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Case report

Successful recovery of MERS CoV pneumonia in a patient with acquired immunodeficiency syndrome: A case report

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Middle East Respiratory Syndrome Coronavirus (MERS CoV) may cause severe pneumonia with significant morbidity and mortality, particularly in patients with multiple comorbid condition. MERS CoV pneumonia has not been previously reported in patients with Human Immunodeficiency Virus (HIV). Herein, we report a case of MERS CoV pneumonia with a successful outcome in a patient recently diagnosed with HIV.

1. Why is this case important

Middle East Respiratory Syndrome Coronavirus (MERS CoV) pneumonia has a reported mortality of 60% in the general population [1]. There are no previous reports of MERS CoV pneumonia in patients who are positive for Human Immunodeficiency Virus (HIV).

The immunosuppressive effect of HIV as well as steroids may lead to disseminated viral infections. However, previous data on MERS CoV pneumonia in patients with a low CD4 count due to HIV and steroids are lacking. Herein, we report MERS CoV pneumonia in a patient recently diagnosed with HIV, who has been on prednisone for *pneumocystis jirovecii* pneumonia (PJP).

2. Case description

In April 2014, a 51 year old gentleman was admitted with shortness of breath, dry cough and diffuse pulmonary infiltrates on radiological imaging. His HIV ELISA test was positive, which was subsequently confirmed with a positive Western blot. Trimethoprim/sulfamethoxazole (TMP/SX) 1920 mg orally every 8 hours in addition to prednisone 40 mg once daily were initiated empirically to treat PJP pneumonia. The patient’s symptoms rapidly improved and he was sent home on the above mentioned treatment. He was not started on antiretroviral treatment, as a CD4 count was not yet available at that point. Moreover, the diagnosis of PJP was a presumptive one, as a spumum sample could not be collected and a bronchoscopy was not done in view of the rapid improvement of the patient’s clinical condition in response to TMP/SX. He was admitted fifteen days later with a two day history of fever, shortness of breath and a productive cough. He had not had recent contact with camels or people with a similar illness. Physical examination revealed a temperature of 38.6 °C, respiratory rate of 22 min⁻¹, and a blood pressure of 106/90. Auscultation revealed bilateral vesicular breathing with no added sounds.

Blood examination revealed a white blood cell count 5.6 x 10⁹/L (absolute neutrophil count 4.3 x 10⁹/L, absolute lymphocyte count 1 x 10⁹/L); hemoglobin 9.9 g/dl, platelet count 335, lactate dehydrogenase 211 U/L, C-reactive protein (CRP) 140.7 mg/L, alanine amino transferase (ALT) 138 U/L. Plasma HIV viral load reverse transcription polymerase chain reaction (RT-PCR) was 30 345 copies/ml (COBAS® amplicor assay). The remainder of the patient’s laboratory testing was essentially normal.

Serologic testing for cytomegalovirus (CMV), Epstein Barr virus (EBV) revealed past infection. Chest X-ray revealed patchy air space opacity in the right lower lobe (Fig. 1).
Diagnosis with MERS CoV pneumonia was confirmed using two real time RT-PCR assays; one targets the upstream of the E protein gene (upE) and the other targets the region within open reading frame (ORF)1b on a sputum sample on April 25th [2]. Both RT-PCR tests were done on the light cycler machine. He was placed in an isolation room and was started on a combination of interferon α2a 180 μg subcutaneously once weekly in combination with ribavirin (a loading dose of 2 gm., followed by 600 mg orally every 12 hours). Upon completion of his PIJP treatment, his TMP/SX dose was reduced to secondary prophylaxis dose of 960 mg orally once daily. Based on recent data regarding superior in vitro efficacy of interferon β [3], and due to lack of improvement in the patient’s clinical condition, interferon α2a was switched to interferon β1a 44 μg subcutaneously three times weekly and ribavirin was continued. T-cell subset testing revealed a CD4 count of 58 cells (L/mm³), and CD8 count 321 cells (L/mm³), CD4/CD8 ratio 0.18.

The patient was promptly started on antiretroviral treatment that consisted of a combination of tenofovir/emtricitabine (TDF/FTC) 300/200 mg orally once daily, in combination with ritonavir boosted atazanavir (atazanvir 300 mg in addition to ritonavir 100 mg) orally once daily. The patient then complained of increased sputum production and his oxygen requirement had increased to a maximum of 12 L/min. Sputum culture revealed E. coli, which was treated with meropenem as per susceptibility studies. The patient’s respiratory symptoms and oxygen requirements subsequently improved.

His hospital admission course was complicated with persistent diarrhea. Bacterial stool culture, Clostridium difficile PCR, and stool microscopy for ova and parasites were negative. Serum cytomegalovirus (CMV) quantitative PCR was 10,000 copies/ml. Computed tomography (CT) of the abdomen revealed circumferential recto sigmoid wall thickening. Ganciclovir 5 mg/kg intravenously every 12 hours was promptly initiated to treat CMV colitis, followed by valganciclovir 900 mg orally twice daily. Diarrhea resolved four days after initiating ganciclovir. Cytomegalovirus treatment was administered for a total of 21 days.

Serial sputum MERS CoV PCR tests were done at 5 day intervals to determine the duration of MERS CoV shedding, and were persistently positive until June 2nd (Fig. 2). Two consecutive sputum samples were negative for MERS CoV PCR 1 day apart. The patient had an oxygen saturation of 96% on room air. The patient became depressed and it was at least partially attributed to interferon treatment, therefore both interferon β1a and ribavirin were discontinued prior to achieving negative respiratory tract RT-PCR samples given the patient’s stable clinical condition. No other side effects were noted.

He received interferon α2a followed by interferon β1a in combination with ribavirin for a total duration of 9 and 17 days, respectively. The patient had clinical as well as radiological improvement, evidenced by resolution of the air space opacity with residual atelectasis, which resolved on a follow up chest X-ray in July.

He went home on the above mentioned antiretroviral treatment in addition to prophylactic trimethoprim/sulfamethoxazole 960 mg daily. The T-cell subsets repeat on June 17th revealed a CD4 count of 237 cells (L/mm³), and a CD8 count of 744 cells (L/mm³), CD4/CD8 ratio 0.32.

3. Other similar and contrasting cases in the literature

There have been no previously reported cases that describe MERS CoV infection in HIV positive patients.

4. Discussion

Pneumonia caused by MERS CoV is associated with significant morbidity and mortality. The effect of HIV with low CD4 count on the course of MERS CoV illness is unknown. Here, we report successful recovery of a patient with HIV/AIDS from MERS CoV pneumonia. The clinical presentation of this patient with MERS CoV pneumonia is similar to previously reported non-HIV infected cohorts in terms of symptoms, laboratory and radiological abnormalities [1]. Given the patient’s lack of contact with similarly ill patients at home and the recent hospital admission during a period where several patients were confirmed to have MERS CoV infection, it is likely that the patient had contracted the virus during his hospital stay. The patient continued to shed MERS CoV, evidenced by the persistently positive MERS CoV RT-PCR sputum samples, for 38 days. CD4 helper cells play an integral role in initiating an effective immune response to clear MERS CoV [4]. Viral shedding (positive MERS CoV RT-PCR sputum samples) was prolonged in immunocompromised patients compared to healthy individuals in cases of seasonal influenza [5,6], as well as H1N1 pandemic virus [7]. In a case series, six of 10 HIV-infected individuals had H1N1 pandemic virus detected by RT-PCR 2–10 days after starting treatment with oseltamivir [8]. However, since no data exist regarding the duration of MERS CoV shedding in immunocompetent population, it is difficult to determine whether the duration of shedding in this patient was prolonged and whether
the patient’s low CD4 count in addition to steroids have slowed the clearance of MERS CoV.

The decision to initially treat with interferon α2a in combination with ribavirin was based on in vitro studies that showed strong inhibitory effects of interferon α2b on MERS CoV replication [9], which was supported by studies on animal models that received early treatment with interferon α2b in combination with ribavirin [10]. Interferon α2a was used instead of interferon α2b due to lack of availability of the latter. This may have played a role in the initial lack of improvement in the patient’s clinical condition. Moreover, recent data by Hart et al. demonstrated superior in vitro activity of interferon β compared to other different interferon products, including interferon α2a and α2b [3]. Therefore, in view of the lack of improvement in the patient’s clinical condition coupled with persistence of sputum samples positivity for MERS CoV PCR. The decision was made to switch interferon α2a to interferon β1a. Given the lack of data regarding the effective doses, we initiated therapy with interferon β1a 44 μg subcutaneously 3 times weekly. While the only human data available on utilizing the combination of interferon α2b and ribavirin was a case series of 5 patients, and a mortality rate of 100% [11], there are no human data regarding the efficacy of interferon β1a in combination with ribavirin to treat MERS CoV pneumonia. Therefore, it is not possible to simply attribute the successful outcome in this patient to this treatment. Nonetheless, interferon α and interferon β are necessary to activate CD8 T-cell response. It maybe possible, that the exogenous administration of interferon α followed by interferon β have led to activation of CD8 cells [12], and hence aided in subsequent clearance of the MERS CoV virus. This however, should be verified in a prospective controlled manner. In summary, we report a successful recovery of a patient with HIV/AIDS from MERS CoV pneumonia. To date, this is the only reported case of MERS CoV pneumonia in a patient with HIV/AIDS. The difference in the viral shedding duration between immunocompetent and immunocompromised patients and the impact of this on treatment decisions deserve evaluation in comparative studies.

Future research should be directed to address the effect of HIV positivity on the clinical course of MERS CoV infections in large cohorts particularly in relation to varied CD4 counts. Additionally, the efficacy of exogenous interferon α and interferon β in combination with ribavirin should be tested prospectively in a randomized controlled manner.

Authors contribution

S.S. has reviewed the literature and written the manuscript. R.S. and A.Z. provided aid in interpreting the molecular virology results and contributed to the manuscript. A.M. contributed to the manuscript. All authors have approved the final manuscript.

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Competing interests

None declared.

Ethical approval

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