Acute Influenza A Virus-Associated Encephalitis with Bilateral Lateral Geniculate Body Hemorrhagic Infarction-Complicating Pregnancy

Sir.

Involvement of the central nervous system (CNS) in influenza virus infection is very rare. India witnessed a surge in influenza cases in the year 2017, with 37,463 people testing positive. [1] What is alarming though was, 1 in every 20 affected succumbed to their illness.

A 22-year-old female at 36 weeks of gestation presented wisth 1-day history of fever, running nose, cough, and expectoration. In view of fetal distress and maternal pyrexia, she underwent an emergency lower segment cesarean section. On postoperative day 1, throat swab for H1N1 viral polymerase chain reaction (PCR) was sent. On postoperative day 5, she developed sudden-onset blurring of vision with swaying to both the sides on walking and slurring of speech. Examination showed normal vitals, normal higher mental functions, normal cranial nerves, and a scanning speech. Unaided visual acuity was found to be 6/9 in both the eyes, with normal color vision, extraocular movements, and fundus examination. Cerebellar examination revealed to have an impaired finger nose and heel-knee-shin test and impaired gait on tandem walking. Blood investigations were within normal limits. Fever workup, including test for malaria, typhoid, and blood and urine cultures, was negative. Chest X-ray showed haziness in the lower zone of the left lung. Throat swab for influenza H1N1 pdm09 RNA was positive. Cerebrospinal fluid (CSF) analysis showed normal opening pressure with normal protein and sugar and no pleocytosis. CSF viral PCR panel for herpes simplex, Japanese encephalitis, and varicella zoster was negative. Visual-field testing was done after 10 days of onset of symptoms, showed right inferior quadrantanopia and left centrocecal scotoma.

Magnetic resonance imaging (MRI) of the brain showed multiple T2 and fluid-attenuated inversion recovery hyperintensities in the bilateral lateral geniculate body (LGB), pons, external capsule, and middle cerebellar peduncles [Figures 1 and 2] with gradient echo images suggestive of microhemorrhages in LGB [Figure 3]. Diffusion-weighted sequences showed

evidence of bilateral symmetrical diffusion restriction in lateral geniculate bodies, pons, and external capsule. There was no contrast enhancement in the above-mentioned areas. In view of clinical picture and throat swab proven to be due to H1N1 illness and the CNS manifestations immediately following it, a diagnosis of H1N1 viral encephalitis was made.

Acute bilateral blurring of vision is usually caused by postgeniculate optic pathway lesions. Another rare and unusual anatomical localization is bilateral-isolated lesions of the LGBs. Since the 1930s, there are only nine case reports in the literature of lesions in LGBs, resulting in bilateral acute painless vision loss.^[2,3] The different etiologies for bilateral lesions described include the following: pancreatitis, cirrhosis with hyponatremia, febrile gastroenteritis, preeclampsia, anaphylactic shock, and stroke. The mechanisms causing damage to LGBs are as follows: infarction, myelinolysis, or hypoperfusion with predilection to young females.^[2,3] None of these were associated with pregnancy and influenza infection as in our case.

Influenza A virus-associated encephalitis always presents a diagnostic dilemma for neurologists and is difficult to distinguish it from other infective and metabolic causes. During the pandemic influenza (H1N1) infection, various neurological complications were described such as seizure, aseptic meningitis, encephalitis, acute disseminated encephalomyelitis, and acute necrotizing encephalopathy.^[4]

CSF findings in previously reported cases of influenza-associated encephalitis are unremarkable or with little inflammation; hence, diagnosis is based on the detection of viral RNA by real-time PCR or demonstration of virus by immunofluorescence or virus culture from the throat or nasopharyngeal swab. As the influenza virus is not demonstrated in the CSF, in suspected cases and appropriate clinical setting, nasopharyngeal swab should be collected at the earliest. [4]

In most of the reported cases, influenza virus was not isolated from CSF or brain tissue.^[5] In the only case report described

in a pregnant woman, CSF study was normal, but influenza A/Hong Kong virus (H3) was isolated from the CSF. The imaging was normal in that patient.^[6]

Brain imaging in influenza encephalopathy may range from normal MRI to single or multifocal T2 hyperintensities, bilateral necrotizing thalamic lesions, splenium hyperintensities, diffuse brain edema, and T2 hyperintensity with restricted diffusion in the thalami, cerebellar hemispheres, brain stem, and centrum semiovale bilaterally.^[7] In a largest case review published, of the 33 patients with influenza encephalitis, only one patient was pregnant. In addition, influenza virus RNA in CSF was detected in 5/32 cases (16%). MRI data were available in 21 cases, of which 13 were abnormal and only 10 of these cases showed multiple lesions in CNS.^[8]

Imaging in our patient was unique in two ways. First, there were demyelinating lesions involving external capsule, adjacent putamen, middle cerebellar peduncle, and pons [Figures 1 and 2]. This pattern has not been reported in acute setting of influenza encephalopathy, where necrotizing lesions are more common. Second, there was clear imaging evidence to suggest hemorrhagic infarction of bilateral LGB, which produced blurring of vision [Figure 3]. This has not been reported yet as a manifestation of CNS involvement in influenza.

The pathogenesis of influenza A virus-associated encephalitis is poorly understood. It can be either due to direct invasion of the virus that causes acute illness or more typically an autoimmune/vasculitic/demyelinating encephalopathy triggered by significant inflammation elsewhere. Literature search showed that evidence of direct CNS invasion was found to occur through the olfactory nerve in only one study. [9]

The evidence for influenza virus not directly invading the CNS is more robust. A significant inflammation elsewhere sets off an abundant immune response resulting in the disruption of the blood–brain barrier at the localized areas, which eventually leads to the brain lesions seen in acute influenza encephalitis. [10] The second mechanism is more likely in our patient. In addition, pregnancy being an immune-dysregulated state, we propose that this too would have contributed to the CNS manifestations.

At present, there is no definitive treatment for acute influenza encephalitis. Our patient was treated with oral oseltamivir and intravenous injection of methylprednisolone. She made a rapid recovery with improvement in ataxic symptoms in 5 days and vision improvement in 2 weeks.

To the best of our knowledge, our patient is the first female with term pregnancy and Influenza A virus-associated encephalitis described in the literature and the first description of viral etiology for bilateral LGB lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his



Figure 1: Magnetic resonance imaging brain: T2 fluid-attenuated inversion recovery imaging showing hyperintense lesions in bilateral lateral geniculate bodies

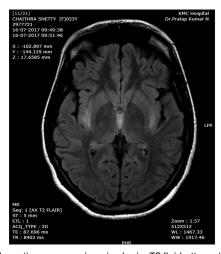


Figure 2: Magnetic resonance imaging brain: T2 fluid-attenuated inversion recovery imaging showing hyperintense lesions in bilateral external capsule, insular cortex

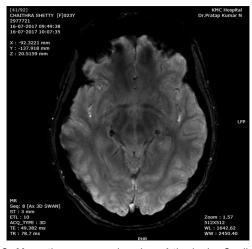


Figure 3: Magnetic resonance imaging of the brain: Gradient echo showing blooming suggestive of bilateral hemorrhagic infarction of lateral geniculate bodies

consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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DOI: 10.4103/aian.AIAN_319_18