

# Posterior reversible encephalopathy syndrome associated with Hantavirus infection in Sri Lanka: A case report

Adassuriya AANSS<sup>1</sup>, Udurawana AMJB<sup>1</sup>, Pattiyakumbura TT<sup>2</sup>, Muthugala MARV<sup>2</sup>, Herath NB<sup>1</sup>


<sup>1</sup> *Department of Radiology, National Hospital, Kandy 20000, Sri Lanka*

<sup>2</sup> *Department of Virology, National Hospital, Kandy 20000, Sri Lanka*

**Keywords:** Hemorrhagic fever with renal syndrome, Zoonoses, Asia, Atypical presentation, Posterior reversible encephalopathy syndrome

**Correspondence:** Adassuriya AANSS, Department of Radiology, National Hospital, Kandy, 20000, Sri Lanka

E-mail address: nisalsrisanka@gmail.com

 <https://orcid.org/0000-0002-1825-0097>

**Copyright:** Adassuriya AANSS

DOI: <https://doi.org/10.4038/slj.v9i1.120>

## Introduction

Hantavirus infections are emerging zoonoses transmitted by inhalation of aerosolized rodent urine. Hantaviruses cause two main clinical entities; hemorrhagic fever with renal syndrome (HFRS) in Euro-Asia, and hantavirus pulmonary syndrome (HPS) in America.<sup>1</sup> In Sri Lanka, the hantavirus commonly manifests as HFRS.<sup>2</sup> However, mixed clinical syndromes of HFRS and HPS have also been reported. We present a case of a middle-aged paddy farmer from the north-central part of Sri Lanka, who presented with predominant HFRS and subsequently

developed neurological manifestations and was diagnosed with posterior reversible encephalopathy syndrome (PRES).

## Case History

A 32-year-old otherwise healthy paddy farmer presented to a hospital in the north-central part of Sri Lanka with a 5-day history of fever, headache, and myalgia. His symptoms were associated with gradually worsening shortness of breath for a 1-day duration. On admission to the hospital, the patient looked ill, tachypneic, and dyspneic. His peripheral oxygen saturation was 88% without supplementary



This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution and reproduction in any medium provided the original author and source are credited.

oxygen. He was intubated, mechanically ventilated, and transferred to the medical intensive care unit (MICU) at a tertiary care hospital for further investigations and management.

Being a paddy farmer who worked at the paddy field recently with the above-mentioned symptoms, he was suspected of having leptospirosis. The initial blood investigations showed neutrophilic leukocytosis ( $WBC-15 \times 10^3/\mu L$ ) with normal hemoglobin platelet count. The C-reactive protein level was moderately elevated at 82mg/ml. The blood urea level was four times the upper limit of normal (100mg/dL) and the serum creatinine level was 5-6 times the upper limit of normal (677mg/dL). The liver functions test was marginally elevated. Ultrasonography of Kidney-Ureter-Bladder (USS-KUB) revealed signs of acute renal injury. A series of chest X-rays revealed bilateral progressive bronchopneumonia. Electrocardiogram (ECG) showed non-specific T elevations. However, the serum troponin I level was negative.

According to the local epidemiology, seasonal influenza and SARS-CoV-2 were excluded by the rapid antigen detection method as causative agents for his respiratory infection. The bacterial culture of endotracheal secretion was negative.

Even though the patient was suspected of having leptospirosis as per his clinical picture, it was excluded by the leptospira-specific IgM antibodies in the lateral-flow assay which was done on day seven of the illness. Then the other possible diagnosis which can give rise to a similar clinical presentation with his occupational exposure were suspected and serological testing was arranged for the diagnosis of hantavirus infection. Hantavirus-specific IgM antibodies were detected on day nine of the illness by using a locally validated commercial enzyme-linked immunosorbent assay (ELISA) [Anti-Hanta Virus Pool 1" Eurasia" ELISA (IgM), Euroimmune, Germany]. Additionally, the serum sample was tested with the immunoblotting test (Mikrogen diagnostik, Germany). It revealed the patient had been infected with the Hantaan or Seoul type of hantavirus.

The patient received three cycles of therapeutic plasma exchange, whole cell transfusion for transient low haemoglobin, and supportive care with intravenous broad-spectrum antibiotics. After ten days of mechanical ventilation and several cycles of hemodialysis, the patient showed clinical and biochemical improvement and was discharged from the MICU and transferred to the nephrology ward to

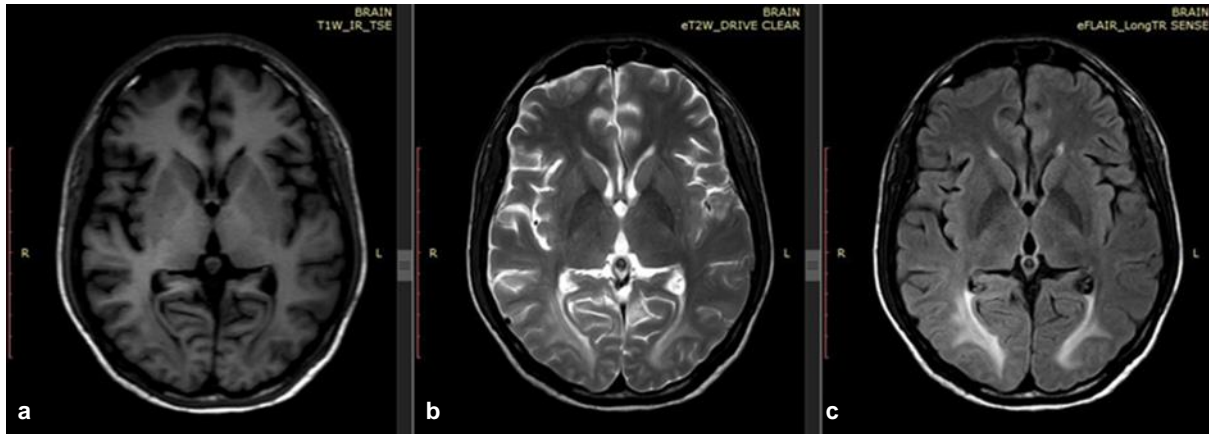
continue management of acute kidney injury.

During the ward stay, the patient developed moderate to severe headache, and right upper limb weakness. The rest of the limbs had normal function and power. He had no other neurological symptoms including seizures and visual symptoms. Initially, a non-contrast-enhanced computerized tomography (NCCT) brain was done due to newly developed neurological symptoms to exclude any cerebral ischemic event. The NCCT of the brain showed ill-defined hypoattenuations in the sub-cortical white matter in bilateral frontal, parietal, and occipital cortices. The changes were prominent in the bilateral parietal and occipital lobes. There was no evidence of ischemic infarctions or haemorrhages owing to the patient's neurological symptoms (Figure 1).

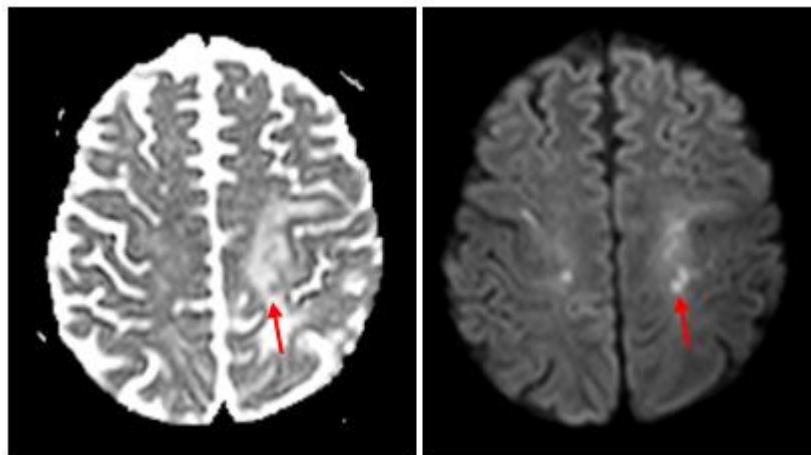
Further imaging proceeded with Magnetic Resonance Imaging (MRI) of the brain. MRI was limited to a non-contrast study due to high serum creatinine level caused by acute renal failure. MRI-Brain revealed symmetrical FLAIR (Fluid attenuated inversion recovery) and T2W signal hyperintensities distributed predominately in the cortical and subcortical white matter of the occipital and parietal lobes bilaterally (Figure 2). Particular hyperintense areas demonstrated T1W hypo intensity. Subtle areas of restricted diffusion seen in bilateral parietal white matter (Figure 3). Other than these MRI findings SWI (Susceptibility-weighted imaging) sequence demonstrated blooming which represents microhemorrhages scattered in both cerebral hemispheres involving all the lobes bilaterally (Figure 4).



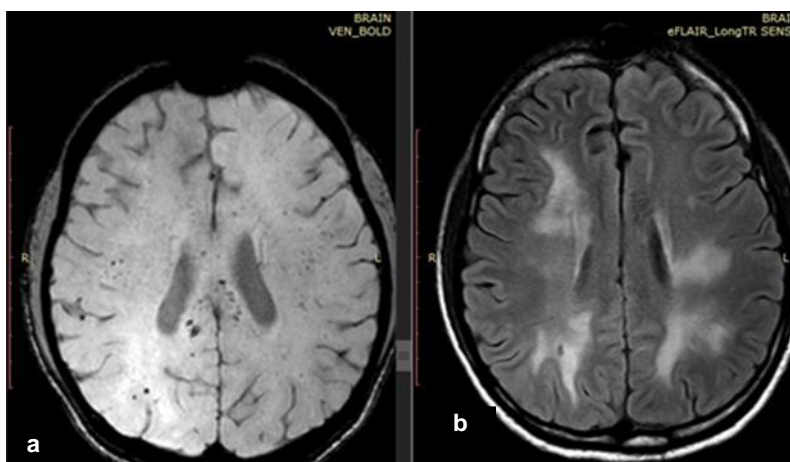
**Figure 1:** Non-enhanced CT brain demonstrating bilateral white matter hypodensities within frontal, parietal, and occipital regions



**Figure 2:** Non-enhanced MRI brain demonstrating a)T1W hypointense, b)T2W and c)FLAIR hyperintense white matter signal changes.



**Figure 3:** ADC map and DWI images showing subtle areas of diffusion restriction (red arrow)



**Figure 4:** a)SWI sequence demonstrating blooming in both hemispheres indicating microhemorrhages. b) FLAIR image showing bilateral hyperintense white matter changes.

When considering the recent hantavirus infection followed by neurological symptoms, MRI signal characteristics of cerebral edema confirmed posterior reversible encephalopathy syndrome (PRES). The patient had a good clinical improvement with supportive care and was discharged after 3 weeks of hospital stay. Follow-up MRI- Brain study was arranged in 3 month time, but the patient did not attend the follow up study.

## Discussion

This patient presented with clinical features suggestive of leptospirosis infection. However, the leptospira-specific antibody was not detected in serological tests, and subsequent investigations were directed to hantavirus serology as both leptospirosis and hantavirus infections have similar occupational exposure and share similar clinical characteristics features. On day nine of the illness, hantavirus infection was confirmed by serological tests. Mechanical ventilation, plasmapheresis, hemodialysis, and supportive care improved the clinical outcome significantly. However, the patient developed sudden onset moderate to severe headache, and right upper limb monoparesis after 2 weeks of his initial

clinical illness. There were no other neurological symptoms. The patient was initially investigated with NCCT-Brain.

Initial NCCT-Brain features were suggestive of subcortical and deep white matter edema with a more or less symmetrical distribution in both cerebral hemispheres. The ischemic event was the clinical diagnosis that warranted a NCCT brain. However, when considering recent Hantavirus infection, NCCT brain findings were suggestive of Posterior reversible encephalopathy syndrome. Imaging was escalated and subsequent MRI-Brain revealed the signal characteristics of the radiological diagnosis of PRES. Considering the patient's clinical characteristics, hantavirus infection was identified as the possible causative agent in our patient.

Posterior reversible encephalopathy syndrome was originally described in 1996 and since then has gained increasing attention.<sup>3</sup> PRES is characterized by a combination of clinical and neuroimaging findings. It has been documented in all age groups, but young or middle-aged adults are the most affected. The pathophysiology of PRES has been linked to immune system activation, endothelium activation, and damage, as well as cytokine release. Multiple etiological agents and risk factors have been identified for PRES such as infections, autoimmune disorders, chemotherapeutic drugs, altered renal functions, high blood pressure, and

transplantation. The clinical symptoms and signs of PRES are extremely non-specific. Encephalopathy and seizures are the most frequent symptoms, followed by headache, visual abnormalities, and focal neurological impairments.<sup>4</sup> Brain imaging is key to establishing a PRES diagnosis because over 90% of individuals exhibit common radiological and clinical characteristics.<sup>5</sup> Although PRES was initially assumed to be a benign condition with a positive outcome, mortality has been reported. The prognosis is highly dependent on the etiological factor.<sup>4</sup> Unfortunately our patient was lost to follow up.

Hantaviruses are zoonotic viruses associated with rodents. The virus is transmitted to humans by contact with aerosols of rodent excreta. In Sri Lanka, the hantavirus commonly manifests as HFRS, fever, thrombocytopenia, and nephritis.<sup>2</sup> Symptoms also include headaches, backaches, abdominal pain, fever, chills, nausea, and impaired vision; subsequent symptoms include low blood pressure, acute shock, vascular leakage, and acute kidney failure.<sup>1</sup> This patient had predominant HFRS clinical manifestations. The pathogenesis of PRES in hantavirus infection has not been widely studied. There was no documented evidence of similar clinical presentations associated with hantavirus infection in Sri Lanka.

Ermira Muco *et al* have described a similar presentation in Albania in a 45-year-old wood cutter with HFRS and subsequently developed PRES.<sup>6</sup> Immune-mediated endothelial cell dysfunction with increased vascular permeability induced by hantavirus infection is proposed as a possible mechanism for hantavirus-associated PRES.<sup>7</sup> Treatment for hantavirus infection is mostly supportive with hemodynamic and pulmonary support. The use of intravenous ribavirin to treat has been studied. However, in limited studies, ribavirin showed no therapeutic effect on the patients.<sup>8</sup>

In Sri Lankan patients with clinical symptoms suggestive of leptospirosis, hantavirus infection should be considered as a differential diagnosis.<sup>2</sup> Although posterior reversible encephalopathy syndrome is a very rare neurological manifestation of hantavirus infection, it should be considered as a differential diagnosis in a patient with hantavirus infection with neurological symptoms.

### Acknowledgments

The authors acknowledge the contribution made by the Medical Intensive Care Unit (MICU), Nephrology unit National Hospital, Kandy, Sri Lanka in providing patient's clinical data.

### Consent statement

Informed consent was obtained from the



patient for the publication of this case report. There are no patient identification details included in the case report.

### Competing interests

The authors declare that they have no competing interests

### Funding

The authors did not receive funding support from any organization for the submitted work.

### References

1. Bennett J. E., Dolin R., and M. J. Blaser. *Mandell, douglas, and bennett's principles and practice of infectious diseases E-book*. Elsevier Health Sciences, 2019.
2. Muthugala R., Dheerasekara K., Manamperi A., et al. Hantavirus Hemorrhagic Fever with Renal Syndrome - Suspected Cases in Sri Lanka: Clinical Picture and Epidemiology from 2013-2021. *Japanese Journal of Infectious Diseases*. 2022 Sep;75(5):533–536. DOI:10.7883/yoken.JJID.2021.837.
3. Hinchey J, Chaves C, Appignani B, et al. Reversible Posterior Leukoencephalopathy Syndrome. *New England Journal of Medicine*. 1996 Feb;334:494-500. DOI:10.1056/NEJM19960223340803.
4. Lee VH, Wijdicks EFM, Manno EM, et al. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. *Archives of neurology*. 2008 Feb;65(2):205–210. DOI:10.1001/archneurol.2007.46 .
5. Legriel S, et al. Determinants of Recovery from Severe Posterior Reversible Encephalopathy Syndrome. *PLOS ONE*. 2012 Sep;7(9):e44534. DOI:10.1371/journal.pone.0044534.
6. Mucó E, Hasa A, Rroji A, et al. Posterior Reversible Encephalopathy Syndrome in a Patient with Hemorrhagic Fever with Renal Syndrome. *Case Reports in Infectious Diseases*. 2020 Feb;2020: 1017689. DOI: 10.1155/2020/1017689.
7. Jonsson CB, Figueiredo LTM, Vapalahti O. A Global Perspective on Hantavirus Ecology, Epidemiology, and Disease. *Clinical Microbiology Reviews*. 2010 Apr;23(2):412–441. DOI: 10.1128/CMR.00062-09.
8. Mertz GJ, et al. Placebo-Controlled, Double-Blind Trial of Intravenous Ribavirin for the Treatment of Hantavirus Cardiopulmonary Syndrome in North America. *Clinical infectious Diseases*. Nov. 2004;39(9):1307–1313. DOI: 10.1086/425007.