Herpes Simplex Virus Induced Anti-NMDAR Encephalitis
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INTRODUCTION

• N-methyl-D-aspartate receptor (NMDAR) is a glutamate receptor on nerve cells that controls synaptic plasticity and memory function.
• Anti-NMDAR encephalitis is a rare autoimmune disease in which IgG antibodies against GluN1 subunit of the NMDAR causes inflammation of the brain tissue.
• Preceding Herpes simplex virus-1 encephalitis (HSVE) is a well-recognized infectious trigger for this condition.
• It is most often seen in young adults and children and was first identified in patients with associated ovarian teratoma.

CASE PRESENTATION

• A 61-year-old male presented with agitation, behavioral changes and confusion.
• Eight months prior the patient was diagnosed with HSVE, and treated with 21 days of intravenous (IV) acyclovir.
• Following HSVE, he suffered from residual cognitive and personality changes with slow recovery up until 3 months prior to presentation with worsening encephalopathy again.
• An extensive investigation was unrevealing except for a CSF lymphocytic pleocytosis, positive anti-NMDAR antibodies titer (1:64), EEG and MRI changes consistent with post-viral encephalitis.
• He was diagnosed with HSV induced anti-NMDAR encephalitis at that point. Two cycles of plasmapheresis were attempted over 4 months period with limited success in improving his worsening neurologic deficits.
• PET scan did not reveal any occult malignancy.

IMAGING

Fig 1: T1 Pre-contrast image                             Fig 2: T1 Post contrast ring enhancing lesion in the Rt. temporal lobe
Fig 3: T1 Pre-contrast image                             Fig 4: T1 Post contrast ring enhancing lesion in the Rt. temporal
Fig 5: T2/FLAIR with hyperintense lesion in the Rt. frontal lobe.  Fig 6: T2/FLAIR with hyperintense lesion in the Rt. temporal lobe with encephalomalacia in the Rt temporal lobe (from prior HSV encephalitis)

DISCUSSION

• HSVE induced anti-NMDAR encephalitis is a rare autoimmune disease, primarily affecting children under 3 years of age and young adults.
• Anti-NMDAR antibodies develop 1 to 4 weeks after HSVE. Antibody titer in CSF is highly sensitive and specific for the diagnosis.
• Two proposed mechanisms: either viral reactivation, or a post-infectious autoimmune process.
• In young children, symptoms include choreoathetosis and/or orofacial dyskinesia. Teenagers and young adults are more likely to develop behavioral and psychiatric symptoms. In almost all the cases, involvement of the temporal region can be seen on MRI.
• First line immunotherapy (corticosteroids, IV immunoglobulin, or plasma exchange) with tumor resection (if present) has been promising with less frequent need for second line therapy (cyclophosphamide and/or rituximab) compared to those without tumors who are treated with similar initial therapy.
• HSV related anti-NMDAR encephalitis has not been associated with teratoma and resistance to first line therapy is observed. Symptoms improves in reverse order with declining antibody titer.
• The unique feature of this case is the age of the patient and preceding HSVE which triggered this autoimmune process.
• Physicians should consider anti-NMDAR encephalitis in the differentials for relapsing patients post HSVE.

REFERENCES