

Covid-19 associated Acute Haemorrhagic Leukoencephalomyelitis

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Case Report

Keywords: Acute Haemorrhagic Leukoencephalomyelitis, Covid-19, ADEM

Posted Date: August 18th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-58993/v1>

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Version of Record: A version of this preprint was published at Neurological Sciences on September 2nd, 2020. See the published version at <https://doi.org/10.1007/s10072-020-04703-z>.

Abstract

Since the first appearance of Covid-19 in December 2019 in Wuhan, China, the disease has spread worldwide infecting more than 13 million people and causing approximately five hundred eighty-five thousand deaths. The disease which was initially thought to primarily involve respiratory and cardiovascular system only, over time has been reported to involve central and peripheral nervous system with varying frequency. The importance of identifying neurological symptoms cannot be over emphasised by the fact that loss of sense of smell is now considered as one of the earliest features of Covid-19. Although, impaired consciousness has been reported in approximately 17% patients with Covid-19, acute haemorrhagic leukoencephalomyelitis (AHL) as its cause has been reported in a very few cases. It is imperative for the emergency and respiratory physicians to be aware of this condition as mostly they are the ones who initially come in contact with the Covid-19 patients, as early diagnosis and aggressive treatment would greatly help in improving the prognosis and reducing the morbidity in this otherwise fatal disease. We herein report a case of acute haemorrhagic leukoencephalomyelitis secondary to Covid-19 from a tertiary care centre in India. To the best of our knowledge, this is the first case of Covid-19 associated AHL to be reported from India.

Introduction

Since the first appearance of Covid-19 in December 2019 in Wuhan, China, the disease has spread worldwide infecting more than 13 million people and causing approximately five hundred eighty-five thousand deaths [1]. The disease which was initially thought to primarily involve respiratory and cardiovascular system only, over time has been reported to involve central and peripheral nervous system with varying frequency. The importance of identifying neurological symptoms cannot be over emphasised by the fact that loss of sense of smell is now considered as one of the earliest features of Covid-19 [2]. The incidence of neurological manifestations was seen in up to 36% patients presenting with Covid-19, out of which two third had central nervous system (CNS) involvement and only one third had features suggestive of peripheral nervous system (PNS) impairment [3]. Although, impaired consciousness has been reported in approximately 17% patients with Covid-19, acute haemorrhagic leukoencephalomyelitis (AHL) as its cause has been reported in very few cases [4]. AHL is characterized by rapidly progressive, fulminant inflammatory haemorrhagic demyelination mainly involving the white matter and is almost always monophasic. Aetiology is most likely post infectious and is usually associated with poor prognosis [5]. We herein report a case of acute haemorrhagic leukoencephalomyelitis secondary to Covid-19 from a tertiary care centre in India. To the best of our knowledge, this is the first case of Covid-19 associated AHL to be reported from India.

Case Presentation

A 33-year-old male known case of Chronic Kidney Disease (on Maintenance Haemodialysis: 3/week) and hypertension was admitted to our hospital with chief complaints of fever for 5 days, acute onset rapidly progressive weakness of both upper and lower limbs since 3 days and altered sensorium since 1 day. Patient had an episode of generalised tonic clonic seizures in the emergency and was started on injection lacosamide. On examination, patient was hemodynamically stable, tachypnoeic with respiratory rate as 30/minute with Glasgow Coma Score (GCS) as E2 V1 M4. Brainstem reflexes were well elicitable. Deep tendon reflexes were absent in all four limbs with bilateral extensor plantar response. No neck rigidity was appreciable. He was intubated in view of poor GCS to protect the airway and to provide respiratory support. A clinical diagnosis of encephalitis was kept and patient was started on Acyclovir, ceftriaxone, lacosamide and other supportive treatment. Routine blood investigations showed normocytic normochromic anaemia (Hb:8.8g%) with elevated Urea (84.20 mg/dL) and Creatinine (6.74 mg/dL). Chest X ray findings were consistent with bilateral hilar dominant opacities. Inflammatory markers were elevated i.e. Interleukin (IL-6): 8.30 pg/ml (normal 0-7); D dimer: 0.98 mcg/ml (Normal: 0-0.5) and S. ferritin levels: 2973 ng/ml (Normal: 21.8-274). COVID-19 PCR test from nasopharyngeal swab was positive. USG abdomen showed changes consistent with medical renal disease with no other noteworthy finding. Patient's electroencephalogram (EEG) was suggestive of diffuse background slowing with no epileptiform discharges.

In view of altered sensorium, a brain Magnetic Resonance Imaging (MRI) was advised which revealed symmetrical FLAIR hyperintensities involving bilateral subcortical fronto-parietal lobes, splenium of corpus callosum, medulla and visualised cervical cord with petechial haemorrhages and evidence of diffusion restriction involving splenium of corpus callosum (Figure 1-4). Following the MRI, a lumbar puncture was done to rule out any infective cause explaining the above MRI changes. Cerebrospinal (CSF) fluid examination revealed normal protein: 35 mg%, sugar: 75 mg% and cell count: 5 cells (all lymphocytes). Viral RT-PCR panel (including Herpes simplex 1 and 2), Gene X-pert for Tuberculosis and cryptococcal antigen were negative. Thus, a final diagnosis of Acute Haemorrhagic Leukoencephalomyelitis secondary to Covid-19 was made and patient was started on Methyl Prednisolone 1gm IV per day for 5 days. This resulted in good neurological improvement of the patient as he became conscious and responsive to verbal commands. He started showing improvement in motor deficits too with power in upper and lower limbs improving to grade 3/5 as per Medical Research Council (MRC) grading by 5th day of IV steroid therapy. But his respiratory features and X-ray findings continued to deteriorate and his ventilatory requirement progressively increased. At day 10 of hospitalisation he was not able to maintain adequate oxygen saturation in spite of full ventilatory support and subsequently went into shock and cardiac arrest.

Discussion

Although, Covid-19 has been reported to be associated with central as well as peripheral nervous system impairment, deficits involving CNS fairly outnumber PNS with impaired consciousness seen in approximately 17% of admitted Covid-19 patients [3]. Possible mechanism by which Covid-19 affects

nervous system is still under study, but few hypotheses include direct damage to receptors, cytokine related injury, retrograde travel along the nerve fibres and immune mediated. Mechanism of encephalitis in patients with Covid-19 is not totally clear, but likely possibilities include inflammatory injury and direct viral infection [6]. A number of case series have shown association of CNS manifestations with severe Covid-19 infection and elevated inflammatory markers like D-Dimer and interleukin-6 (IL-6) [3,7]. Our case report supports the hypotheses of association between CNS manifestation and severe form of Covid-19 infection and raised inflammatory markers.

AHL is one of the aggressive variants of acute disseminated encephalomyelitis (ADEM), which is found in less than 2% of patients with ADEM and is most often triggered by an upper respiratory tract infection [5]. A few clinical and radiological clues help in differentiating ADEM from its rare and more aggressive variant. Although, AHL and ADEM share a common aetiology i.e. autoimmune process directed against CNS myelin, clinically, hyperacute onset, rapid progression and high mortality seen in AHL helps in differentiating it from ADEM [8]. Similarly, both ADEM and AHL on imaging are characterised by perivenular demyelination and inflammation predominantly involving white matter, but asymmetric or symmetric subcortical white matter involvement of posterior fronto-parietal lobes with relative sparing of the cortex is characteristic of AHL. Involvement of Basal ganglia which is quite common in ADEM is relatively rare in AHL and thus, helps in differentiating the two [9]. Our patient had an almost sudden onset and a very rapidly progressive downhill course associated with MRI showing bilateral asymmetric confluent FLAIR hyperintensities in subcortical white matter involving the posterior fronto-parietal lobes and splenium of corpus callosum suggestive of demyelination and inflammation, with sparing of basal ganglia and cortex with punctate haemorrhages noted in the splenium. FLAIR hyperintensity in cervical cord was suggestive of myelitis. Thus, clinico-radiological manifestation of our patient was suggestive of AHL and although, it has a poor prognosis, our patient had a good neurological response to steroids but unfortunately, severe respiratory dysfunction due to Covid-19 led to his mortality. Other conditions which share the common imaging findings are: progressive multifocal leukoencephalopathy (PML), vasculitis and lymphoma. Hyperacute onset and rapidly progressive course help in differentiating the above conditions from AHL, as all of these have a subacute to indolent course [9]. Various treatments which have been described to be effective in AHL include high dose steroids, IV Immunoglobulins, plasmapheresis and cyclophosphamide [4].

Conclusion

As there is huge amount of research going on in recognising new clinical presentations of Covid-19, evidence favouring neurological manifestations in Covid-19 is increasing with each passing day. It is quite clear that CNS is quite often involved in Covid-19 and sometimes quite early during the course of illness, like in our patient. AHL is a fulminant disease characterised by hyperacute onset and rapidly deteriorating course with almost certain mortality if not treated early and aggressively. Thus, it is imperative for the emergency and respiratory physicians to be aware of this condition as mostly they are the ones who initially come in contact with the Covid-19 patients, as early diagnosis and aggressive

treatment would greatly help in improving the prognosis and reducing the morbidity in this otherwise fatal disease.

Declarations

The Ethics committee of our hospital was informed about the case report. As it didn't involve any trial or any new treatment to be tried and neither was it a study its approval was not required. It only involves reporting of a case. Consent was taken for sharing of clinical details and images for case report to be published in medical literature or journal. As it would be published in medical literature or journal and will be available online, it would be available to general public It was made clear that name of the patient will not be published and every effort will be made to conceal the identity. Consent was taken in local language from the father, as the patient didn't survive the illness.

Acknowledgements:

We received no grant for this case.

There is no financial and intellectual conflict of interest.

References

1. World Health Organization. Coronavirus disease (COVID-19): situation report, 179.
2. Özdağ Acarli AN, Samanci B, Ekizoğlu E, et al. Coronavirus Disease 2019 (COVID-19) From the Point of View of Neurologists: Observation of Neurological Findings and Symptoms During the Combat Against a Pandemic. *Noro Psikiyatrs Ars.* 2020;57(2):154-159.
3. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China [published online ahead of print, 2020 Apr 10]. *JAMA Neurol.* 2020;77(6):1-9.
4. Markus R, Brew BJ, Turner J, Pell M. Successful outcome with aggressive treatment of acute haemorrhagic leukoencephalitis. *J Neurol Neurosurg Psychiatry.* 1997;63(4):551.
5. Marin SE, Callen DJ. The magnetic resonance imaging appearance of monophasic acute disseminated encephalomyelitis: an update post application of the 2007 consensus criteria. *Neuroimaging Clin N Am.* 2013;23(2):245-266.
6. Bridwell R, Long B, Gottlieb M. Neurologic complications of COVID-19. *Am J Emerg Med.* 2020;38(7):1549.e3-1549.e7.
7. Li Z, Liu T, Yang N, et al. Neurological manifestations of patients with COVID-19: potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain [published online ahead of print, 2020 May 4]. *Front Med.* 2020;1-9.
8. Vartanian TK, Monte S. Weekly clinicopathological exercises. Case1–1999. *N Engl J Med* 1999;340:127–135.

9. Kuperan S, Ostrow P, Landi MK, Bakshi R. Acute hemorrhagic leukoencephalitis vs ADEM: FLAIR MRI and neuropathology findings. *Neurology*. 2003;60(4):721-722.

Figures

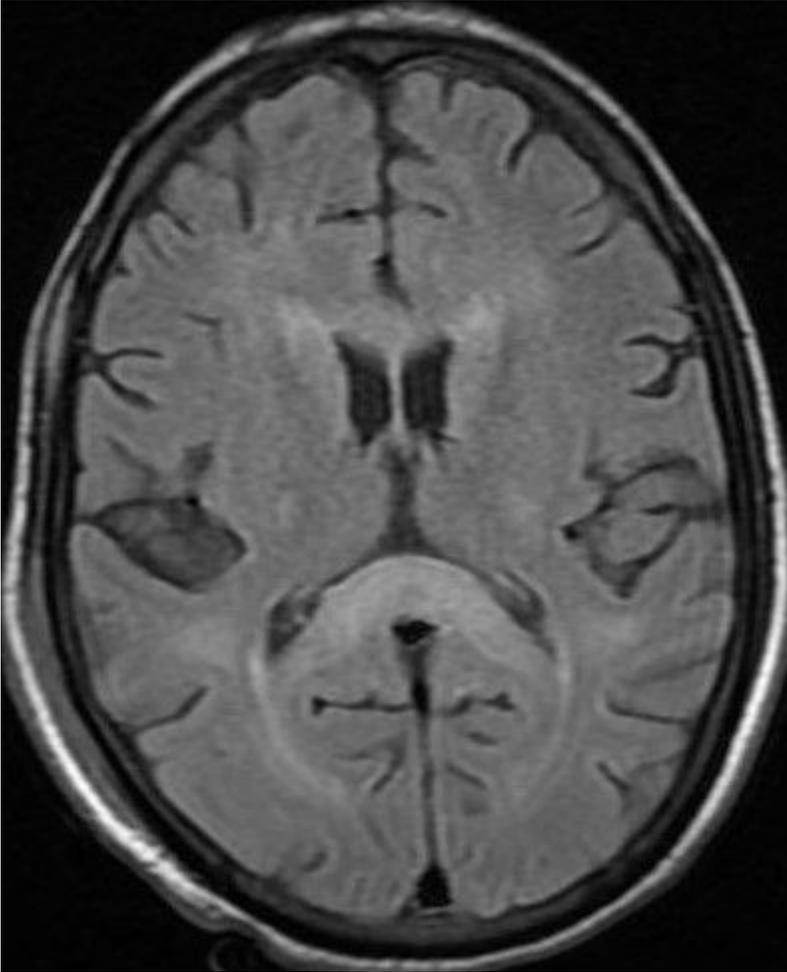


Figure 1

MRI FLAIR image showing hyperintensity in splenium of corpus callosum

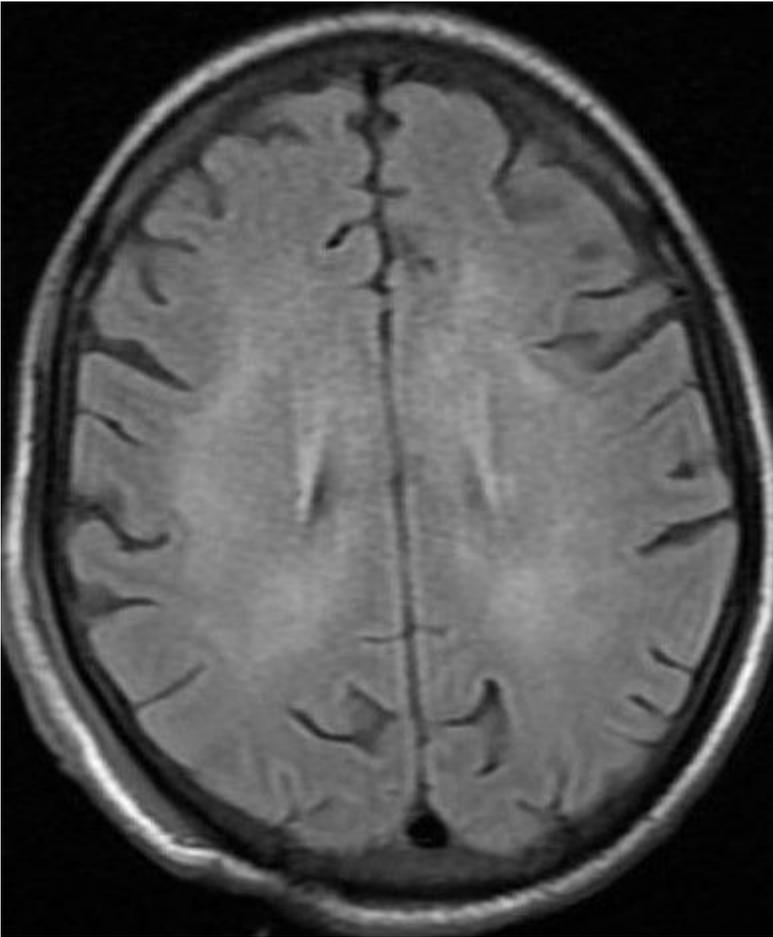


Figure 2

MRI FLAIR image showing confluent hyperintensities involving bilateral subcortical posterior fronto-parietal lobes

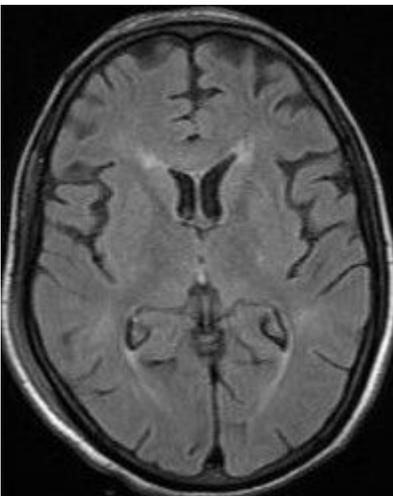


Figure 3

MRI FLAIR image showing sparing of Basal Ganglia



Figure 4

MRI T2W image showing hyperintensity involving medulla and cervical cord