

Infectivity of an Asymptomatic Patient With Middle East Respiratory Syndrome Coronavirus Infection

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During the MERS outbreak in Korea, one case of asymptomatic or mild MERS-CoV infection was noted. Eighty-two persons were exposed to the case without protection. They were isolated and RT-PCR and serology for MERS were performed. There was no transmission through an asymptomatic MERS case in this study.

Keywords. MERS; asymptomatic; infection.

Following the first Middle East respiratory syndrome (MERS)-coronavirus (MERS-CoV) infection in May 2015, there was a large outbreak in Korea with 186 laboratory-confirmed MERS-CoV infections that included 36 fatalities [1]. Asymptomatic or mild cases of MERS-CoV infection have been noted in Saudi Arabia [2, 3], and during the MERS outbreak, 1 case of asymptomatic or mild symptomatic MERS-CoV infection was noted in Korea. There are little data on the infectivity of those asymptomatic or mild MERS-CoV infections, and in this study, we investigated the infectivity of an asymptomatic or mild patient with MERS-CoV infection.

METHODS

On June 2015, MERS-CoV infection was confirmed in a healthcare provider (HCP) without symptoms of MERS at a university hospital, where MERS-CoV infected patients were hospitalized. A nurse was isolated for 2 weeks after contacting the hemodialysis patient with confirmed MERS without proper personal protective equipment (PPE). After the isolation, real-time reverse transcriptase polymerase chain reaction (RT-PCR) for MERS-CoV was done for surveillance prior to returning to work. The result of RT-PCR test reported after 36 hours was positive, but she had no symptoms. During the 36 hours, she continued her

work and might have inadvertently exposed coworkers to MERS-CoV. But until PCR result was available, she did not contact the patients. All the HCPs that had contact with the asymptomatic MERS-CoV positive nurse without proper PPE were isolated at home for 2 weeks, and their contact was graded according to timing and closeness of the contact [4]. A grade 1 contact meant that the person contacted the index patient directly or stayed within 2 meters from the index patient and without having personal protective equipment. A grade 2 contact was for the person staying in the same space of 2 meters or more, separated from index patient, but without personal protective equipment. A grade 3 contact had the person staying in the same space of the index patient at different times without personal protective equipment, and possibly contacting the patient indirectly. The symptoms of these persons were monitored by daily telephone.

When the isolated person reported symptoms possibly related to MERS, RT-PCR was performed. At the end of the isolation period, RT-PCR for MERS-CoV was performed for surveillance for all 82 healthcare worker (HCWs) before returning to work. DiaPlexQ™ MERS Virus Detection Kit II (SolGent, Korea), targeting 3 genes (upE, ORF1a, and ORF1b) was used for RT-PCR.

Blood samples were collected for a serologic test for MERS at 2 and 4 weeks after the exposure and for those who consented to the test. We performed an enzyme-linked immunosorbent assay (ELISA) (Euroimmune, Lübeck, Germany) to screen for the presence of MERS-CoV immunoglobulin G (IgG). When the optical density of ELISA exceeded cut-off value of >50% of the reference, an indirect immunofluorescence test (IIFT) (euroimmun) was performed to confirm MERS-CoV IgG and quantify antibody titers. Serum was diluted 100-fold, according to the protocol suggested by the manufacturer. Antibody titer measurement was conducted by 2-fold dilution from 1:100 to 1:3200.

RESULTS

For 36 hours, 82 HCWs had contact with the asymptomatic or mildly symptomatic but MERS-CoV positive HCW. All 82 HCWs were isolated at home for 2 weeks. The mean age of these workers was 34.5 ± 11.1 years, and 34.1% of them were male. There were 33 HCWs with grade 1 contact (40.2%), 30 HCWs with grade 2 contact (36.6%), and 19 HCWs with grade 3 contact (23.2%) (Table 1).

During the isolation, 4 HCWs had symptoms possibly related to MERS. One person had mild diarrhea, another had diarrhea and rhinorrhea, 1 had some mucus in throat, and 1 had dyspnea and sore throat. Three of them had grade 1 contact with the

Received 9 November 2016; editorial decision 7 February 2017; accepted 7 February 2017.

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Clinical Infectious Diseases® 2017;64(10):1457-8

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Table 1. Characteristics of the HCWs

	No. of patients (10)
Age	34.5 ± 11.1
Male sex	28 (34.1)
Grade of contact	
Grade 1	33 (40.2)
Grade 2	30 (36.6)
Grade 3	19 (23.2)
Symptoms	4 (4.9)
Negative RT-PCR for MERS	82 (100.0)
Negative serology for MERS	45/45 (100.0)

Abbreviations: HCW, healthcare worker; MERS, Middle East respiratory syndrome; RT-PCR, reverse transcriptase polymerase chain reaction.

index person without personal protective equipment. RT-PCR tests during those symptoms were all negative.

The results of surveillance RT-PCR for MERS at the end of isolation were negative for all 82 HCWs. Serology for MERS was done for 45 persons, and the results were all negative.

CONCLUSIONS

MERS is known to be transmitted by droplet, contact, and air-borne spread among humans [5]. Clinical symptoms of MERS range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome, resulting in death [6]. Asymptomatic infections have been detected previously [2, 3, 7].

Although many patients have had severe disease, some reports have described individuals with a mild respiratory illness as not requiring hospitalization [8, 9]. A nationwide serological study in Saudi Arabia showed that anti-MERS-CoV antibodies were confirmed in 0.15% of the general population with seroprevalence of MERS-CoV antibodies being significantly higher in shepherds (2.3%) and slaughterhouse workers (3.6%) [10]. It is possible that there were some asymptomatic or mild cases during the MERS outbreak.

It appears that many individuals who have been reported as being asymptomatic even though they had some signs and symptoms. In a study of the healthcare facility associated with the outbreak in Jeddah, Saudi Arabia, there were 64 cases of 255 laboratory-confirmed cases of MERS initially thought to be asymptomatic [2]. But among the 64 asymptomatic patients, 33 patients were interviewed and 26 patients (79%) reported at least 1 symptom consistent with a viral respiratory illness [2].

It is also not clear whether asymptomatic infection can lead to transmission between humans, although there is 1 study

showing possible nosocomial infection through asymptomatic or mild case in Saudi Arabia [7]. During the MERS outbreak in Korea, there were cases without an obvious origin of infection. It is possible that these cases were linked to asymptomatic or mild cases.

To make effective precautionary measures against transmission, knowing the transmission mode and clinical features of all MERS cases is necessary. In particular, the infectivity of asymptomatic or mild MERS cases is an important factor to consider in quarantine measures. In cases of asymptomatic or mild MERS, it is quite difficult to identify the contact persons and the outcome of the contact. In this case report, we could identify the asymptomatic or mild MERS case by surveillance RT-PCR. We could also identify those who contacted the asymptomatic or mild MERS case and follow them for 2 weeks. In this study, there was no transmission by asymptomatic MERS infection. But more data should be collected to confirm the infectivity of the asymptomatic or mild case of MERS.

Note

Potential conflicts of interest. Authors certify no potential conflicts of interest. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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