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## Letter to the Editor

**COVID-19 in a case previously infected with MERS-CoV: No cross immunity**


Dear Editor,

We read with interest the recent study published in this journal suggesting the immunological cross-reactivity between common cold coronaviruses and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as explanation for the reduced incidence of COVID-19 in children.<sup>1</sup> Immunity due to past Middle East respiratory syndrome coronavirus (MERS-CoV) exposure in the Middle East has also been proposed as a potential reason for the lower mortality with COVID-19 in comparison to experience in USA and Europe.<sup>2</sup> In this report, we discuss a confirmed case of COVID-19 in June 2020 in a physician who was diagnosed previously with MERS-CoV infection in February 2019.

Middle East respiratory syndrome (MERS) emerged in the Arabian Peninsula in 2012 mainly causing hospital outbreaks. Oman is one of the countries that has reported local transmission of (MERS-CoV) with total of 24 human cases since 2012, including two healthcare workers from nosocomial outbreaks.<sup>3</sup> The current COVID-19 pandemic caused by SARS-CoV-2 has also affected the country with ongoing transmission activity since the reporting of the first imported case on 24 February 2020.

A healthy 31-year-old physician involved in healthcare outbreak of MERS-CoV in 2019 was reported to have COVID-19 in June 2020. He was born in Sudan and working in a district hospital in Oman covering consults from accident and emergency and the critical care unit.

On 12 February 2019, he admitted two patients with severe pneumonia, one with adult respiratory distress syndrome, the other needed urgent intubation and the procedure was done without protective precautions. Two days later, the physician performing the intubation developed fever with mild nasal congestion. Both patients' died and their respiratory samples were positive for MERS-CoV by RT-PCR and the physician was screened and isolated. The result of the nasopharyngeal swab (NPS) was positive for MERS-CoV. His-family remained symptom-free; their screening samples, taken 3 days following contact, were negative. The physician's symptoms subsided after one day and he was able to join work following an isolation period and repeated negative NPS. MERS-CoV was detected using RT-PCR using RealStar<sup>®</sup> MERS-CoV (N-gene) (Altona Diagnostics, Hamburg, Germany) for the detection of N-gene-specific RNA of MERS-CoV and CT values reported (UpE 35.3, ORF 35.7). The positive results were confirmed using the US CDC confirmatory method to detect the UpE, N2, and N3 genes with CT results 38.9, 39.1, and 38.4, respectively.

The same physician was working in the emergency room during the COVID-19 pandemic when he reported headache and body ache for one day and his NPS was positive for SARS-CoV-2 on 14

June 2020. His-symptoms lasted only one day and otherwise he was well till the end of the 2-week isolation period with no symptoms. Detection of SARS-CoV-2 was done by the novel coronavirus (2019-nCoV) multiplex RT-PCR (Sansure Biotech, Changsha, China). The test was positive (CT values N-gene 33.8 and ORF gene 33.7). The repeated PCR at end of isolation was negative.

All his hematology, biochemistry, and chest x-rays were normal in both the MERS-CoV and the SARS-CoV-2 infections and no secondary infections were found in his family. Serology samples for SARS-CoV-2 and MERS-CoV were collected on 14 and 29 September 2020. Both were negative. MERS-CoV serology was done using the protein microarray and PRNT (Reusken C, Mou H, Godeke GJ, van der Hoek L, Meyer B, Muller MA, et al. Specific serology for emerging human coronaviruses by protein microarray. *Euro Surveill* 2013; 18: 20,441). SARS-CoV-2 Serology was done using LIAISON<sup>®</sup> SARS-CoV-2 S1/S2 IgG (DiaSorin, Saluggia, Italy) and Roche Elecsys<sup>®</sup> Anti-SARS-CoV-2 (Roche, Basel, Switzerland) antibody tests.

This case of a mild human disease with the two zoonotic  $\beta$ -coronaviruses in the same host indicates that earlier infection did perhaps provide some but not complete cross-protection against SARS-CoV-2.

SARS-CoV, MERS-CoV, and SARS-CoV-2 share significant sequence homology and potentially share antigenic epitopes capable of inducing an adaptive immune response. Interestingly, it was observed that there is a high degree of cross-reactivity between T- and B- cell epitopes, and antibodies produced against the relevant viral structural proteins of SARS-CoV-2 and other SARS-like viruses.<sup>4,5</sup> It had been hypothesized that the comparative lack of serious COVID-19 cases in locations where SARS-like infections have been prevalent is due to partial immunity conferred from this cross-reactivity.<sup>2</sup>

Barry et al. recently presented clinical characteristics of the first case series of 99 hospitalized COVID-19 patients admitted to one of three MERS-CoV reference centers in the KSA where no co-occurrence of MERS-CoV among SARS-CoV-2-infected persons were found.<sup>6</sup> There is overall paucity of published data during this pandemic of SARS-CoV-2 from MERS-CoV-endemic areas, especially the large-scale immunological studies that may help understand the potential cross-immunity which might explain the sharp reduction in MERS-CoV cases from KSA, for example during the COVID-19 pandemic, and guide future work on producing one vaccine for the two viruses.

Although in our case, the serology for both viruses were negative after 14 weeks from SARS-CoV-2 infection and 22 months post-MERS-CoV, immunity studies with T-cells showed reaction after 17 years against the SARS-CoV virus emerging in 2003.<sup>7</sup> A large-scale follow-up study from Korea also showed optimistic results of persistence of antibody levels against spike antigen in 70 recovered patients from MERS-CoV for up to three years after the

infection but the titers were showing gradual decline by less than two-fold yearly. It also becoming clear that levels of specific antibody responses and opportunity to recover them in testing is significantly dependent on clinical severity and duration of viral persistence.<sup>8</sup> A recent study showed that anti-SARS-CoV-2 antibodies to the spike protein decreased over 60 days in healthcare personnel with 58% of seropositive individuals becoming seronegative.<sup>9</sup>

T-cell studies found reactions to SARS-CoV2 in blood samples from people who had not been exposed to the virus suggesting the possibility of cross-reactivity with other coronaviruses, including common-cold types. This potential lasting cross-immunity has been leading to speculation that it could be responsible for the wide severity spectrum of COVID-19. The implications for individual reinfection risk depends on whether the SARS-CoV-2 antibodies alone or other factors like memory B- and T-cell responses are playing a role in immunity and disease susceptibility.<sup>5,10</sup>

This case report provides a unique situation that may occur only in the Middle East region where the two viruses are circulating, and potential evidence that can support partial immunity from prior exposure resulting in mild disease but may not be completely protective. Also emphasized is the importance of healthcare workers observing infection prevention and control standards and transmission-based precautions in the workplace.

### Declaration of Competing Interest

The authors declare no conflict of interest

### Author contributions

All authors contributed to conception and design of the report and to the interpretation of the results. All authors critically revised the manuscript for intellectual content and approved the final draft for submission.

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