

Case Report

Atypical presentation of Middle East respiratory syndrome coronavirus in a Lebanese patient returning from Saudi Arabia

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Abstract

Around 2090 confirmed cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) from 27 countries have been reported to the World Health Organization (WHO) between September 2012 and October 2017, the majority of whom occurring in countries in the Arabian Peninsula, mainly in Saudi Arabia. MERS-CoV can have atypical and misleading presentations resulting in delays in diagnosis and is associated with a high mortality rate especially in elderly patients with multiple comorbidities. Herein, we present the first case of confirmed MERS-CoV infection diagnosed at the American University of Beirut Medical Center (AUBMC) - Lebanon in June 2017 presenting without any respiratory symptoms. This is the second confirmed case of MERS-CoV infection in Lebanon since 2014. The first case presented with a febrile respiratory infection with persistent symptoms despite antibiotic treatment.

Key words: Middle East Respiratory Syndrome; MERS-CoV; atypical presentation; Lebanon.

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Introduction

Prior to 2002, four coronaviruses were known to circulate in humans causing only mild disease. Over the past 15 years, two zoonotic introductions of the coronaviruses into the human population occurred, namely the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) first described in 2002 and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) first described in 2012 [1, 2]. MERS-CoV is the first subgroup 2c of the lineage betacoronavirus known to infect humans [3] with a high crude case fatality rate of 34.7% [4]. MERS-CoV clinical presentation can range from asymptomatic carriers to severe respiratory disease, septic shock, multi-organ failure and death [5]. Patients can have atypical presentations such as isolated gastrointestinal symptoms however almost inevitably develop respiratory symptoms [6,7].

We report a case of MERS-CoV infection diagnosed in Lebanon, in a previously healthy patient resident of Riyadh, Kingdom of Saudi Arabia (KSA)

presenting with fever and gastrointestinal symptoms. The patient did not develop respiratory symptoms at any time throughout the course of the disease. To our knowledge, our case is the second documented case of MERS-CoV infection in Lebanon, and one of the few reported cases in the literature with complete absence of respiratory symptoms.

Case Report

The patient is a 40-year-old male, previously healthy gastroenterologist, resident of Riyadh (KSA) for the past 5 years. On June 8, 2017 while still in Riyadh, he developed high grade fever, anorexia and fatigue. At that time, a nasopharyngeal swab for MERS-CoV by Polymerase Chain Reaction (PCR) was negative. The patient had no contact with dromedary camels and did not drink camel milk. He also had no documented contact with any confirmed MERS-CoV patients and is not practicing in a hospital with known MERS-CoV cases. However, he reported that he examined patients returning from Makkah for Umrah

several days prior to his illness. He failed to improve on a 7-day course of oral ciprofloxacin started on June 9. The patient reported taking a 5-day course of metronidazole started on June 11 after developing diarrhea.

He presented to AUBMC on June 15 for severe abdominal pain and a significant 6 Kilograms weight loss since the onset of symptoms. On presentation, he was afebrile (on antipyretics) and hemodynamically stable with pulse oximetric oxygen saturation of 98% on ambient air. Throughout his illness he did not have any respiratory symptoms. Physical exam was significant for right basal crackles and mild tenderness on deep palpation of the epigastric and right upper quadrant areas. His white blood cell count (WBC) was 5,300/mm³, with 69% neutrophils. His platelet counts, aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase, gamma-glutamyl transferase, and direct bilirubin levels were all within normal limits. Chest X-ray was normal. Abdominal CT scan done to investigate his abdominal symptoms failed to reveal any abnormalities, however, cuts through the lower chest revealed bilateral air space opacities. A subsequent CT of the chest confirmed the presence of multi-lobar infiltrates (Figure 1). Based on the patient's CT chest findings, fever, and residence in Saudi Arabia, MERS-CoV was considered. He was placed on contact isolation in an Airborne Infection Isolation Room (AIIR). Bronchoalveolar lavage (BAL) was performed. No organisms were identified on direct microscopy or culture of the BAL samples, and PCR for multiple respiratory viruses including adenovirus, coronavirus 229E, HKU1, NL63, OC4, Influenza A and B among others all returned negative. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) for MERS-CoV (using *PrimerDesign*TM *genesig* Kit for Human Coronavirus 2012 (HCoV_2012) Genomes, detecting open reading frames 1 a/b and 5/E, kit by PrimerDesign, Cambridge, United Kingdom) tested on the BAL samples returned positive. The patient's course in the hospital was uncomplicated, he remained afebrile during his stay and was subsequently discharged from the hospital to be isolated at home under the close supervision of the Ministry of Public Health (MOPH) staff. The case was promptly reported to the WHO, making it the second case of MERS-CoV to be reported from Lebanon since 2014. The MOPH and the Infection Control and Prevention Program (ICPP) at AUBMC investigated all possible hospital contacts. All 51 exposed staff tested negative by nasopharyngeal swab for MERS-CoV PCR and

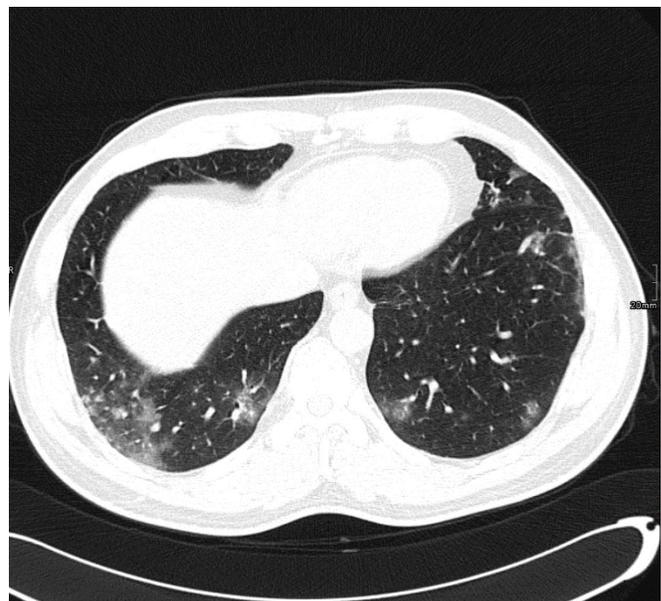
remained asymptomatic throughout the 2 weeks' observational period.

Discussion

Multiple lines of evidence suggest that bats are the primary hosts of MERS-CoV, however, given the limited bat-human contact, dromedary camels are currently thought to be intermediate hosts contributing to spread of the disease in humans [1]

Clusters of nosocomial infection identified in KSA, South Korea, France among others [6, 8-11] present a conclusive evidence that human- to- human transmission, although self-limited, is possible [2,12]. Expression of dipeptidyl peptidase 4 (DPP4), a receptor needed for MERS-CoV entry into host cells, in the upper respiratory tract of camels but in the lower respiratory tract of humans [13] suggests a respiratory route of transmission from camels to humans and might explain the limited human-to-human transmission. There is still debate on the extent of infectivity of asymptomatic carriers of MERS-CoV [14]. Ongoing viral shedding for 6 weeks has been detected by PCR from an asymptomatic healthcare worker [15]. Our patient, similar to many others reported in the literature, had no direct contact with a confirmed infected case suggesting that acquisition from an asymptomatic or mildly symptomatic carrier could be an important contribution to ongoing transmission [15,16]. Interestingly, 60 new cases of MERS-CoV infection were reported to the WHO in KSA between April 21

Figure 1. Non-enhanced CT scan of the chest.



The CT scan shows multiple patches of ground glass opacities within the lower lobes bilaterally in keeping with multilobar pneumonia.

and June 10, 38 of which being from Riyadh [17], coinciding with the period in which our patient is thought to have acquired the infection.

In a descriptive study of 47 patients diagnosed with MERS-CoV in KSA, 96 % had underlying comorbidities such as diabetes, heart disease or chronic kidney disease [7]. Increasing age seems to be an independent risk factor for a poorer outcome and increased mortality [7,18]. Fever, chills, cough, and shortness of breath were among the most common presenting symptoms of MERS-CoV infection while gastrointestinal symptoms were less frequent [7]. MERS-CoV infections can have atypical presentations leading to a delayed or missed diagnoses [6,19], however almost all patients eventually develop respiratory symptoms through the course of their disease. The Ministry of Public Health in KSA published their revised guidelines in January 2017 on the infection prevention and control for MERS-CoV Infection [20]. A visual triage checklist based on clinical symptoms and risks of exposure to MERS was devised, aiming to rapidly identify patients with acute respiratory illness suspected to have a MERS infection and who should be placed in isolation [20]. Retrospectively, our patient did not meet the criteria for isolation at any time throughout his hospital stay despite having a confirmed MERS-CoV infection. This sheds light on the limitations of conventional screening questionnaires and checklists for the detection of MERS-CoV infection especially in patients presenting with no respiratory symptoms.

One patient reported from King Fahd Medical City (KFMC) in 2015 presented with fever, abdominal distention, deteriorating hepatic and renal function and eventually developed pulseless electrical activity and passed away in the Intensive Care Unit (ICU). This patient was diagnosed with MERS-CoV and was not reported to have any respiratory symptoms at any time throughout the course of her disease [21].

Our patient was treated conservatively and improved clinically. He was sent on home isolation and given preventive instructions to follow based on the CDC and WHO recommendations [22,23]. Nasopharyngeal samples were taken for MERS-CoV PCR after hospital discharge and all returned negative. He was released from home isolation on June 23, 2017. His MERS-CoV infection was not transmitted to any of the exposed family contacts nor to the healthcare workers who examined him in the hospital before he was placed on contact and airborne isolation.

Conclusion

MERS-CoV infection has a high fatality rate especially in elderly patients with multiple comorbidities. Human-to-Human transmission is well documented and asymptomatic carriers may play a big role in the transmission cycle. Our case proves that patients with confirmed MERS-CoV infection can have an atypical presentation with no respiratory symptoms making identification and adequate patient isolation a challenging task. It is possible that MERS-CoV is underdiagnosed in patients with the above clinical picture. Therefore, it is very important to keep a high index of suspicion in all patients who present with fever of unclear etiology and have a direct epidemiological link to a MERS-CoV endemic area even with no history of exposure to a confirmed case within the past 14 days prior to presentation. Successful diagnosis will help in early isolation of the patient to prevent potential transmission to household members, travelers and healthcare workers and to avoid unnecessary antibiotics use.

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