developed fever and malaise on the 20th of August. She took symptomatic treatment and tested herself on 28th August for COVID-19. The RTPCR turned out to be positive. On 29th August she was tested again with a fresh sample to confirm. The results for RTPCR and Rapid Antigen (RAT) both came positive. She was isolated as per protocol and given treatment. Her Anti-SARS CoV2 IgG Antibody on 3rd September came negative. The CT scan of the chest detected no abnormality. Three contacts, two-family and one at the workplace were identified and quarantined. The family members tested positive around the 5th day of last exposure. The workplace contact was previously COVID positive and did not re-test positive at the end of the quarantine period. Antibodies had developed in the workplace contact due to her previous infection. Repeat RTPCR of the index case on 5th and 9th September was also positive for RTPCR but she was already asymptomatic by this time. A repeat RTPCR of 13th September was negative. Later on 15th October, a repeat Antibody test was done by COVID KAWACH IgG MICROLISA detecting presence of Anti SARS CoV2 IgG Antibody this time.

The third case is a 57 years old male, support staff in the hospital (no direct contact with any patient), had been exposed to a COVID positive person, developed body aches within a week of contact, and subsequently tested positive by RTPCR for COVID-19 for the first time on 30th June 2020. He had taken Hydroxychloroquine prophylaxis for 3 weeks. He is a known case of Diabetes and Hypertension on medications. Two of his family members who were his contacts were quarantined and tested negative at the end of the quarantine period. He was hospitalized and subsequently discharged on 10th July after testing negative by RTPCR. The case did not report to work for 6 weeks even after discharge due to personal reasons. He resumed work on the 1st of September. On the 2nd of September, he developed fever and cough for which he took symptomatic treatment. Within 4-5 days he also had diarrhea and the previous symptoms did not subside. He tested positive for COVID by Rapid Antigen (RAT) and RTPCR on the 10th of September. The Anti-SARS CoV2 IgG Antibody came negative. He was admitted to the COVID ward as per protocol. The patient was hospitalized longer due to changes in chest radiograph (patchy consolidation), HRCT chest (consolidation in lungs, CT score-moderate), and oxygen requirement. He tested negative by RTPCR on the 1st of October and was discharged on the 3rd of October.

DISCUSSION

After reviewing similar cases found around the world, there are three possibilities where a person turns positive

again after being cured for the first time-reactivation, reinfection and RDP (Table1).

Other possibilities are that the tests done in between were false-negative tests which can be due to faulty technique in collection or processing of the samples, or due to the virus mainly residing in the lower respiratory tract and the viral load and multiplication in the upper respiratory tract is low during the later course of the disease when the cases were discharged.⁷⁻⁹

Antibodies have a great role in predicting herd immunity, and vaccine efficacy, and longevity. As observed, the case 1 had developed antibodies (IgG) which directs us towards the possibility that it could be inactivated viral remnant particles which may have been detected in RTPCR testing and hence RAT was detected to be negative. If this is the situation, the case is no longer infective to the community and isolation is questionable.¹⁰ However, there are no clear guidelines regarding this.

In the second case, both RTPCR and RAT were positive. In this scenario, viral genomic sampling (or viral culture) is the only way to confirm if its re-infection or reactivation. As the previous samples were discarded this couldn't be pursued. No antibody testing was done during the period between the two episodes. Even if antibodies are present, the titer should be significant enough to neutralize the virus as antibodies are expected to wane off over time.^{11,12} It is also possible that the virus was residing in the lower respiratory tract during the later stages of the first infection and when the immunity of the individual dropped, it was reactivated, multiplied and hence, tested positive for the next time with symptoms. None of the contacts during the first infection contracted the infection, which could be because she was already in quarantine. Whereas during the second infection, household contacts did get infected. A false positive test during the first time is also a rare possibility as there were no secondary contacts, no symptoms and no antibody response.

The third case, was similar to the second case concerning diagnostic tests outcome and contact history but clinically this case showed more severe symptoms compared to case 2. The second infection was more severe than the first in this case. Reinfection, reactivation are both a possibility and couldn't be confirmed due to non-availability of previous samples. However both of them developed antibodies post the second infection which was not seen in the first infection.

In two of the three cases (cases 2 and 3) the symptoms were aggravated and a longer period before turning negative was observed during the second infection. The first infection was with mild symptoms. Cases of reinfection can be more taxing to the health of an individual pathophysiologically, psychologically, and socially. The period observed in the above cases between 2 infections is two to three months.

Prolonged shedding of virus can be another possibility. But as all the three were tested negative once and/or twice at the time of discharge after the first infection, re-detected positive due to prolonged positive status can be possible only due to false-negative tests in these cases.

According to the latest COVID-19 discharge policy of the Ministry of Health and Family Welfare, India, a swab is not required before discharge.¹³ In such cases, we would not know if the post-discharge positive status is due to prolonged viral RNA shedding or reinfection.

Table 1: A comparison of mechanism of reactivation, reinfection and RDP.

Recurrence patterns	Reactivation	Reinfection	Re-positive/re-detected positive (RDP)
Cause	Clinical improvement and negative RT-PCR, doesn't conclude viral clearance. The residual virus may reside in the lungs and certain circumstances may lead to reactivation. ⁷	Once infected with the virus, immunity is built up which may wear off and give chance to be infected once again. Or the 1st infection was due to another strain of the virus than the 2nd infection and hence previous antibodies do not offer protection to reinfection.	Detection of inactivated viral particles (Viral RNA neutralized by Antibody) (or can be Reinfection/Reactivation). ⁸
Process	Endogenous	Exogenous	Inactivated virus particles
Lab investigation	RAT +/-	RAT +/-	RAT -
	RTPCR +	RTPCR +	RTPCR +
	Antibody +/-	Antibody +/-	Antibody +

As per guidelines only Quality control laboratories store all samples for long duration, hence it may not be possible to confirm the diagnosis in all cases of recurrence. Wherever, paired samples are available attempt for genomic sequencing should be done. A close surveillance is required on such occurrences to understand the epidemiology and clinical course in such patients.

Limitations

Due to limitations in availability of paired samples (as samples are stored for a month only due to space constraints) viral genomic sampling could not be performed in any of the cases.

CONCLUSION

Second infections in the case of COVID-19 are possible. It is still difficult to comment on whether a particular factor might be related to the reappearance of the virus. The second infection is expected to present with more severe signs and symptoms and take longer period of time to be free of virus. General precautions should be taken even after recovery from the disease, especially in the case of HCWs who are constantly exposed. Distinct guidelines for reporting and isolation of cases infected for the second time is the need of the hour. With releasing of lockdown restrictions, awareness about this should be enforced. Presence and waning of Antibodies should be studied in more detail to get clear picture of the longevity of immunity against SARS-CoV-2.

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