Glatiramer Acetate-Induced Acute Liver Failure and Liver Transplantation: A Case Report

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Background

- Glatiramer acetate (GA) has been used for multiple sclerosis (MS) since 1996.
- Regular liver function test monitoring is not required for the medication because there have not been any reported cases of liver toxicity (1).

Case Presentation

- 59-year-old woman with well-controlled MS presented to the emergency department with three weeks of jaundice and dark-colored urine.
- She took GA, which was her only medication since 2008.
- Liver enzymes were normal one year prior to presentation, and she has no family history of autoimmune or liver disease.

Initial Physical Exam and Laboratory Data

- Physical exam was notable for mild asterixis. Patient was alert and oriented.
- Chemistry: AST 2527 IU/L (81x ULN), ALP 210 IU/L (2x ULN), ALT 2512 IU/L (81x ULN), Total bilirubin 22.7 mg/dL
- INR 2.65
- Anti-smooth muscle antibody 1:40, normal ceruloplasmin, alpha-1-antitrypsin, and IgG. Negative hepatitis, HSV, VZV, T-spot, HIV, ANA, anti-mitochondrial antibody, and anti-LKM antibody.
- CT A/P showed patent vasculature and no evidence of cirrhosis; MRI/MRCP showed no evidence biliary obstruction.
- Liver biopsy demonstrated submassive necrosis (70%) consistent with drug-induced liver injury **(Fig1A).**

Hospital Course

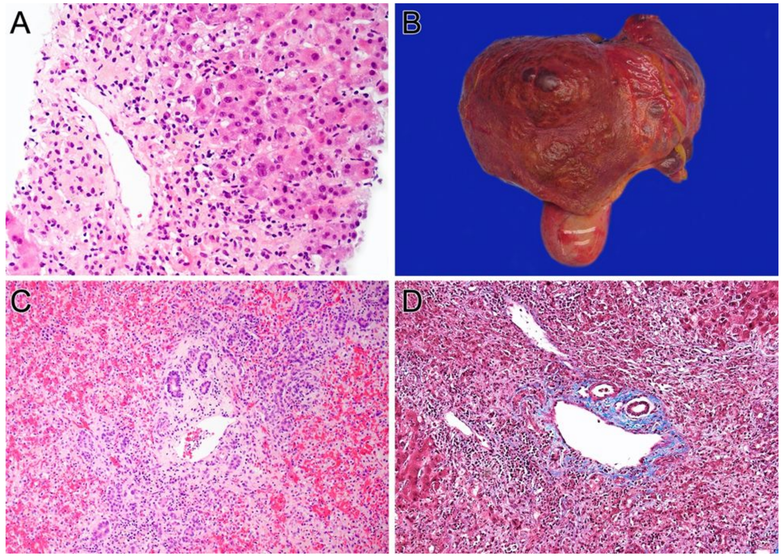

Figure 1. Histological analysis of pre-transplant and explant liver. A. Hematoxylin and eosin (H&E) stain of the pre-transplant biopsy showed extensive necrosis including zone 3 (x100). B. Gross picture of explant (weight 500.3 gram). The surface showed wrinkles, which were characteristics of acute liver failure with massive hepatocyte necrosis. C. H&E stain of explant showed massive hepatocytes necrosis. (x200). D. Masson trichrome stain showed no fibrosis, which confirmed the acute process (x200).

- GA was thought to be the most likely etiology of her liver injury and was held on admission. Neurology was in agreement.
- DAY 3-5 - Patient was given 3-day course N-acetylcysteine
- DAY 6 – Liver enzymes downtrended and mental status improved, AST 699 IU/L (934), ALT 910 IU/L (1194), ALP 188 IU/L (199), Total bilirubin 21.3 mg/dL (22.7), INR 2.57 (2.47), so liver transplant was deferred and patient discharged.

Hospital Course

- DAY 10 – Patient developed severe abdominal pain, lethargy, and was slow to respond. Physical exam notable for scleral icterus and asterixis. Labs showed AST 909 IU/L, ALT 839 IU/L, total bilirubin 27.2 mg/dL, and INR 2.94. She underwent expedited liver transplant evaluation and was listed on the same day.
- DAY 13 – Patient successfully underwent deceased donor liver transplant. Liver explant showed mixed zone 1 and 3 liver necrosis (50%) with associated inflammation-mild lobular inflammation and cholestasis **(Fig1B-D).**

Discussion

- This case illustrates the first case of GA-induced ALF requiring liver transplantation.
- Previous reports have showed that patients with GA drug-induced-liver injury recovered completely in 1-5 months after drug withdrawal and time of presentation ranges from 1-8 months. This contrasts with 14 years in our case.

Conclusion

Given this case of GA-induced ALF requiring liver transplantation, patients on GA should have long term regular liver monitoring.

References

(1) Biolato M, Bianco A, Lucchini M, Gasbarrini · Antonio, Mirabella M, Grieco · Antonio. The Disease-Modifying Therapies of Relapsing-Remitting Multiple Sclerosis and Liver Injury: A Narrative Review. CNS Drugs. 123AD;35:861-880. doi:10.1007/s40263-021-00842-9