Drug-Induced Liver Injury Secondary to Gabapentin

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Introduction

We are reporting a case of drug induced liver injury (DILI) secondary to gabapentin therapy with risk factors for underlying non-alcoholic fatty liver disease (NAFLD).

Case Description

A 56-year-old male with hypertension, hyperlipidemia, diabetes with neuropathy, obesity, chronic kidney disease stage 3, and obstructive sleep apnea presented as an outside hospital (OSH) transfer for evaluation of liver transplantation after discovery of acute liver injury. He initially presented to the OSH for jaundice. Admission labs were notable for AST 87, ALT 61, ALP 1252, total bilirubin (Tbili) 23.4, INR 1.1, and creatinine 1.98 (baseline 1.2). Prior lab review showed liver enzymes within normal limits until one month prior to admission, when his ALP was 851. He started taking gabapentin, without introduction of any other medications, one month prior to the initial rise in ALP (two months prior to admission). Evaluation for viral, inherited, and metabolic causes of liver disease were negative. Liver biopsy showed multifocal hepatocyte cholestasis predominantly involving zone 3 with associated hepatocyte feathery degeneration and neutrophil and lymphocyte infiltration. There was patchy portal edema, mild portal inflammation with neutrophil and lymphocyte infiltrates, and bile duct injury. Trichrome stain highlighted periportal and focal bridging fibrosis appearing to be unrelated to cholestasis, most likely due to underlying NAFLD. The leading differential for cholestasis was drug induced liver injury (DILI) versus biliary obstruction. Magnetic resonance cholangiopancreatography showed no biliary abnormalities. After gabapentin was discontinued, liver enzymes began to downtrend with final discharge values being AST 16, ALT 35, ALP 413, Tbili 9.3 and INR 1.1.

Figure 1: A Trend of Alkaline Phosphatase and Total Bilirubin in Relation to Gabapentin Administration

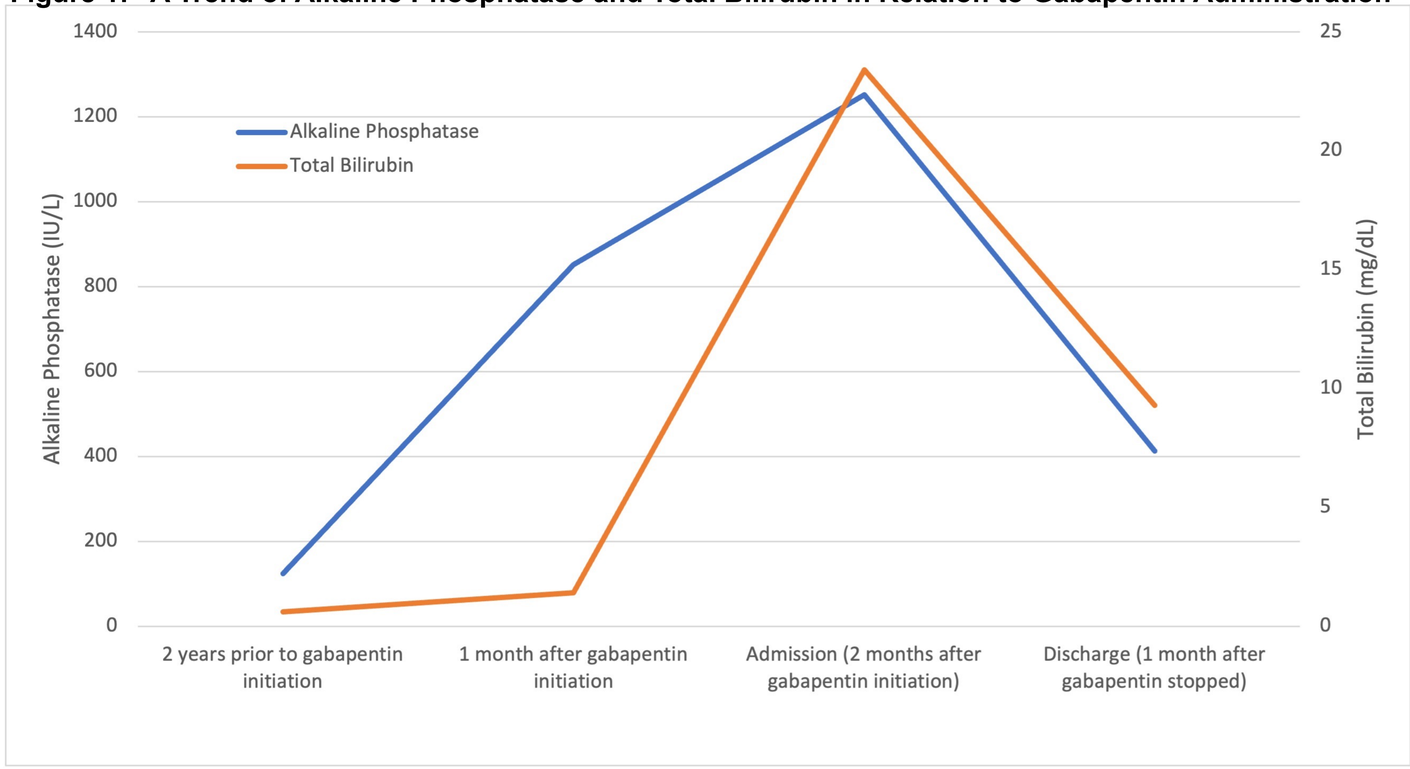

Figure 1: Depicts the trend of alkaline phosphatase (Left Y-Axis) and total bilirubin (Right Y-Axis) over time. The initial values note a baseline 2 years prior to exposure to gabapentin with the subsequent rise and fall in ALP and Tbili as gabapentin was added and then removed.

Discussion/Conclusion

Gabapentin induced liver injury is rare with few reported cases, many of which did not exclude other etiologies (1-3). In this case, the key elements of diagnosing DILI were met including gabapentin initiation closely preceding liver injury, other etiologies excluded, and discontinuation of gabapentin leading to improvement. The severity of this patient's DILI and general recommendation to avoid future exposure precluded him from being rechallenged with gabapentin. Given the extensive use of gabapentin in medical practice, this case represents an extremely uncommon but severe complication of its use. This is also an example of DILI with suspected underlying NAFLD. While NAFLD has not been shown to predispose to DILI, it is suspected to be associated with more serious liver injury in patients who develop DILI (4).

References

1. Contreras-Mota M, Rosales-Cortés V. Hepatotoxicidad probablemente asociada a gabapentina [Hepatotoxicity probably associated with gabapentin]. Rev Med Inst Mex Seguro Soc. 2021 Jun 14;59(2):157-162. Spanish. PMID: 34232226.

2. Jackson CD, Clanahan MJ, Joglekar K, Decha-Umphai ST. Hold the Gaba: A Case of Gabapentin-induced Hepatotoxicity. Cureus. 2018 Mar 4;10(3):e2269. doi: 10.7759/cureus.2269. PMID: 30128217; PMCID: PMC6093755.

2. Lasso-de-la-Vega MC, Zapater P, Such J, Pérez-Mateo M, Horga JF. Gabapentin-associated hepatotoxicity. Am J Gastroenterol. 2001 Dec;96(12):3460-2. doi: 10.1111/j.1572-0241.2001.05357.x. PMID: 11774985.

4. Regev A, Palmer M, Avigan MI, et al. Consensus: guidelines: best practices for detection, assessment and management of suspected acute drug-induced liver injury during clinical trials in patients with nonalcoholic steatohepatitis. Aliment Pharmacol Ther. 2019;49(6):702-713. doi:10.1111/apt.15153