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Case Report

A case of acute necrotising encephalitis in an adult with H1N1 pneumonia

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ABSTRACT

Acute necrotising encephalitis is a severe and rapidly progressive neurological disorder seen after Respiratory or Gastrointestinal tract viral infections mostly affecting children and very rarely affecting adults with only few case reports published worldwide. Common organisms implicated in the etiology are influenza, Enteroviruses, COVID-19, It was reported in adult patients after influenza and COVID-19 pneumonia. Diagnosis requires a high index of suspicion with clinical and radiological evidence precisely MRI findings with characteric features. Treatment has to be initiated early with high dose steroids and IVIG where indicated because this condition is associated with a very high mortality. ANEC can mimic sepsis with a cytokine storm and hence awareness of this entity is very crucial for early diagnosis and treatment initiation. We report the case of a middle aged man presenting with altered mental status after H1N1 influenza and diagnosed with ANEC based on the characteristic MRI and CSF findings after excluding other causes with biochemical and imaging workup.

Keywords: Acute necrotising encephalitis, Adult, Claustral sign, H1N1, MRI

INTRODUCTION

Influenza viruses are highly contagious and pose a significant economic burden worldwide due to their complications mostly affecting the respiratory and occasionally neurological system. Common neurological manifestations are seizures and encephalopathy Acute necrotising encephalitis is a rare complication triggered by an immune response to the virus.

It was first described in Japanese children by Mizuguchi et al in 1995 and later reports came from many parts of Asia.[1,2] It is associated with multiple viruses like influenza, A and B, enteroviruses, dengue, SARS COV2, HHV 6 and atypical bacteria like mycoplasma pneumonia. A genetic predisposition has also been proposed in some cases where the disease has occurred spontaneously had recurred or has a familial association. A mutation in RANBP2 is linked to ANE 1 a specific subtype of ANE.[3] ANEC is mostly described in the pediatric population and very few cases have been reported in adults.[4,5]

CASE REPORT

A 55 years old male presented with altered sensorium since one day, generalised weakness and decreased urine output with facial puffiness and cough with expectoration since 4 days. He gave a h/o fever with chills 6 days ago which subsided with antipyretics. On examination he was anxious, irritable and disoriented with involuntary movements. He had mild tachycardia, was afebrile and had basal crept. His spo2 was 98% on RA.

On evaluation CBP showed leukocytosis with thrombocytopenia, patient had borderline raised creatinine 1.29 with moderate hyponatremia. Flu panel was positive for influenza A with H1N1. Tropical fever panel was negative. ABG showed non anion gap metabolic acidosis,

LFT showed transaminitis, PCTQ was raised 1.22. Patient developed hypotension and required vasopressor support.

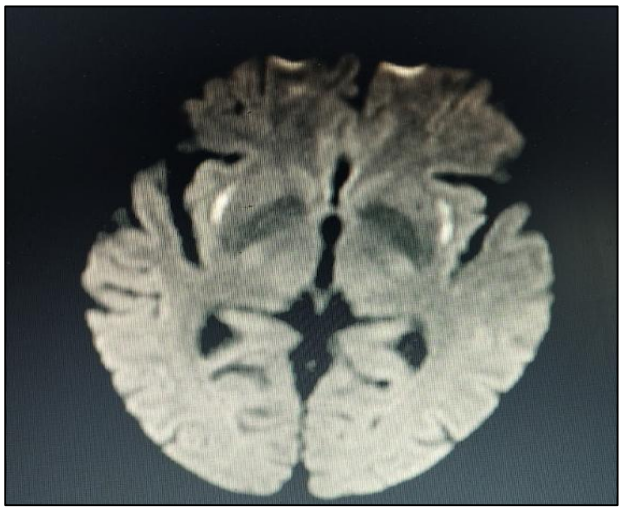

Figure 1: Dwi hyperintensity.

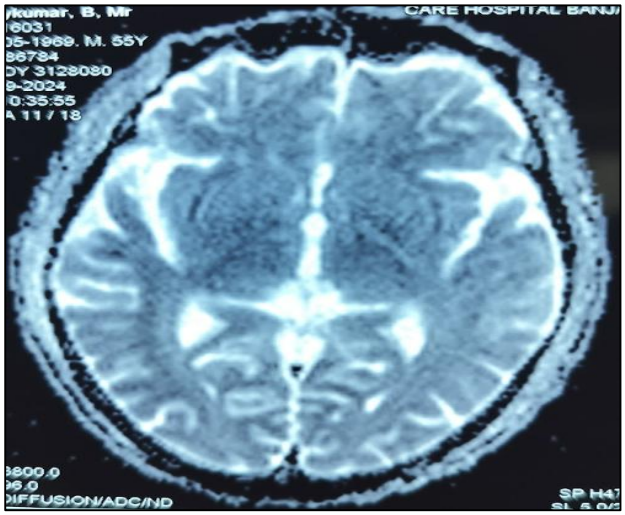

Figure 2: ADC reduction.

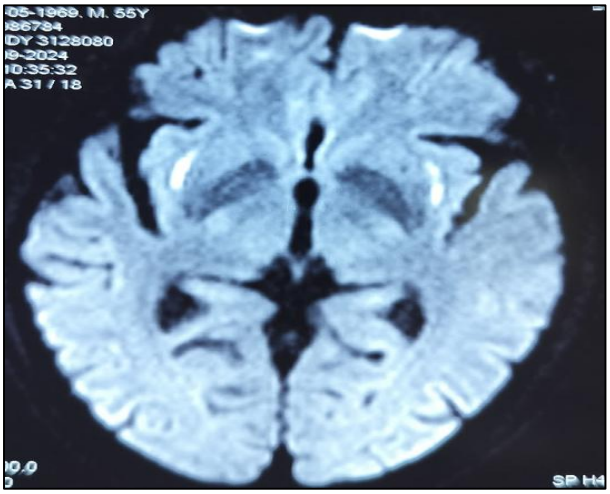

Figure 3: FLAIR hyperintensity.

Patient was electively intubated in view of increasing irritability not controlled with sedatives and anxiolytics. HRCT chest showed features suggestive of aspiration pneumonia with infection, cardiomegaly, pulmonary arterial hypertension and bilateral trace pleural effusion. USG abdomen show edematous gall bladder wall, urine and blood cultures were sterile. EEG was normal. CSF analysis showed high protein with no pleocytosis. Meningo encephalitis panel and AIE panel was negative, while CSF for cultures were sterile. MRI brain showed linear areas of diffusion and flair hyperintensities with corresponding ADC reduction in bilateral claustral regions which was suggestive of acute necrotizing encephalitis.

Treatment was initiated with IVIG for 5 days. BAL for pneumonia plus panel showed presence of influenza A corona virus, *Staphylococcus aureus* and pseudomonas, while culture sensitivity showed presence of *Pseudomonas aeruginosa* which was pan drug resistant. Antibiotics were escalated accordingly.

Patient had worsening AKI, thrombocytopenia and hypotension. CRRT was initiated in view of refractory shock. Patient had worsening thrombocytopenia and coagulopathy with hemorrhagic shock over next 3 days and he succumbed due to refractory shock.

DISCUSSION

Altered mental status is a common clinical presentation in patients with acute febrile illness. Most common causes are viral meningo-encephalitis, febrile encephalopathy, septic encephalopathy and dyselectrolytemias due to inadequate intake in the febrile phase. This patient had hyponatremia with S. Na 125 meq/l, other electrolytes were normal. We initially suspected hyponatremia to be the cause of altered mental status, but next day he became very irritable warranting intubation.

Authors suspected post viral gram-negative sepsis with encephalopathy in view of hypotension, AKI and thrombocytopenia. But persistent irritability prompted us to do CSF analysis and MRI on day 3 of admission which showed the characteristic claustral sign on MRI T2 and flair hyperintensity T1 hypointensity) characteristic of cytokine mediated Encephalitis. Differential diagnosis of claustral sign on MRI include FIRES (febrile infection related epilepsy syndrome), COVID-19 encephalopathy, Autoimmune encephalitis and Immune effector cell-associated neurotoxicity syndrome (ICANS). MRI findings of ANEC are bilaterally symmetric lesions involving thalamus, internal and external capsule, putamen and brainstem.[6]

Differential diagnosis for ANEC include all etiologies for encephalitis i.e., infective, autoimmune and paraneoplastic. ADEM, REYE syndrome, Leigh syndrome, Wernicke encephalopathy, reversible posterior leukoencephalopathy syndrome. Our patient did not have

the hypoglycemia, hyperammonaemia and characteristic features of REYE or leigh's. MRI findings were not supportive of ADEM and wernickie encephalopathy and other conditions. Autoimmune and paraneoplastic panels were negative. Authors treated him with IVIG for 5 days. Steroids were not chosen in view of bacterial sepsis. The inflammatory response could not be curtailed and the patient succumbed due to coagulopathy and subsequent hemorrhagic and septic shock. The clear pathogenesis of ANEC hasn't been defined but evidence suggests that the encephalitis is due to an exaggerated systemic immune response mediated by cytokines, interleukins and natural killer cells which cause extensive inflammation leading to disruption of blood brain barrier causing cerebral edema, hemorrhage and necrosis.

Systemic inflammation also leads to hypotension, AKI and DIC mimicking gram negative sepsis with septic shock. Patients present with altered mental status, vomiting, focal seizures progressing to GTCS, refractory seizures with some cases progressing to brain death. This condition carries high morbidity and mortality and early diagnosis and treatment plays a significant role in improving the outcomes. Mizuguchi proposed diagnostic criteria for ANEC encephalopathy preceded by febrile viral illness with rapid deterioration in level of consciousness and convulsions.

Absent CSF pleocytosis, symmetric multifocal brain lesions, elevation of AST, exclusion of similar diseases. Multiple treatment strategies have been advocated for this condition which has high mortality and neurological morbidity Early institution of pulse steroids within 24 hours has been shown to improve outcomes.[7] Though IVIG is also advocated clear evidence of benefit is not available.[8]

Tocilizumab an IL-6 inhibitor used during SARS COV2 epidemic, also found to be beneficial in reducing the inflammation.[9-11] PLEX is another modality used in treatment of ANEC shown to reduce the levels of CRP and procalcitonin and improvement in liver function but efficiency with neurological outcome isn't proved.[12]

CONCLUSION

Acute necrotising encephalitis is very rare in adults and has a high mortality. With this case we would like to increase the awareness of this rare complication of H1N1 pneumonia which presents with altered mental status.

Early diagnosis with the help of radiological and laboratory findings notably MRI and CSF along with prompt initiation of steroids within 24 hours of presentation and early IVIG therapy and use of PLEX when disease in severe may improve the outcome in these patients. Currently available treatments are those extrapolated from their use in pediatric patients and their benefit in adults has to be demonstrated with their use in this population.

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