Published in final edited form as:

Clin Gastroenterol Hepatol. 2006 April ; 4(4): xxvi. doi:10.1016/j.cgh.2005.10.013.

Eosinophilic Hepatitis Caused by Lamotrigine

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A 20-year-old woman with seizures was started on lamotrigine 6 weeks before presenting with fatigue, jaundice, pruritus, rash, chest pain, and dyspnea. She had no known history of liver disease or drug allergies and took only occasional acetaminophen in addition to lamotrigine. She denied use of herbal products. On presentation, she was febrile, tachycardic, and developed wheezing and respiratory distress. She had jaundice and a tender liver edge, but no ascites, asterixis, or cutaneous stigmata of chronic liver disease. Laboratory studies showed a white blood cell count of 9600 cells/mm³ with 15% eosinophils, a platelet count of 162,000/mm³, an international normalized ratio of 1.1, an albumin level of 3.2 g/dL, a total bilirubin level of 10.4 mg/dL, an aspartate transaminase level of 190 U/L, an alanine transaminase level of 233 U/L, and an alkaline phosphatase level of 171 U/L. Liver enzyme levels were normal 3 years earlier. She had negative tests for hepatitis A, B, and C, hepatitis C RNA, and antinuclear antibody, and a normal ceruloplasmin level. The acetaminophen level was 7 mg/L and anti-smooth muscle antibody was borderline positive (titer, 1:40). Imaging showed a 14-cm spleen, normal liver, no biliary ductal dilatation, bilateral patchy ground-glass opacities in the lungs consistent with hypersensitivity pneumonitis (Figure A), and numerous subcentimeter mediastinal, axillary, and inguinal lymph nodes. Liver biopsy examination showed prominent eosinophilic portal and lobular inflammation, necrotic hepatocytes, and focal confluent necrosis, with no granulomas or fibrosis, with hematoxylineosin staining (Figure B, 200×).

The patient showed several features of hypersensitivity including fever, rash, lymphadenopathy, eosinophilia, pneumonitis, increased liver enzyme levels, and eosinophilic hepatitis on biopsy examination. Lamotrigine was stopped, glucocorticoids were initiated for apparent hypersensitivity pneumonitis, and liver enzyme levels improved over several weeks. Lamotrigine generally is safe¹ but a potentially life-threatening hypersensitivity syndrome, including severe liver injury, has been associated rarely with its use.² This report of severe hepatotoxicity includes pneumonitis and highlights the importance of close monitoring in patients treated with lamotrigine.

Acknowledgments

Dr Fix has received funding from the American Association for the Study of Liver Diseases Advanced Hepatology Fellowship Award.

The authors thank Robert K. Kerlan Jr, MD, from the Department of Radiology, and Grace E. Kim, MD, from the Department of Pathology.

References

1. Fayad M, Choueiri R, Mikati M. Potential hepatotoxicity of lamotrigine. *Pediatr Neurol.* 2000; 22:49–52. [PubMed: 10669206]
2. Overstreet K, Costanza C, Behling C, et al. Fatal progressive hepatic necrosis associated with lamotrigine treatment. *Dig Dis Sci.* 2002; 47:1921–1925. [PubMed: 12353830]