Progressive hippocampal sclerosis after viral encephalitis: Potential role of NMDA receptor antibodies

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PURPOSE
Survivors of viral encephalitis can develop refractory epilepsy and hippocampal sclerosis. Both the initial infectious insult and the secondary effects of recurrent seizures have been implicated in chronic disease progression. Recently, post-infectious autoimmunity, involved in acute relapses, has also been proposed as a pathomechanism for chronic disease progression. Our case series suggests a potential role of antibodies against the N-methyl-d-aspartate receptor (NMDAR) in chronic inflammatory disease beyond acute manifestations.

METHODS
Retrospective chart review of four patients with epilepsy, hippocampal sclerosis following viral encephalitis and NMDAR-antibodies in CSF.

RESULTS
The four patients were female, developed hippocampal sclerosis (in 3/4 in a step-wise progression) after Herpes simplex or Varicella zoster virus encephalitis and harboured immunoglobulin G antibodies against the NMDAR in their CSF. Two patients were treated with short-term immunosuppression but did not benefit.

CONCLUSION
This case series presents the first tentative evidence in support of chronic autoimmune inflammation driving disease progression after viral encephalitis beyond the known acute immune-mediated relapses. The anecdotal nature of the data does not, however, permit conclusive judgement on causality. Should our findings be replicated in larger cohorts, the treatment of post-infectious epilepsy could potentially be expanded to include immunosuppressive strategies in antibody-positive cases.