LETTER TO THE EDITOR

Anti-N-Methyl-D-Aspartate receptor Encephalitis as a potential cause of worsening Herpes Simplex Virus Encephalitis

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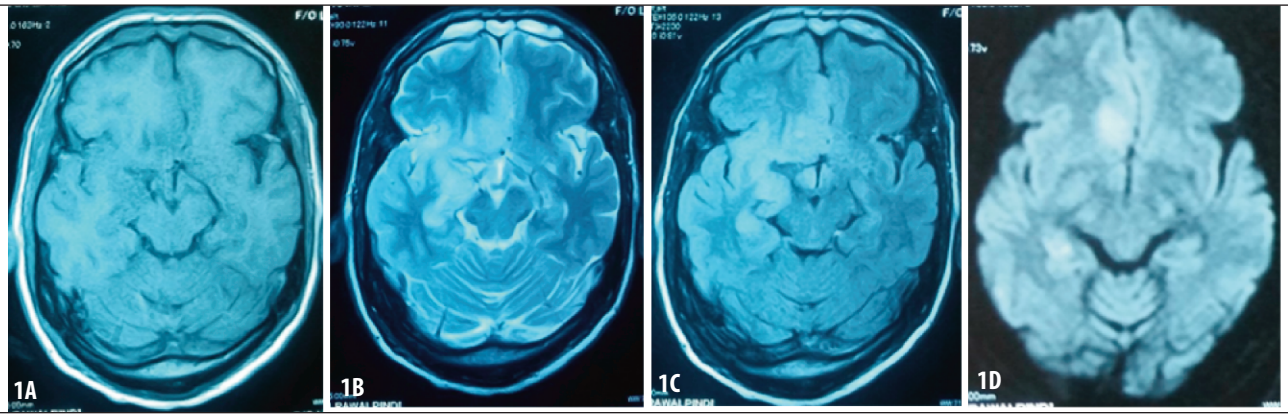

Figure-1: MRI of a 60 years old male with Herpes Simplex Virus Encephalitis. Magnetic resonance imaging of patient showing hyper-intense lesions on T2WI & FLAIR sequences (Figure: 1B &1C), involving insular cortex, hippocampus, medial frontal and temporal lobes bilaterally. These lesions appeared hypo-intense on T1WI (Figure 1A) and show restricted diffusion on DWI sequence (Figure 1D).

Madam, Herpes Simplex Virus Encephalitis (HSVE) though rare tends to be lethal if left without treatment. The mortality of untreated HSE is up to 70%[1] and most patients don't return to normal function.[1] That said with prompt recognition and treatment with antiviral therapy the prognosis is considerably better.[1] HSVE may become complicated by the presence of autoimmune encephalitis particularly Anti-N-Methyl-D-Aspartate receptor Encephalitis (NMDAR).[2] When this occurs the differentiation between two is not possible clinically and radiologically. In such situations the understanding and awareness of autoimmune encephalitis profile which also includes test for NMDAR antibodies becomes very important. Although such expensive tests have become available in Pakistan but the facility is present at only a handful of centers along with unawareness of this possible condition making the situation worse.

We encountered such a situation with our 60-years-old patient who initially presented with altered behaviour and recurrent episodes of focal seizures of left arm with secondary tonic clonic generalization. He was subsequently diagnosed with HSVE on cerebrospinal fluid (CSF) HSV polymerase chain reaction (PCR) and was treated with intravenous acyclovir. Magnetic resonance imaging of the patient showed lesions in the insular cortex, hippocampus, medial frontal lobes and temporal lobes bilaterally (Figure 1). The patient had resolution of symptoms with relapse of altered behaviour eight weeks later. On CSF PCR for HSV this time was negative, with positive serum Anti-N-Methyl-D-Aspartate receptor (NMDAR) antibodies. This condition was treated with plasmapharesis and intravenous methylprednisolone without acyclovir.

HSV has been postulated to induce autoimmunity against neuronal cell proteins.[3,4] Moreover, NMDAR Encephalitis has also been described in the literature as an etiology of "Relapsing Post-HSVE", which is amenable to immune modulation if diagnosed and treated timely. Although one of the considered differential diagnosis in cases of relapse of HSVE, at the same time, NMDAR Encephalitis can also be a reason of worsening or lack of improvement of patients suffering from HSVE.[1,2] These clinical situations may be missed by clinicians. So, it is important to differentiate among these clinical situations timely, which can be done easily by the antibody tests. This is important because the direction of therapy changes with initiation of immunotherapy if anti-NMDAR antibodies are tested positive. This may result in improvement in a large subset of patients.[5]

Therefore, in all cases of worsening HSVE anti-NMDAR antibodies should be done to rule out concurrent

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autoimmune Encephalitis, which if timely treated through immunosuppression would improve patient outcomes.

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