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HERPES SIMPLEX VIRUS-1 ENCEPHALITIS CAN TRIGGER ANTI-NMDA RECEPTOR ENCEPHALITIS: CASE REPORT

Gordon J. Gilbert, St. Petersburg, FL: Leypoldt et al.¹ reported an interesting case in which herpes simplex encephalitis (HSE) probably triggered the production of reactive NMDA receptor (NMDAR) antibodies. Within weeks of being treated with acyclovir for HSE, the patient had what the authors believed was recurrent HSE, yet it later proved to be NMDAR limbic encephalitis.

Since the viral encephalitic episode closely resembled the autoimmune encephalitic attack, it is difficult to know when the NMDAR limbic encephalitis first manifested. At initial discharge after having 3 weeks of acyclovir therapy, the patient had slow recovery, residual retrograde and anterograde amnesia, and impaired executive function. Some of these residua could have reflected the developing autoimmune encephalitis. The NMDAR immunoglobulin G (IgG) antibody level was 0 at day 1 but 1:800 by day 42. These IgG levels might have become clinically relevant by week 3 of the illness. Following subsequent treatment with IV methylprednisolone, it would be interesting to know whether the patient's condition improved beyond initial discharge.

Since this is the first case reported, it is unclear how often NMDAR antibodies develop in the context of HSE. It is possible that joint use of antiviral and corticosteroid medications may become the standard for the treatment of herpes simplex virus considering the potential for NMDA antibodies to effect prolongation or recurrence of the limbic encephalitis.

Author Response: Frank Leypoldt, Josep Dalmau, Barcelona, Spain: Relapsing symptoms post-HSE usually occur within a few weeks and represent either a true viral relapse or a disorder postulated to be

immune-mediated. This patient belonged to the second category. He did not have a true relapse of HSE, but anti-NMDAR encephalitis.

Our goal was to demonstrate a new synthesis of NMDAR antibodies that started after the viral infection. It is unclear whether some of the residual deficits from the first admission represented the initial manifestation of anti-NMDAR encephalitis. Only the relapsing symptoms responded to immunotherapy and this may suggest that the viral encephalitis caused the baseline deficits.

In recent studies with 6 additional patients, we confirmed that HSE can trigger anti-NMDAR encephalitis, usually between 4 and 6 weeks after HSE, but sometimes occurs without clear interval improvement of HSE. There are currently 13 patients reported with anti-NMDAR encephalitis as relapsing symptoms post-HSE^{2–5} and there is evidence that HSE triggers NMDAR antibodies.^{2,3} Most patients were children and developed choreoathetosis and dyskinesias, and immunotherapy seemed effective.

We agree that these findings may provide another reason to add steroids during treatment of HSE⁶ yet it is unclear whether this would prevent the development of anti-NMDAR encephalitis.

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