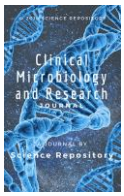

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Case Report

A Febrile Return from Mecca: is it the obvious?

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ABSTRACT

We describe a 53-year-old female patient with diabetes mellitus and mild hypertension who made the ritual Hajj pilgrimage to Mecca. On the return trip to Jerusalem, she developed a respiratory illness, high fever and chills. We describe the initial and subsequent management of this patient, epidemiological aspects and the surprising final diagnosis. The take-home messages are: first, emergency department staff should demonstrate a high index of suspicion and put patients in isolation who meet specific case definition criteria. Second, even if a certain disease, in this instance MERS-CoV is the obvious diagnosis, open-mindedness and a differential diagnosis are always necessary in order to avoid misdiagnosis.

Introduction

Patients with fever and acute respiratory symptoms with a recent travel history to Saudia Arabia should be considered to have Middle East Respiratory Syndrome (MERS) [1]. The causative pathogen MERS-CoV (Coronavirus) was first described in 2012. The disease is endemic in dromedary camels of the Middle East and these are evidently the only animals responsible for transmission to human contacts [2]. Stored dromedary camel sera suggest that the virus was present in these camels several decades ago [3]. At the end of December 2018, there have been a total of 2279 laboratory-confirmed cases of MERS-CoV (Coronovirus) infection, with 806 associated deaths, a case fatality rate of 35.3% [4]. The majority of these patients were reported from Saudi Arabia: 1901 cases, including 732 related deaths 38.5%. Because of the high rate of transmission in medical settings, most hospitals have adopted official case definitions of MERS-CoV and isolate travelers from endemic countries meeting these definitions until laboratory tests have ruled out this infection [5].

Case presentation

A 53-year-old female patient with diabetes mellitus and mild hypertension made the ritual Hajj pilgrimage to Mecca, carefully continuing the medications prescribed for these conditions. On the return trip to Jerusalem, she developed weakness, muscle aches, a runny nose, sore throat, and mild cough. After 2-3 mildly symptomatic days, she developed a 39^0C fever and chills, general weakness, a harsh cough and shortness of breath. The next day, the 13^{th} day after her pilgrimage, she presented at our hospital's emergency department. The physical examination revealed tachycardia and tachypnea, an O2 saturation of 85% at room air, her blood pressure was 100/64, and there were right lower lobe crackles. The peripheral blood count was 19,000/mm^3 with 85% neutrophils; blood chemistry included glucose 268 mg/dl, HgBA1c was not available, sodium 134 meq/L, potassium 4.0 meq/L, and creatinine was 0.55 mg/dl BUN 12 mg/dl. Markers of inflammation included CRP of 3 mg/dl (normal 0-0.5) and lactate was 5.4 mmol/L

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(normal 0.7–2.1). The chest radiogram showed large bilateral opacities, suggestive of pulmonary edema. The electrocardiogram showed ST-T changes in the antero-lateral leads and serum troponin was 0.44 ng/L (normal 0.04-0.3); 3 hours later troponin increased to 0.99. The patient was admitted to the coronary care unit with a diagnosis of non-ST elevation myocardial infarction and secondary pulmonary edema. An infectious disease specialist was consulted, who immediately raised the possibility of MERS-CoV infection. Blood, sputum, and urine cultures were obtained, in addition to viral serology and nasal culture for viruses. The patient was started on ceftriaxone, azithromycin and oseltamivir, and she was transferred to a high-efficiency particulate air (HEPA) filtered isolation room in the medical department. Revision of the admission chest radiogram led to suspicion of adult respiratory distress syndrome (ARDS).

Within 45 minutes after admission to the medical department the patient collapsed. She was successfully resuscitated and intubated and transferred to the intensive care unit; follow-up blood tests showed severe leukocytosis of 34,500 with 85% neutrophils, acute kidney injury with creatinine 1.36 mg/dl, BUN 21 mg/dl, lactate 6.13 mmol/L and her liver enzymes showed signs of liver shock. The patient died 12 hours after her admission to the intensive care unit. Cultures revealed a surprising abundance of clues regarding this unfortunate patient's final illness. First, the nasal culture was positive for Respiratory Syncythial Virus (RSV). Second, the sputum culture was positive for *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*. Third, two blood cultures were positive for *Streptococcus agalactiae* (*Streptococcus* group B, GBS). Finally, serology and PCR were negative for influenza and MERS CoV.

The probable cause of death was post-RSV bacterial pneumonia and sepsis due to *Streptococcus agalactiae*, complicated by ARDS and septic shock.

Discussion

Our patient developed a febrile, respiratory tract illness on the return trip from the Hajj to Mecca. She met case definition criteria of MERS-CoV and should have immediately been placed in isolation; however, only after several hours in hospital was, she transferred to a HEPA-filtered isolation room [5, 6]. If she had been confirmed ill with MERS-CoV quite likely a secondary outbreak with disastrous consequences could have occurred as has been described extensively from Korea and elsewhere [5, 7, 8].

Hajj associated infections include mainly minor viral, respiratory illnesses, including influenza and RSV, but also vaccine-preventable meningitis and MERS-CoV.[1] Our patient most probably had a non-specific viral infection, quite likely RSV, with a secondary bacterial infection due to *Streptococcus agalactiae* (Group B *Streptococcus*, GBS) The latter organism - although often associated with peri-natal infection - due to prophylactic antibiotics given to parturient women previously shown to be GBS carriers, currently is more often encountered in medical departments [9, 10]. Post viral bacterial infection is most commonly due to *Streptococcus pneumoniae* and *Staphylococcus aureus*; a PubMed search did not detect any description of *Streptococcus agalactiae* pneumonia or sepsis in the aftermath of a respiratory tract infection [11]. Diabetes mellitus, malignancy, HIV infection, and advanced hepatic and renal disease have been identified as risk factors for invasive GBS infection [12]. GBS associated pneumonia or sepsis in these patients carry a case fatality rate in excess of 40%.

The presumed initial diagnosis of this patient was non-ST elevation myocardial infarction and secondary pulmonary edema. Only subsequently did the combination of clinical and laboratory factors lead to the consideration of possible pneumonia and sepsis – with initiation of antibiotic treatment and vasopressor support. The international multicenter prevalence study on sepsis (the IMPreSS study) has shown that adherence with all components of the surviving sepsis bundle various between hospitals and countries, with associated varying rates of survival [13, 14]. Accordingly, early diagnosis and institution of appropriate treatment is essential.

In conclusion, emergency department staff should demonstrate a high index of suspicion and put patients in isolation who meet certain case definition criteria. Even if a certain disease, in this instance MERS-CoV is the obvious diagnosis, open-mindedness and a differential diagnosis are always necessary in order to avoid misdiagnosis.

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