age, creating a vicious cycle of increasing addiction and brain damage.

A magnetic resonance imaging scan would likely provide only equivocal information on the extent of brain damage because brain mass remains constant, despite the continued loss of brain functional capacity. The SPECT scan was useful for outlining the functional capacity of the brain and might be a useful adjunct in the future for assessing brain impairment from substance inhalation.

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Anticonvulsant Hypersensitivity Syndrome From Addition of Lamotrigine to Divalproex

TO THE EDITOR: Lamotrigine is an efficacious, well-tolerated treatment for bipolar disorder and seizure disorders. The initial dosing requires gradual dose escalation, especially when lamotrigine is added to valproic acid to avoid the risk of inducing serious rashes with features within the spectrum of Stevens-Johnson syndrome and hepatitis.

Ms. A, a 50-year-old woman with bipolar depression who was admitted for worsening depression was taking 0.05 mg/day of clonidine, 1000 mg/day of divalproex, 450 mg/day of lithium, 50 mg of trazodone at bedtime, 150 mg b.i.d. of bupropion, 0.5 mg/day of clonazepam, and lamotrigine, which was started 2 weeks before at 25 mg/day, and was recently increased to twice daily. A baseline lithium level was not available.

Three days after admission, Ms. A developed a fever of 101°F, nausea, mild headache, and loose stools, and 2 days later, she had a generalized fine macular rash. A CBC, blood chemistries, a urinalysis and stool studies, a chest X-ray, computerized tomographies of her sinuses, and plain abdominal films were all normal. She developed pancytopenia with a WBC count of 5,500 with 16% segs, 43% bands, platelets of 81,000, mild eosinophilia at 5%, and an elevation of her alanine transaminase level at 186 units/liter (normal range=0–36) and her aspartate transaminase level at 82 units/liter (normal range=0–33) and normal alkaline phosphatase and bilirubin levels. Lamotrigine was discontinued when the rash developed, and divalproex was discontinued 2 days later. The rash began to decrease; the fever remitted; the headache, loose stools, and pancytopenia resolved; and the aspartate transaminase and alanine transaminase levels decreased. A lithium level obtained during hospitalization was subtherapeutic at 0.3 mmol/liter (therapeutic range=0.6–1.2 mmol/liter). The lithium dose was increased, and Ms. A was given hydroxyzine for anxiety resulting in effective control of her symptoms.

Anticonvulsant hypersensitivity syndrome is an uncommon immune-mediated disorder associated with older aromatic anticonvulsants. It is also seen with lamotrigine and characterized by fever, rash, eosinophilia, lymphadenopathy, pharyngitis, and malaise. It typically develops between 2 and 8 weeks after starting therapy but can occur after 12 weeks or longer. Liver involvement is common, ranging from mild (two- to threefold) elevation in transaminases to fulminant and lethal hepatocellular necrosis.

Although lamotrigine can be added to valproic acid with an acceptable incidence of side effects (1), 60% of the patients with anticonvulsant hypersensitivity syndrome related to lamotrigine also were taking valproic acid (2). The overall rate of rashes for patients taking lamotrigine is 13% and of serious rashes, 0.1% (3). Any rash is potentially serious and should be evaluated promptly (4). Although prolonged symptoms and fatalities have been reported, early recognition and discontinuation of offending agents often result in rapid improvement, as with our patient.

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Bipolar Disorder and Niemann-Pick Disease Type C

TO THE EDITOR: A number of neurodegenerative disorders that appear in adolescence or early adulthood are associated with the development of major mental illness. We present the case of a young man who was seen with a bipolar illness in the setting of the early-life diagnosis of Niemann-Pick disease type C.

Mr. A was a 25-year-old man who was hospitalized for behavioral disturbances, including disturbed sleep and appetite, sexualized behavior, and disorientation. Born prematurely, he was diagnosed with jaundice and hepatosplenomegaly. Fibroblast testing confirmed deficient cholesterol esterification and positive filipin staining, and later mutation analysis revealed homozygosity for the I1061T mutation of the NPC1 (Niemann-Pick disease type C) gene. He attended a special educational program and was able to work and participate in musical theater. At age 18, he exhibited early cognitive decline, and at 23, his behavior became disturbed, with periods of increased wakefulness, elation, poor judgment, and disinhibition that lasted 2–3 weeks, every 1–2 months, with interepisode euthymia.

At a mental status examination, Mr. A was highly elevated, euphoric, and markedly sexually disinhibited, with sexualized thought content. There were no delusions, for-