Case Report

ISSN: 1735-0344 *Tanaffos 2015; 14(4): 262-267*

TANAFFOS

Health Care Associated Middle East Respiratory Syndrome (MERS): A Case from Iran

Afshin Moniri [1], Majid Marjani [2], Payam Tabarsi [2], Davood Yadegarynia [3], Seyed Alireza Nadji [1]

[1] Virology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2] Clinical Tuberculosis and Epidemiology Research Center, NRITLD, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [3] Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Received: 7 July 2015
Accepted: 16 September 2015

Correspondence to: Nadji SA
Address: Virology Research Center, NRITLD, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Email address: s.a.nadji@sbmu.ac.ir

Middle East respiratory syndrome coronavirus (MERS-CoV) Infection, has caused recurrent outbreaks worldwide. It is associated with severe morbidity and mortality, and is not treatable with the currently available antiviral therapies. We present a case of a 43 year-old male healthcare provider, who admitted with productive cough, dyspnea, myalgia, pleuritic chest pain and fever. Computed tomography (CT) showed bilateral ground glass opacities and consolidation. Sputum polymerase chain reaction (PCR) for MERS-coronavirus was positive.

Key words: MERS-Coronavirus, Infection control, Respiratory

INTRODUCTION

Middle East respiratory syndrome coronavirus (MERS-CoV) Infection, has caused recurrent outbreaks worldwide. It is associated with severe morbidity and mortality, and is not treatable with the currently available antiviral therapies (1). Since its emergence in 2012, about 1595 laboratory-confirmed cases of MERS have been reported with a fatality rate of more than 30% (global deaths 571) (2).

Clinical manifestation of MERS-CoV infection is variable, ranging from asymptomatic to very severe pneumonia with acute respiratory distress syndrome, septic shock and multi-organ failure resulting in death. There is growing evidence that dromedary camel is a reservoir for the virus and a source of human infection (3).

Although it is likely that zoonotic transmission is the starting point of most clusters, person-to-person transmission is the most common form of transmission for MERS-CoV. Nosocomial transmission amplified the spread of MERS, and the majority of cases so far have been reported from hospital outbreaks in Saudi Arabia, the United Arab Emirates and South Korea (4). The MERS situation in the republic of Korea can be highlighted as evidence. To date, a total of 186 MERS-CoV cases, including 36 deaths, have been reported in the Republic of Korea (5). The outbreak in the Republic of Korea has been associated with health care facilities and all cases reported so far include healthcare workers caring for confirmed cases, patients who were being cared for at the same healthcare facilities as confirmed patients, and family

members of confirmed patients (6, 7). Thus, infection prevention and control measures are critical to prevent the possible spread of MERS-CoV in the health care facilities. In this article we describe the first health care–acquired MERS-CoV infection in Iran.

CASE SUMMARY

A 43 year-old male anesthesiologist who was also a cigarette smoker from Kerman province of Iran presented with productive cough, dyspnea, myalgia, pleuritic chest pain and fever since 10 days prior to admission on June 16, 2014.

He was well up until 14 days prior to admission. He gave a history of intubating a patient in an emergency situation without standard protective measures. The intubated patient was later diagnosed with MERS-CoV. Four days later, he developed dyspnea, fever, myalgia, pleuritic chest pain and cough (first dry and then became productive). The patient was referred to Dr. Masih Daneshvari Hospital – NRITLD in Tehran. Upon admission, the patient's body temperature was 38.1°C, blood pressure was 95/50 mmHg, pulse rate was 106 beats/min, respiratory rate was 32/min and percutaneous oxygen saturation was 63% in room air. Pulmonary auscultation revealed fine crackles over the lung bases and wheezing in the middle zone. Physical examination was otherwise normal. The patient's white blood count was 3,600 cells/mm^3 (lymphocytes: 26%, neutrophils: 61%, monocytes: 13%), platelets: 104,000, urea: 20mg/dL, Cr: 0.9 mg/dL and AST: 61 IU/L, ALT: 76 IU/L and alkaline phosphatase: 163 IU/L. Arterial blood gas showed pH: 7.43, PO_2: 53 mmHg, PCO_2: 42 mmHg, bicarbonate: 28.1 mmol/lit.

Computed tomography showed bilateral ground glass opacities and consolidation with air bronchogram (Figure 1). He was admitted to the ICU and diagnostic workups were done. With the impression of severe pneumonia, vancomycin, meropenem, ciprofloxacin (when he developed hyper-sensitivity reaction to ciprofloxacin, it was changed to co-trimoxazole) and oseltamivir were started.

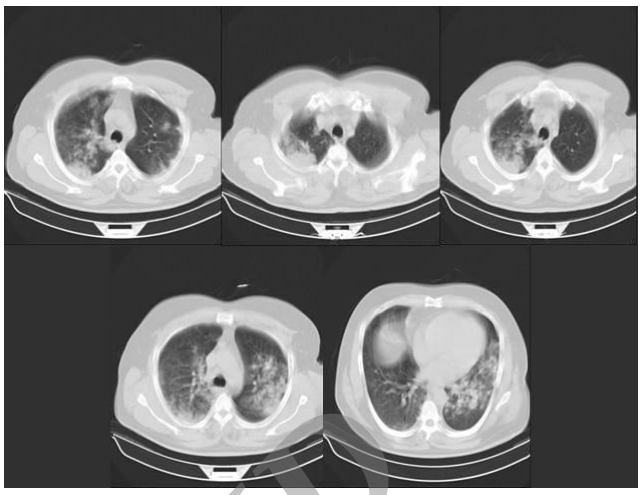

Figure 1. Chest CT scan at the time of admission

During the hospitalization period, liver enzymes raised (two-three folds, AST: 145, ALT: 195) but renal function test was normal. Blood cultures, urine culture and sputum smear and culture were negative for bacterial infections. Viral agent screening results for influenza viruses A and B, parainfluenza viruses 1, 2 and 3, coronavirus OC43, 229E and NL63, RSV, hMPV, CMV and Adenovirus were negative in sputum by real-time RT-PCR/PCR assays. But molecular tests became positive for MERS-CoV using upstream of E gene region real-time RT-PCR assay (upE assay) (8) with a threshold cycle of 31.34. The positive result was confirmed by real-time RT-PCR assay of 1A gene region (9) with a threshold cycle of 32.76. The RdRpSeq and NSeq gene sequences were amplified (9) (Figure 2) and then the sequence of RdRpSeq PCR product was determined with the Big-Dye terminator cycle sequence kit and an ABI 377A sequencer (Applied Biosystems Inc.). Figure 3 shows the phylogenetic tree of the MERS-CoV isolate.

With supportive care and antimicrobial agents he became better and no longer needed oxygen therapy at the third day of admission, and chest X ray revealed significant improvement at the 4th day of admission (Figure 4). Complete blood count changed to normal (WBC 7100 cells/mm^3, lymphocytes: 35%, neutrophils: 60%, monocytes: 5%, and platelets: 297,000 cell/mm^3) and liver enzymes significantly decreased. The patient was discharged without any sequel after four days.

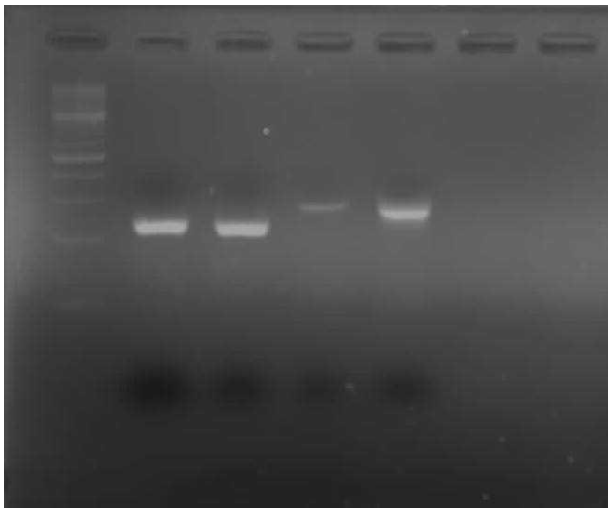

Figure 2. Gel electrophoresis of the resulting products of both RdRpSeq and NSeq assays.

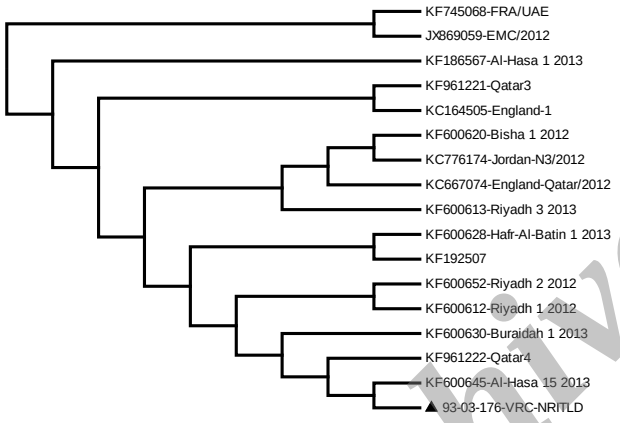

Figure 3. Phylogenetic analysis of RdRpSeq gene sequence in studied MERS-CoV isolate. The tree was constructed by the Maximum Composite Likelihood method using MEGA6

Figure 4. CXR at the 4th day of admission

DISCUSSION

Middle East respiratory syndrome is a viral respiratory illness that was first identified in Saudi Arabia in September 2012. It is caused by a novel coronavirus (called MERS-CoV) (1). Coronaviruses are a large family of viruses that produce a wide spectrum of illnesses in humans, from the common cold to the severe acute respiratory syndrome (SARS). The MERS-CoV genetically and epidemiologically differs from the previously recognized coronaviruses such as the SARS coronavirus (SARS-CoV), which caused the SARS pandemic in south east of Asia in 2003–2004. A number of viruses in this family also cause disease in animals.

The World Health Organization (WHO) was informed of a total of 1595 laboratory-confirmed cases of MERS-CoV infection, including 571 deaths (current outbreak situation in the Republic of Korea and China as of 11 September 2015 with 186 confirmed causes and 36 deaths) (2). The main source of MERS-CoV has not yet been clearly understood. Although not established, the infection could be primarily zoonotic in nature, with limited human-to-human transmission. Molecular investigation indicated that bats in Saudi Arabia might play a role in human infection (10). Previous experience with animal and human coronaviruses and seroepidemiological studies from dromedary camels demonstrated a high prevalence of antibody reactive to MERS-CoV (3). Strains of MERS-CoV that contest human strains have been isolated from camels in Egypt, Qatar, and Saudi Arabia. These investigations supported a scenario of a virus reservoir in bats with a peridomestic animal such as the camel as intermediate host, which may in fact be the immediate source of human infection (11). Genetic sequencing data revealed a close link association between the virus found in camels and that found in human (12). These studies supported the hypothesis that camels or camel related products are the expected source of infection in humans (3).

Most MERS-CoV cases have been reported in adults (median age approximately 50 years, and male

predominance), although children and the elderly have also been infected (range 9 months to 94 years) (13).

Clinical features of MERS-CoV infection are variable, ranging from asymptomatic infection to acute upper respiratory illness, and rapidly progressive pneumonitis, respiratory failure, septic shock and multi-organ failure resulting in death (1,13,14). Most hospitalized MERS-CoV patients have had underlying medical disorders such as diabetes, hypertension, chronic cardiac disease, and chronic renal disease or immunosuppression but MERS-CoV infections were seen in previously healthy cases (14).

Data suggest that MERS-CoV presents primarily with respiratory symptoms (similar to those found in SARS-CoV) as a flu-like illness with signs and symptoms of pneumonia. Common symptoms in patients with MERS-CoV include fever, chills/rigors, headache, non-productive cough, dyspnea, shortness of breath, myalgia and gastrointestinal symptoms. However, SARS infections did not cause renal failure, unlike MERS-CoV (13, 14).

Among confirmed MERS-CoV cases reported to date, the case fatality ratio is approximately 28-30% (2, 13). Although MERS-CoV has low overall person-to-person transmission potential, most MERS-CoV cases are acquired through person-to-person transmission (15), including the most recent South Korean outbreak of MERS in 2015 (4, 5, 6, 7, 16). Human-to-human transmission of MERS-CoV can occur in health care providers and may be associated with substantial morbidity and occasionally mortality (10). A significant fraction of MERS cases were linked to the healthcare setting, ranging from 49% for the nosocomial outbreak in Jeddah and Saudi Arabia in 2014 (17) to 100 % for both the outbreak in Al-Hasa, Saudi Arabia, in 2013 (10) and the recent outbreak in South Korea in 2015 (16).

An analysis showed that 59% of cases were secondary cases with an epidemiologic relation to other confirmed cases and infection in these cases has occurred more frequently in healthcare settings (63.2%) than due to family contacts (13.7%) (18). In a recent update by the WHO, it was noted that the number of laboratory-confirmed MERS-CoV cases increased sharply in relation to the occurrence of health-care-associated outbreaks (6).

One screening of contacts was done in Kingdom of Saudi Arabia and three patterns of transmission were described (sporadic, within families, nosocomial transmission to healthcare workers). The true incidence of the disease in the community is not known. Of the 1,695 healthcare contacts and 462 family contacts of confirmed MERS cases, a positive result was obtained from 19 (1.12%) healthcare workers and 14 (3.6%) cases of family contacts. As a result, the rate of secondary transmission among family contact is higher than other contacts (19). Thus, Infection in the healthcare setting is an important risk factor for human-to-human transmission and close and prolonged contact with the index case seems to be a necessity for the disease transmission (20). Potential routes of transmission included respiratory droplets (was the most likely mode of transmission), with the possibility of direct or indirect contact and airborne transmission during aerosol-generating procedures as other possible routes of transmission (20). One study showed that many healthcare workers were involved in aerosol generating procedures, such as intubation (71.4%), airway suctioning (57%) and sputum induction (28.6%) (21).

Base on the WHO disease outbreak news, 6 cases of MERS-CoV infection have been reported from Iran; 5 cases in Kerman Province during May–July 2014 and 1 case in Kahnooj city in March 2015 (22). Since most cases of disease have been reported in the Middle East especially Saudi Arabia, the risk of returning Hajj pilgrims contracting and spreading MERS-CoV from Saudi Arabia is high (23) and owing to the nosocomial nature of the last outbreak, it is particularly important to identify cases and stop similar preventable tragic outbreaks, with training of the epidemiological determinants, molecular diagnostic tests and management in health care workers and reporting suspected and confirmed cases. The center for disease control recommend that travelers to countries in or

near the Arabian Peninsula protect themselves from respiratory diseases, including MERS, by washing their hands often and avoiding contact with persons who are ill. If travelers to these regions have fever and symptoms of respiratory illness during their trip or within 14 days of their return, they should seek medical care (24).

Prevention and control measures are critical to prevent the possible spread of MERS-CoV Infection in health care services. It is not always possible to detect patients with MERS-CoV early enough because, like other respiratory infections, the early symptoms of MERS-CoV are non-specific. Therefore, health-care workers should always follow standard precautions for all patients, regardless of their diagnosis. Droplet precautions should be added to the standard precautions when providing care to patients with symptoms of acute respiratory infection; contact precautions and eye protection should be added when caring for probable or confirmed cases of MERS-CoV infection; airborne precautions should be applied when performing aerosol generating procedures (25).

At this time there is no definite therapy or effective vaccine for MERS-CoV. The clinical experience from SARS suggests that a number of interventions including ribavirin with and without corticosteroids, interferon alpha with corticosteroids, ribavirin with lopinavir and ritonavir, and convalescent plasma may advance the outcome in patients but the data are not conclusive (26).

CONCLUSION

MERS outbreaks are significantly augmented in the healthcare facilities, and infection in the healthcare setting is an important risk factor for person to-person transmission. It is not easy to recognize patients with MERS-CoV during the early stages of the disease based on clinical presentations alone. Thus, enhanced infection control practices in medical facilities should be attempted to protect those at risk of MERS. Since no specific treatment or effective vaccine is available, development of an effective vaccine is an important public health priority.

REFERENCES

1. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. ***N Engl J Med*** 2012; 367(19): 1814-20.
2. Middle East respiratory syndrome coronavirus (MERS-CoV) – Saudi Arabia, Disease outbreak news 12 October 2015 available at http://www.who.int/csr/don/12-october-2015-mers-saudi-arabia/en/
3. European Centre for Disease Prevention and Control. Factsheet for health professionals, MERS-CoV 2014. Available from: http://www.ecdc.europa.eu/en/healthtopics/coronavirus-infections/mersfactsheet/Pages/default.aspx
4. Müller MA, Meyer B, Corman VM, Al-Masri M, Turkestani A, Ritz D, et al. Presence of Middle East respiratory syndrome coronavirus antibodies in Saudi Arabia: a nationwide, cross-sectional, serological study. ***Lancet Infect Dis*** 2015;15(5):559-64.
5. Middle East respiratory syndrome coronavirus (MERS-CoV) – Republic of Korea, Disease outbreak news 17 July 2015 available at http://www.who.int/csr/don/17-july-2015-mers-korea/en/
6. Middle East respiratory syndrome coronavirus (MERS-CoV): Summary and Risk Assessment of Current Situation in the Republic of Korea and China – as of 19 June 2015 available at http://www.who.int/emergencies/mers-cov/mers-cov-republic-of-korea-and-china-risk-assessment-19-june-2015.pdf
7. Mizumoto K, Endo A, Chowell G, Miyamatsu Y, Saitoh M, Nishiura H. Real-time characterization of risks of death associated with the Middle East respiratory syndrome (MERS) in the Republic of Korea, 2015. ***BMC Med*** 2015;13:228.
8. Corman VM, Eckerle I, Bleicker T, Zaki A, Landt O, Eschbach-Bludau M, et al. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. ***Euro Surveill*** 2012; 17(39). pii: 20285.
9. Corman VM, Müller MA, Costabel U, Timm J, Binger T, Meyer B, et al. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. ***Euro Surveill*** 2012;17(49). pii: 20334.

10. Memish ZA, Mishra N, Olival KJ, Fagbo SF, Kapoor V, Epstein JH, et al. Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. ***Emerg Infect Dis*** 2013; 19(11): 1819-23.
11. Perera RA, Wang P, Gomaa MR, El-Shesheny R, Kandeil A, Bagato O, et al. Seroepidemiology for MERS coronavirus using microneutralisation and pseudoparticle virus neutralisation assays reveal a high prevalence of antibody in dromedary camels in Egypt, June 2013. ***Euro Surveill*** 2013;18(36):pii=20574.
12. Memish ZA, Cotten M, Meyer B, Watson SJ, Alsahafi AJ, Al Rabeeah AA, et al. Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, 2013. ***Emerg Infect Dis*** 2014; 20(6):1012-5.
13. Middle East Respiratory Syndrome (MERS), MERS Clinical Features available at http://www.cdc.gov/coronavirus/mers/clinical-features.html
14. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. ***Lancet Infect Dis*** 2013;13(9):752-61.
15. Chowell G, Abdirizak F, Lee S, Lee J, Jung E, Nishiura H, et al. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. ***BMC Med*** 2015;13:210.
16. Lim PL. Middle East respiratory syndrome (MERS) in Asia: lessons gleaned from the South Korean outbreak. ***Trans R Soc Trop Med Hyg*** 2015;109(9):541-2.
17. Drosten C, Muth D, Corman VM, Hussain R, Al Masri M, HajOmar W, et al. An observational, laboratory-based study of outbreaks of middle East respiratory syndrome coronavirus in Jeddah and Riyadh, kingdom of Saudi Arabia, 2014. ***Clin Infect Dis*** 2015; 60(3): 369- 77.
18. Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, Cummings DA, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. ***N Engl J Med*** 2013; 369 (5): 407- 16.
19. Memish ZA, Al-Tawfiq JA, Makhdoom HQ, Al-Rabeeah AA, Assiri A, Alhakeem RF, et al. Screening for Middle East respiratory syndrome coronavirus infection in hospital patients and their healthcare worker and family contacts: a prospective descriptive study. ***Clin Microbiol Infect*** 2014; 20(5): 469- 74.
20. Al-Tawfiq JA, Memish ZA. Middle East respiratory syndrome coronavirus: transmission and phylogenetic evolution. ***Trends Microbiol*** 2014; 22 (10): 573- 9.
21. Memish ZA, Zumla AI, Assiri A. Middle East respiratory syndrome coronavirus infections in health care workers. ***N Engl J Med*** 2013; 369 (9): 884- 6.
22. Middle East Respiratory Syndrome coronavirus (MERS-CoV) – Iran, Disease outbreak news 8 May 2015 available at http://www.who.int/csr/don/8-may-2015-mers-iran/en/
23. 23.Kumar A, Beckett G, Wiselka M. Middle East respiratory syndrome coronavirus (MERS-CoV) in pilgrims returning from the Hajj. ***BMJ*** 2015; 351: h5185.
24. Rha B, Rudd J, Feikin D, Watson J, Curns AT, Swerdlow DL, et al. Update on the epidemiology of Middle East respiratory syndrome coronavirus (MERS-CoV) infection, and guidance for the public, clinicians, and public health authorities - January 2015. ***MMWR Morb Mortal Wkly Rep*** 2015; 64 (3): 61-2.
25. Middle East respiratory syndrome coronavirus (MERS-CoV) – Republic of Korea, Disease outbreak news 25 October 2015 Available from: http://www.who.int/csr/don/25-october-2015-mers-korea/en/
26. Momattin H, Mohammed K, Zumla A, Memish ZA, Al-Tawfiq JA. Therapeutic options for Middle East respiratory syndrome coronavirus (MERS-CoV)--possible lessons from a systematic review of SARS-CoV therapy. ***Int J Infect Dis*** 2013; 17(10): e792-8.