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A Case of Drug-Induced Liver injury Secondary to Clobenzorex use

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INTRODUCTION

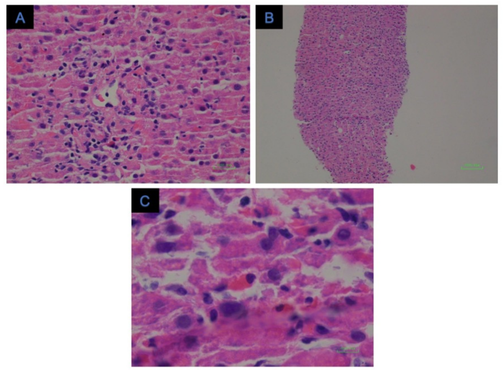
- Drug-induced liver injury (DILI) is a cause of both acute and chronic liver disease and can be a challenging condition for clinicians.
- DILI is a diagnosis of exclusion that requires a detailed history and workup to ensure other potential causes have been ruled out before affirming the diagnosis.
- There are numerous offending agents with varied presentations, often idiosyncratic in nature, with an additional challenge being a lack of specific testing or biomarkers to aid diagnosis.
- This case report documents a unique instance of drug-induced liver injury secondary to Clobenzorex use.
- This case highlights the importance of a detailed social history and should encourage clinicians not to neglect to ask about over-the-counter (OTC) medications to help elucidate potential causes of liver injury.

BACKGROUND

- DILI is a significant cause of acute liver failure in the western world. It is also the most common adverse drug reaction that leads to the withdrawal of medication from both clinical and preclinical settings.
- A wide spectrum of disease exists as those who experience DILI range from asymptomatic to acute or chronic liver failure. DILI has been reported to account for over 50% of acute liver failure along with the most common cause of acute liver failure in the USA and the UK reiterating the importance of early clinical suspicion and identification (1,2).
- DILI is not limited to prescription medication as there have been numerous reported instances of over-the-counter herbal products and dietary supplements also causing liver injury globally (2).
- The list of offending agents is constantly growing which prompted The National Institutes of Health (NIH) to develop a searchable database that is accessible to the public and healthcare providers which is constantly updated (4).
- Here we present a case report of a unique instance of drug-induced liver injury secondary to Clobenzorex use.

THE CASE

- A 25-year-old male who immigrated from Mexico 4 months ago, with no reported past medical history, presented to the emergency department for a two-day history of postprandial non-radiating right upper quadrant and epigastric pain.
- The patient worked as a driver in Mexico and was taking two different formulations of 30mg Clobenzorex, an amphetamine pro-drug, daily for two years to help him stay awake for work. These medications were available over the counter.
- He had not taken Clobenzorex since he moved to the US four months prior. He denied the use of illicit drugs, contact with any inmates or Tuberculosis patients. At the time of his presentation, he worked in a wooden floor-making company.
- Labs revealed a markedly elevated total bilirubin of 4.4 mg/dL, INR 1.1, AST 1325 IU/L, ALT 3151 IU/L, LDH 745 IU/L and a mildly elevated ALP 220 IU/L. Acute hepatitis and autoimmune panels were not reactive. Serum acetaminophen level was also within normal limits. Ultrasound of the abdomen and MRCP showed no biliary dilatation or pathology.
- The patient subsequently underwent a core-needle liver biopsy that displayed lobular infiltrates of inflammatory cells of predominantly lymphocytes (Figure 1).
- Given the absence of positive viral and autoimmune serology, a diagnosis of drug-induced liver injury (DILI) was concluded.



- **Figure 1**: Core needle liver biopsy showing lobular infiltrates of inflammatory cells consisting of predominantly lymphocytes.

DISCUSSION

- DILI can be classified based on a few different criteria, including clinical presentation, the mechanism of hepatotoxicity, and histologic findings. The clinical presentation is often used to characterize the type of DILI.
- This can be reflected by laboratory findings suggesting hepatocellular injury, cholestatic injury, or a combination of both.
- There are two mechanisms by which a drug can cause liver injury; either directly via a dose-dependent and predictable way or in an idiosyncratic and unpredictable manner.
- Acetaminophen toxicity is the archetypal drug that causes hepatotoxicity in a dose-dependent and predictable manner. Although a liver biopsy is not required for a diagnosis it can help assess the extent of hepatoxicity and allow for further sub-classification of the DILI (7).
- The diagnosis is one of exclusion that requires an extensive and detailed history including ascertaining details regarding over-the-counter medications.
- Another important step in diagnosis is the exclusion of common causes of liver injury.
- Although a liver biopsy is not a requirement for diagnosis it can aid in the determination of the cause of liver injury (8).
- Amphetamines have been shown to cause DILI with a hepatocellular pattern and can mirror a viral hepatitis-type picture (9).

CONCLUSIONS

- Drug-induced liver injury (DILI) is a cause of both acute and chronic liver disease and is often a challenging condition for clinicians.
- It is a diagnosis of exclusion that requires a detailed history and workup to ensure other potential causes have been ruled out before affirming the diagnosis.
- This case highlights the importance of obtaining a thorough history, especially in the subset of patients from countries outside the United States who have access to a variety of OTC medications that are potentially hepatotoxic.

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