中文題目:案例報告: Phenobarbital 造成肝損傷合併淋巴血管增生

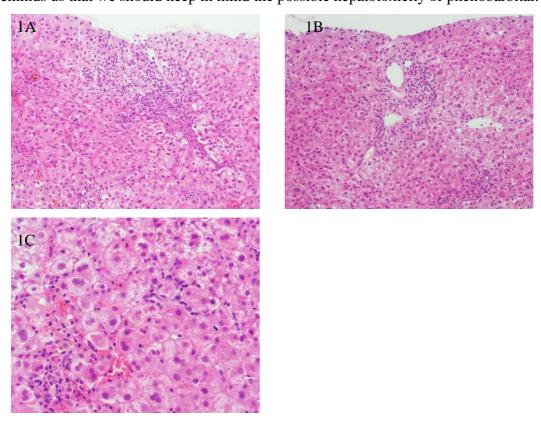
英文題目: Phenobarbital-induced Liver Injury with Nodal Angiomatosis

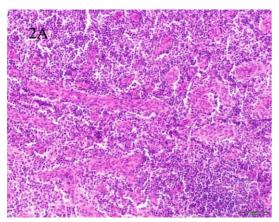
作 者:鄭立廷¹,黃正皓²,劉峰誠²,盧俊吉²

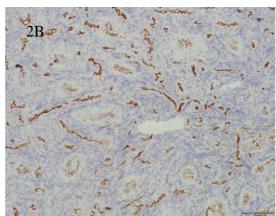
服務單位:1三軍總醫院一般內科;2三軍總醫院風濕免疫過敏科

Drug-induced liver injury (DILI), a rare and challenging disorder, is diagnosed based on drug exposure, detailed history taking, and by excluding other liver diseases. Phenobarbital has infrequently been reported to cause liver injury. According to previous literature, the most common clinical presentations of phenobarbital-induced liver injury are fever, rash, and eosinophilia. (1) Generalized lymphadenopathy with histologic finding is rarely reported. Here we present a unique case of phenobarbital-induced liver injury with nodal angiomatosis. An 18-year-old woman presented with a two-week history of spiking fever after three weeks of daily phenobarbital, amoxicillin, chlorphenamine, ergotamine, and cinnarizine for acute sinusitis and chronic migraine. Her medical history was unremarkable. She did not drink, take herbal or dietary supplements (HDS), and had no history of animal contact. Physical examination revealed enlarged nontender superficial lymph nodes (LNs) in her neck. Laboratory evaluation revealed a normal white blood cell count, atypical lymphocytes of 8.6%, platelet count of 146 × 109/L, aspartate aminotransferase of 288 U/L, alanine aminotransferase (ALT) of 452 U/L, total bilirubin of 4.3 mg/dL, direct bilirubin of 3.6 mg/dL, gamma-glutamyl transpeptidase of 469 U/L, alkaline phosphatase (ALP) of 290 U/L, and lactate dehydrogenase of 619 U/L. An ultrasound of her neck showed several ovoid LNs bilaterally. A computed tomography (CT) scan of the abdomen revealed mild periportal lucency, 14.8-cm splenomegaly, mild ascites, and several enlarged LNs (size < 1.5 cm) along the hepatoduodenal ligament, paraaortic space and bilateral inguinal regions. No dilation of the common bile duct or hepatic duct was noted. Her spiking fever continued, and newly developed lymphadenopathy of the bilateral axillary region was noted. A contrast CT scan of the chest showed bilateral pleural effusions and lymphadenopathy in the axillary fossae. She underwent biopsies of liver and axillary LN (Figs. 1 and 2). Histological analysis of the liver revealed interface hepatitis, increased lobular apoptotic bodies (Fig. 1A), prominent portal lymphocytic cells infiltrates, many binucleated and even multinucleated hepatocytes with rosette formation (Fig. 1B), ballooning degeneration

of hepatocytes and canalicular cholestasis (Fig. 1C). Bone marrow examinations revealed normal cellularity without abnormal blasts or malignant cells. Histological features of the axillary lymph nodes showed a marked proliferation in the sinus area of small blood vessels lined by hyperplastic endothelial cells, compatible with nodal angiomatosis without malignant cells (Figs. 2A and 2B). Histological finding from the lymph node displayed nodal angiomatosis, which is a benign vascular proliferation of lymph node and usually an incidental finding when resected for suspected malignancy. Bacillary angiomatosis and Kaposi sarcoma should be ruled out. The patient had not experienced an animal scratch, and no bacteria were identified from a nodal biopsy. There was no evidence of HIV infection or skin lesion. Therefore, cat-scratch disease and Kaposi sarcoma were excluded. We present a rare case of phenobarbital-induced liver injury with fever, atypical lymphocytosis, and generalized lymphadenopathy with unique histologic finding of nodal angiomatosis. Although use of phenobarbital has decreased, it remains easily available in the world. This case reminds us that we should keep in mind the possible hepatotoxicity of phenobarbital.







References

- 1. Evans WE, Self TH, Weisburst MR. Phenobarbital-Induced Hepatic Dysfunction. Annals of Pharmacotherapy. 1976;10:439-443.
- Chalasani N, Bonkovsky HL, Fontana R, et al. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN prospective study.
 Gastroenterology. 2015;148:1340-1352.e7.
- 3. Chalasani NP, Hayashi PH, Bonkovsky HL, Navarro VJ, Lee WM, Fontana RJ. ACG Clinical Guideline: The Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. Am J Gastroenterol. 2014;109:950-966.
- 4. Suzuki, A., Brunt, E. M., Kleiner, D. E., Miquel, R., Smyrk, T. C., Andrade, R. J., Isabel Lucena, M., Castiella, A., Lindor, K. and Björnsson, E. The use of liver biopsy evaluation in discrimination of idiopathic autoimmune hepatitis versus drug-induced liver injury. Hepatology, 2011;54: 931–939.
- 5. Chan JKC, Warnke RA, Dorfman RF. Vascular transformation of sinuses in lymph nodes. A study of its morphological spectrum and distinction from Kaposi's sarcoma. Am J Surg Pathol 1991;15:732-743.