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CASE REPORT | LIVER

Cyproheptadine-Induced Acute Liver Failure

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Abstract

We present the case of a 55-year-old white female with no history of liver or gastrointestinal disease, admitted with acute liver failure following a trial of cyproheptadine for appetite stimulation. The patient was managed with supportive care, symptomatic treatment, and discontinuation of cyproheptadine. To our knowledge, this is the first described case of cyproheptadine-induced acute liver failure in over 20 years.

Introduction

Cyproheptadine is a first-generation antihistamine indicated for allergic reactions, cyclic vomiting syndrome, and appetite stimulation.[1] Although hepatitis, jaundice, and acute liver failure are reported as adverse effects from the use of cyproheptadine, only a few cases have been reported in the literature.[1]

Case Report

A 55-year-old white female with a past medical history of lung adenocarcinoma presented with altered mental status, confusion, and lethargy. Due to significant confusion, history could only be ascertained through chart review of outside medical records. Her exam was significant for lethargy with poor orientation and an oxygen saturation of 93% requiring 4 L of oxygen via nasal cannula. Laboratory evaluation was significant for evidence of acute kidney injury, elevated liver associated enzymes, leukocytosis, and coagulopathy (Table 1). Her abdominal ultrasound with Doppler was unremarkable.

She was admitted and treated with intravenous fluids for acute kidney injury and started empirically on N-acetylcysteine for acute liver failure suspected from drug ingestion. Repeat labs the next day showed improved leukocytosis and kidney function, but continued increase in transaminases. Work-up included negative bloodwork for viral hepatitis and autoimmune etiologies. An infectious work-up of blood and urine cultures was negative. Abdominal, pelvic, and chest computed tomography (CT) did not show abnormalities or findings consistent with metastatic disease.

She was continued on N-acetylcysteine for an additional 3 days. On day 2, the patient's mental status improved, and she stated that the only new substance she had been taking was cyproheptadine for appetite stimulation, begun 3 weeks prior to admission. She had not been on any other chronic medical therapy, or recently ingested alcohol or any other recreational drugs. Cyproheptadine was not started on admission. Over the course her hospitalization, the patient's mental status improved and her laboratory evaluation showed continuous improvement. She was discharged on day 6 with instructions to follow up for laboratory evaluation in 2 days, which showed continued improvement.

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Table 1. Laboratory Values

Day	ALT, U/L	AST, U/L	Total Bilirubin, mg/dL	PT, sec	INR
1[a]	1195	776	2.9	23.2	2.1
2[a]	3156	1607	1.6	23.2	2.1
3	1068	650	2.0	20.8	1.8
4	913	481	2.1	19.7	1.7
5	687	238	2.2	20.2	1.7
6	519	145	1.9	20.0	1.7
7	374	82	1.6	18.0	1.5
8	262	49	1.2	16.5	1.3
2[b]	194	41	1.2	11.6	1.1
15[b]	24	20	0.8	11.9	1.1

ALT = alanine transaminase; AST = aspartate transaminase; INR = international normalized ratio; PT = prothrombin time.
[a]Values recorded at an outside hospital.
[b]Days post-discharge.

Discussion

Introduced in 1961 as an antihistamine, cyproheptadine is a potent anti-serotonin agent and antagonist of histamine that is sometimes used as an appetite stimulant and for symptomatic relief of pruritis.[1–3] In our patient, cyprohepatadine is implicated as the cause of her acute liver failure for several reasons. She did not have a past medical history of liver or biliary disease, and imaging did not demonstrate any underlying liver disease or hepatic vessel abnormalities. Serological work-up for liver disease was negative. Symptoms occurred 3 weeks after taking cyproheptadine, and improved quickly after discontinuation. Symptoms, exam findings, and laboratory results from our patient are similar to findings in other case reports, which describe patients who present with acute elevations in liver enzymes after starting ciprohepatadine but resolve within weeks of discontinuing the drug.[1–5]

The cause for these findings and cyproheptadine's liver toxicity remains unproven, but some have postulated that the cholestatic or mixed-pattern acute hepatitis resulting from cyproheptadine is due to its tricyclic ring, which is similar in structure to other known phenothiazine hepatotoxic drugs like chlorpromazine, imipramine, and ajmaline.[1–5] Our patient had a unique presentation that was more suggestive of hepatitis than cholestastis. Regardless of its mechanism, clinicians should be aware of the rare but life-threatening hepatotoxicity from cyproheptadine so that rapid withdrawal of the drug can be initiated and clinical recovery can begin.

Disclosures

Author contributions: J. Chertoff is the primary author of this manuscript and is the article guarantor. S. Alam assisted with the literature review and some of the manuscript writing. V. Clark supervised the management of this case.

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