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IN THIS ISSUE

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IN BRIEF

A Potentially Fatal Immune Reaction to Lamotrigine

The FDA has warned that the antiepileptic and mood-stabilizing drug lamotrigine (*Lamictal*, and generics) can rarely cause hemophagocytic lymphohistiocytosis (HLH), a serious and potentially fatal immune-related reaction.[1]

HLH, which can be familial, occurs most often in infants, but can occur at any age. Often induced by Epstein-Barr Virus infection (HIV infection and non-Hodgkin's lymphoma are other common triggers), HLH is characterized by an unremitting activation of CD8+ T cells and macrophages.[2] If untreated, it causes organ damage, particularly in the liver, bone marrow, and CNS; organ failure and death occur within months after onset.[3] Clinical features can include fever and rash, splenomegaly, hepatitis, cytopenias, elevated triglyceride levels or low fibrinogen levels, hyperferritinemia, hemophagocytosis, decreased or absent natural killer cell activity, and elevated blood CD25 levels.[4]

The optimal treatment for drug-induced HLH is unclear. Treatment of HLH generally involves use of corticosteroids and blood products, sometimes augmented by aggressive immunosuppression with the cytotoxic drug etoposide (*Toposar*, and generics). The anti-CD52 antibody alemtuzumab *(Lemtrada)* can be added in refractory HLH cases,[5] and allogeneic hematopoietic cell transplantation has been used in genetic cases.

Since lamotrigine first became available in 1994, five confirmed and three suspected cases of HLH associated with its use have been reported. All of these cases occurred within 24 days of starting treatment and required hospitalization. One death was reported; in the other cases, improvement occurred after discontinuation of lamotrigine and treatment of HLH. Because initial signs and symptoms of HLH are nonspecific, the condition can be confused with Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), another potentially fatal, multiorgan, immune-related adverse reaction associated with lamotrigine use.[1,6]

Patients being treated successfully with lamotrigine should continue taking it. Clinicians should monitor patients taking lamotrigine for signs and symptoms of HLH, especially during the first few weeks after starting the drug. ■

1. FDA Drug Safety Communication: FDA warns of serious immune system reaction with seizure and mental health medicine lamotrigine (Lamictal). Available at: www.fda.gov/Drugs/DrugSafety/ucm605470.htm. Accessed June 7, 2018.
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3. SA Parikh et al. Prognostic factors and outcomes of adults with hemophagocytic lymphohistiocytosis. Mayo Clin Proc 2014; 89:484.
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