CASE REPORT

Adult human metapneumovirus encephalitis: A case report highlighting challenges in clinical management and functional outcome

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SUMMARY

We report a rare case of adult human metapneumovirus (HMPV) in a healthy 32-year-old man. There was dramatic deterioration in his condition developing pneumonia with Type-I respiratory failure and encephalitis. He needed mechanical ventilation in the intensive care setting and was treated with intravenous ribavirin. Post-extubation he remained severely physically and cognitively impaired despite rehabilitation. Treatment of HMPV pneumonia is at present, still without specific antiviral therapy. Managing HMPV-encephalitis remained supportive and challenging. More definite treatment strategies are needed.

INTRODUCTION

Human metapneumovirus (HMPV) is a RNA virus commonly presenting in children as upper (URTI) and lower respiratory tract infections (LRTI). Being a member of the Paramyxoviridae family, HMPV was described as early as 2001. HMPV-encephalitis has been documented in children but scarcely so in adult HMPV-meningoencepahilits survivors with cognitive and physical sequelae.[1] We report a 32-year-old man with HMPV pneumonia and encephalitis. We describe the medical treatment, the severe functional deficits from the infectious insult and highlight the medical and rehabilitation challenges.

CASE REPORT

A 32-year-old Chinese man presented in September 2014 with non-specific low backache and fever of one-day duration. He did not have symptoms of URTI preceding hospital admission. There were no complaints of neck stiffness, photophobia, seizures, vomiting or trauma. His family members were well with no travel history.

On examination, his Glasgow Coma Scale was 15 but febrile (39˚C). Blood pressure was 140/76 mmHg, oxygen saturation was 96% on room air and heart rate was 76/min. Auscultation revealed crepitation heard at right lung base. His abdomen was soft and non-tender. Lower limb strength, sensation and reflexes were intact. Anal tone and deep anal sensation were preserved. Kernig sign was negative. Physical examination of the lumbo-sacral spine was unremarkable.

Full blood count showed a reduced total white cell count of 2.7 $x10^9$/L, normal monocyte (23.6%, absolute monocyte count of 0.64 x109/L), normal lymphocyte counts (48.8%, absolute lymphocyte count of 1.32 $x10^9$/L) and low neutrophil counts (24.9%, absolute neutrophil count of 0.66 $x10^9$/L). Electrolytes, glucose, retroviral serology, urinalysis and blood culture were unremarkable. Chest X-ray revealed right upper and lower zone consolidation. He was treated for pneumonia and started on intravenous piperacillin/tazobactam. The magnetic resonance imaging (MRI) of the lumbar spine was reported to be normal.

Patient de-saturated to Spo2 of 80% on room air after admission. Arterial blood gas revealed Type 1 respiratory failure. He was intubated and transferred to the intensive care unit for mechanical ventilation. Computed tomography (CT) chest revealed interlobar septal thickening and consolidation predominantly in the upper lobes [Figure 1]. Bronchoalveolar lavage (BAL) revealed positive antigen and polymerase chain reaction (PCR) to human metapneumonvirus. Lumbar puncture showed normal glucose and protein levels with no leucocytes. Cerebrospinal fluid (CSF) PCR for HMPV was positive. Electroencephalogram was unremarkable.

A clinical diagnosis of HMPV-encephalitis was made and patient was commenced on one week of intravenous ribavirin. Subsequent CXRs revealed resolution of consolidation. He was successfully weaned off the ventilator but cognitive assessment then revealed reduced cognition and intermittent agitation. MRI brain showed multiple T2w/FLAIR hyper-intense foci scattered in the brain in the right fronto-parietal cortex, bilateral basal ganglia, corpus callosum, pons, cerebellar peduncles and cerebellum [Figure.2]. Blood and urine investigations did not reveal any sepsis or electrolyte disturbances that could explain the agitated behaviour. Patient was started on olanzapine at 15mg daily.

This patient was admitted to rehabilitation. He was totally dependent. The Functional Independence Measure (FIM), an instrument to measure disability, was at the lowest score of 18. Despite rehabilitation, there was no functional improvement. At 6months, his FIM scores remained at 20. Agitation improved at 6th weeks and his olanzapine dose was halved daily.

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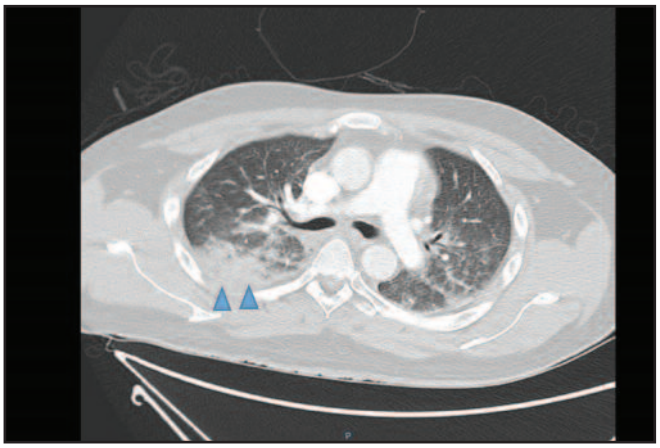

Fig. 1: Computed Tomography of the chest showing increased interlobar septal thickening, air space opacities and consolidation predominantly affecting the upper lobes (see arrowheads).

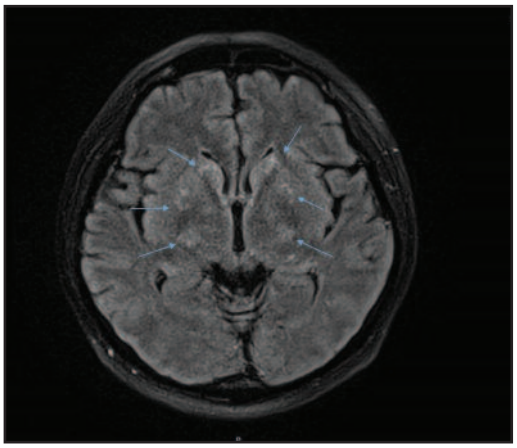

Fig. 2: Magnetic resonance imaging of the brain at 48hrs after withdrawal of sedation demonstrating multiple T2w/FLAIR hyper intense foci scattered in the brain (see arrows).

DISCUSSION

Human metapneumovirus (HMPV) is a single negative-stranded RNA-enveloped virus in the Paramyxoviridae family. HMPV infection can cause URTIs to LRTIs complicated by wheezing, leading to life-threatening bronchiolitis and pneumonia.[1,2] Prevalence of adult HMPV-encephalitis in Malaysia is unknown and previous reports were in pediatric population. There is scarce report regarding the physical and cognitive outcomes of adult HMPV-encephalitis.

Results of the cerebrospinal fluid analysis, bronchoalveolar lavage, endotracheal tube aspirate and MRI imaging in this case supported the diagnosis of HMPV-encephalitis. What was unusual was the lack of symptoms of URTIs other than fever and backache. In previous studies, normal or near-normal CSF leukocyte counts had been reported in HMPV-encephalitis HMPV. Laboratory examination may show lymphopenia and neutropenia. Imaging studies (chest X-ray and CT chest) showed initial signs of acute interstitial pneumonia (ground glass opacity and air-space consolidation) turning into signs of bronchiolitis or bronchitis (bronchial wall thickening or impaction). In this case, the blood counts and CT chest findings resembled previous HMPV cases. The MRI findings were similar to previous studies where cortical and subcortical T2 FLAIR hyper-intensities with evolving DWI hyper-intensities were observed.[3]

Treatment for HMPV remained supportive. No FDA-approved antiviral therapy has been published previously.[4] Ribavirin, known to have activity against respiratory syncytial virus (RSV), is also active in vitro against HMPV and reduces viral replication in experimentally infected mice.[3, 5] The safety and efficacy of ribavirin in humans with HMPV infection are unknown and no vaccine is currently available. Ribavirin has been postulated to augment or terminate T cell immune-mediated damage caused by viral infections. Ribavirin could have accelerated the recovery of this patient.

Encephalitis could cause agitation. We adopted principles of environmental, behavioral management, and pharmacological management. By 6 weeks, the agitation was partially under control but still needing olanzapine. He remained severely disabled at 6 months. Encephalitis is a form of non-traumatic acquired brain injury and more research on the functional outcomes of HMPV-associated encephalitis survivors are needed. It is unclear whether rehabilitation strategies used in acquired brain injury, particularly in the area of pharmacological neuro-modulation can be extrapolated to HMPV-encephalitis.

CONCLUSION

Treatment of adult HMPV-associated pneumonia and impairments related to encephalitis remain supportive and challenging. Principles for the management of the neuropsychiatric sequela of traumatic brain injuries may be considered for the management of similar issues in HMPV-associated encephalitis. This case report can stimulate more discussion on the management of this conundrum.

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