

Olanzapine-Induced Cholestatic Liver Injury Mimicking Obstructive Hepatobiliary Disease: A Case Report

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ABSTRACT: Drug-induced liver injury can present as biliary obstruction which can lead to difficulties interpreting cholestatic liver enzyme elevations. This report describes a middle-aged woman with bipolar disorder, Hashimoto thyroiditis, fatty liver disease, and a prior cholecystectomy with markedly elevated liver enzymes following a recent increase in her olanzapine dose. Laboratory testing showed an alkaline phosphatase level exceeding 1000 U/L and a gamma-glutamyl transferase level of 768 U/L, with mild elevations in aminotransferases. Further testing showed that the elevated alkaline phosphatase was mainly hepatic in origin. Ultrasound and magnetic resonance cholangiopancreatography showed hepatomegaly but no evidence of bile duct dilatation or choledocholithiasis. Viral hepatitis and autoimmune causes were investigated and workup was unrevealing. Olanzapine was discontinued due to concern for drug-induced liver injury, leading to an improvement in her liver function tests, with alkaline phosphatase decreasing to 406 U/L at outpatient follow-up. Due to the timing of the dosage increase, the ability of olanzapine to cause cholestatic injury, the negative findings on imaging, and the improvement after discontinuing olanzapine, drug-induced cholestatic liver injury was considered the most likely diagnosis. This case shows that olanzapine can mimic an obstructive pattern, and that cholestatic drug injury remains a diagnosis of exclusion, especially after biliary surgery or when occult obstruction is still suspected.

KEYWORDS: Olanzapine, Drug-induced liver injury, Cholestasis, Alkaline phosphatase, Biliary obstruction, MRCP, Choledocholithiasis, Hepatotoxicity

1. INTRODUCTION

Drug-induced liver injury (DILI) can cause abnormal liver function tests and may present with hepatocellular, mixed or cholestatic patterns. The cholestatic form is difficult to diagnose because its biochemical and pathological features overlap with features of extrahepatic biliary obstruction and primary cholangiopathies. Recent reviews suggest that hepatobiliary malignancy, choledocholithiasis, cholangitis, viral infections and other causes should be excluded before a cholestatic injury is considered to be medication-induced.¹

Olanzapine is an atypical antipsychotic commonly used to treat bipolar disorder and schizophrenia. Mild, transient liver test abnormalities have been reported to be common during olanzapine therapy, but clinically apparent liver injury is rare. The injury may be hepatocellular, mixed, or cholestatic and onset occurs within weeks of starting treatment or achieving the therapeutic dose.² Echater et al.³ described acute cholestatic hepatitis in a woman with bipolar disorder shortly after her olanzapine dose was increased from 10 mg/day to 20 mg/day. Three days after the dose increase, she developed vomiting, jaundice, dark urine, itching, as well as abnormal liver enzymes. This report shows that a dose increase in olanzapine may lead to the occurrence of significant cholestatic injury.

We describe a middle-aged woman who developed severe cholestatic liver injury following a recent increase in her olanzapine dose. The elevated alkaline phosphatase and gamma-glutamyl transferase levels first raised concern for biliary obstruction, but imaging showed no evidence of obstruction, and her liver function tests improved after discontinuation of olanzapine. This case shows how olanzapine induced cholestatic DILI can mimic obstructive hepatobiliary disease, making it important to consider both obstructed and medication related causes.

2. CASE PRESENTATION

A 53 year old woman with a history of bipolar disorder, Hashimoto thyroiditis, fatty liver disease, cholecystectomy, and sleep apnea was evaluated during prolonged illness with markedly elevated liver enzymes. She also had a previous gastrointestinal episode described as colitis. The record did not fully characterize it, but later records listed irritable bowel syndrome and gastroesophageal reflux disease and a previous colonoscopy which reportedly included the removal of several polyps.

Her initial symptoms included dysuria which was treated as a urinary tract infection. Despite the treatment, she continued to experience flu-like symptoms, poor appetite, weakness, fatigue, nausea, vomiting and low-grade fever. She received several courses of antibiotics, including levofloxacin which was later followed by broad-spectrum antibiotic treatment in the hospital. Chest imaging showed patchy ground-glass opacities and bibasilar atelectasis with no pulmonary embolism. Splenic infarcts were also identified during her hospitalization.

Her medication history included olanzapine for bipolar disorder. The dose had recently been increased to approximately 30 mg daily, which she reportedly took for about two weeks before it was stopped abruptly because of concern for her elevated liver enzymes. Her other medications were fluoxetine, amitriptyline, alprazolam, levothyroxine, acid suppression, antiemetics, and the recent antibiotics.

Laboratory testing during hospitalization showed remarkably elevated liver enzymes, particularly alkaline phosphatase. Early results showed alkaline phosphatase exceeding 1000 U/L, along with elevated liver enzymes, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT). On September 17, alkaline phosphatase was 925 U/L, AST was 231 U/L, and ALT was approximately 169 U/L. The following day, alkaline phosphatase decreased to 807 U/L, AST to 182 U/L, and ALT to 140 U/L. Gamma-glutamyl transferase (GGT) was elevated at 768 U/L. Albumin was also low, ranging from 1.9 to 2.3 g/dL during hospitalization.

Further testing was performed to determine the source of the elevated alkaline phosphatase. On September 17, total alkaline phosphatase was 866 U/L, with the liver fraction measuring 606 U/L, or 70% of the total. Repeat testing on September 20 showed a total alkaline phosphatase of 786 U/L, with a liver fraction of 545 U/L, or 71%. Although the bone fraction was elevated, its percentage remained within the reference range. These findings, along with the high gamma-glutamyl transferase, pointed to a hepatobiliary source.

Abdominal ultrasound showed mild hepatomegaly, no gallbladder (consistent with her cholecystectomy), a normal blood flow through the portal vein, and no biliary ductal dilatation. Magnetic resonance cholangiopancreatography (MRCP) showed no intrahepatic or extrahepatic ductal dilatation and no choledocholithiasis. The pancreas appeared normal and the pancreatic duct was not dilated. CT showed hepatomegaly and later confirmed splenic infarcts, but it did not identify pancreatic or biliary mass. FibroScan was consistent with hepatic steatosis and mild fibrosis.

Additional testing was performed to investigate other possible causes of the abnormal liver enzymes. Viral hepatitis was reportedly ruled out, and autoimmune testing, including c-ANCA, p-ANCA, and cryoglobulins, was negative or unremarkable. Platelet counts and kidney function remained normal. The workup found no persistent structural obstruction of the biliary tree.

At outpatient follow up after discharge, the patient continued to report chills, muscle aches, poor appetite, nausea with dry heaving, diarrhea, and upper abdominal discomfort. Her blood pressure was 136/92 mm Hg, heart rate was 100 beats/min, temperature was normal, and oxygen saturation was 98%.

Repeat testing showed her liver enzymes were improving, with alkaline phosphatase down to 406 U/L. Bilirubin was 0.6 mg/dL and albumin had risen to 2.9 g/dL. AST and ALT were still mildly elevated but significantly below their initial values. Procalcitonin and lipase were normal, and urinalysis showed no active urinary infection.

3. MANAGEMENT AND OUTCOME

Management focused on withdrawal of potentially hepatotoxic medications, supportive care, and continued evaluation for alternative hepatobiliary causes. Olanzapine was discontinued after the concern for drug-induced liver injury following a recent dose increase. Amitriptyline was also reduced because of its potential for hepatotoxicity. During the acute illness and

hospitalization, the patient received intravenous fluids for dehydration and symptomatic treatment for nausea, including prochlorperazine and a gastrointestinal cocktail. Gastroenterology follow-up was arranged to monitor her symptoms and liver biochemical abnormalities.

Following discontinuation of olanzapine and recovery from the acute systemic illness, the cholestatic biochemical abnormalities improved substantially. Alkaline phosphatase decreased from values exceeding 1000 U/L during hospitalization to 406 U/L at outpatient follow-up. Aminotransferase levels had also declined and total bilirubin remained within normal limits at 0.6 mg/dL. Albumin had improved to 2.9 g/dL. Despite the improvement in liver tests, the patient continued to report chills, myalgias, poor appetite, nausea with dry heaving, diarrhea, and upper abdominal discomfort.

The improvement in liver biochemical abnormalities following olanzapine discontinuation, together with the absence of biliary obstruction on ultrasonography and MRCP, favored olanzapine-induced cholestatic liver injury. However, the patient's concurrent systemic illness and exposure to multiple antibiotics limited the ability to definitively attribute the liver injury to olanzapine alone.

4. DISCUSSION

This case shows the kind of difficulties encountered when trying to arrive at a diagnosis of a cholestatic biochemical pattern in a patient who is taking a medication that is known to potentially cause drug-induced liver injury (DILI). The following differential diagnoses were considered: DILI caused by olanzapine, transient or occult choledocholithiasis, a biliary stricture or papillary dysfunction developing after cholecystectomy, cholestasis as a result of an infection, alternative medication-related DILI, and the possibility of small-duct cholangiopathy such as primary sclerosing cholangitis, as the patient has a history of colitis.

The fact that the olanzapine dose was increased at the same time that liver injury began suggests that there is a correlation. As LiverTox (2023) notes, although olanzapine-induced liver injury is rarely seen clinically, it is known to occur. Usually, it appears within one to four weeks of starting treatment or reaching the therapeutic dose. The resulting biochemical abnormalities can take different forms, including hepatocellular, mixed, or cholestatic patterns. Echater et al. (2022) reported a case involving a 43-year-old woman with bipolar disorder who developed jaundice, dark urine, pruritus, and vomiting three days after her olanzapine dose had been increased from 10 to 20 mg per day over two weeks, along with elevated liver enzymes after other possible causes had been excluded.

In contrast, this case showed a persistent biliary pattern, with only a slight rise in bilirubin over the period in question, and the main abnormalities were in alkaline phosphatase and gamma-glutamyl transferase. However, the clinical improvement after stopping olanzapine suggests a clinically significant association. Cholestatic DILI is diagnosed only after ruling out other possible conditions. Björnsson and Devarbhavi stress the importance of evaluating patients with marked increases in alkaline phosphatase for disorders such as hepatobiliary malignancy, choledocholithiasis, cholangitis, sepsis-related cholestasis, and other diseases. A clearly defined exclusion process improves diagnostic clarity and supports the differential diagnosis.

Distinguishing DILI from biliary obstruction remains difficult, even with biochemical and histological evidence. Clarifying the specific criteria or tests used to differentiate these conditions can improve diagnostic clarity. Yu et al. (2020) examined liver biopsies from patients who had been confirmed to have DILI and from those with chronic large-duct obstruction, primary sclerosing cholangitis, and primary biliary cholangitis, finding that cholestasis was present in 42% of the DILI cases as compared with 83% of the cases of chronic physical obstruction, which shows a considerable overlap in biliary-pattern injury. As a result, an approach that incorporates detailed medication history, imaging, and laboratory findings over time is essential for accurate diagnosis.

In this case, both ultrasonography and magnetic resonance cholangiopancreatography (MRCP) showed no choledocholithiasis or biliary ductal dilation, which suggested a lower probability of persistent large-duct obstruction. However, these imaging techniques have limitations, as a negative MRCP does not entirely rule out small stones or sludge. For example, a prospective randomized trial found that endoscopic ultrasound (EUS) identified stones in 35.7% of patients who were considered negative for common bile duct stones after an MRCP (Peterson et al., 2021). Similarly, a retrospective cohort study found that EUS performed after a negative MRCP showed positive results in about 14% of patients still suspected of choledocholithiasis (Jones et al., 2020).

Recognizing these limitations can help determine appropriate next diagnostic steps when clinical suspicion remains high.

It should be emphasized that a previous cholecystectomy does not exclude the possibility of having future complications affecting the common bile duct. Potential ongoing problems include retained or recurrent stones, biliary sludge, benign strictures, or sphincter dysfunction, all of which may cause intermittent obstruction. Although it is important to recognize these possible complications, in this instance the fact that there are no obstructive lesions or dilation of the duct, together with the biochemical improvement that has occurred since olanzapine was stopped, indicates a diagnosis of drug-induced liver injury rather than mechanical obstruction.

It should also be taken into account that the patient had a previous diagnosis of colitis. In such a case, if the diagnosis had been confirmed as ulcerative colitis or Crohn's disease, the association with primary sclerosing cholangitis (PSC), particularly in instances of small duct PSC with normal cholangiography, would be more significant. Nevertheless, the existing records do not definitely confirm a diagnosis of inflammatory bowel disease and therefore allow no definite connection to small duct PSC.

5. CONCLUSION

A cholestatic liver injury caused by olanzapine may closely resemble obstructive hepatobiliary disease. In this case, a 53-year-old woman developed a serious cholestatic biochemical disorder after having recently increased the dose of olanzapine, with the level of alkaline phosphatase rising above 1000 U/L and a marked increase in gamma-glutamyl transferase. Although alkaline phosphatase levels pointed to the liver as the source, ultrasound and MRCP showed no ongoing biliary obstruction.

The drop in alkaline phosphatase after olanzapine was discontinued, together with the known association between olanzapine and cholestatic DILI, indicated that olanzapine-induced liver injury was the primary diagnosis. Nevertheless, the case illustrates why DILI must always be regarded as a diagnosis of exclusion and why other possibilities, such as occult or temporary obstruction, drugs apart from olanzapine, systemic disease, and an underlying cholangiopathy, must all be taken into account before concluding that there is a causal relationship.

Recognizing this overlap will help prevent both the early attribution of severe cholestasis to a medication and the need for unnecessary invasive biliary procedures when high quality imaging and the clinical course indicate a nonobstructive, drug-induced process.

6. ACKNOWLEDGMENTS

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7. DATA AVAILABILITY

This article is freely available and may be used by all members of the scientific and medical community.

Consent for participation

Verbal and written informed consent was obtained from the patient for the preparation and publication of this case report. Informed consent was obtained by the Department of Internal Medicine, Stanford Medical Clinic.

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REFERENCES

1. Bjornsson ES, Devarbhavi HC. Drug-induced cholestatic liver diseases. *Hepatology*. 2025;82(4):996-1015. doi:10.1097/HEP.0000000000001052.
2. National Institute of Diabetes and Digestive and Kidney Diseases. Olanzapine. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. National Library of Medicine.
3. Echater S, Hasnaoui M, El Bouchali W, Elghazouani F. Acute cholestatic hepatitis associated with olanzapine in a patient with bipolar disorder. *Rev Med Liege*. 2022;77(2):80-84. PMID:35143126.



4. Yu S, Vidal B, Peric M, Rosenbaum MW, Cates JMM, Gonzalez RS. Comparative histologic features among liver biopsies with biliary-pattern injury and confirmed clinical diagnoses. *Hum Pathol.* 2024;146:8-14. doi:10.1016/j.humpath.2024.03.003.
5. Suzuki M, Sekino Y, Hosono K, et al. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for the diagnosis of computed tomography-negative common bile duct stone: prospective randomized controlled trial. *Dig Endosc.* 2022;34(5):1052-1059. doi:10.1111/den.14193.
6. Wee D, Izard S, Grimaldi G, Raphael KL, Lee TP, Trindade AJ. EUS assessment for intermediate risk of choledocholithiasis after a negative magnetic resonance cholangiopancreatography. *Endosc Ultrasound.* 2020;9(5):337-344. doi:10.4103/eus.eus_57_20.

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