

Case Report

Letrozole-induced autoimmune hepatitis presenting with decompensated cirrhosis in an elderly woman: a case report

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ABSTRACT

Autoimmune hepatitis (AIH) is a chronic immune-mediated inflammatory liver disease characterized by progressive hepatocellular injury, elevated autoantibodies, and hypergammaglobulinemia. Drug-induced autoimmune hepatitis (DIAIH) is a rare clinical entity that closely resembles idiopathic autoimmune hepatitis in both clinical presentation and histopathological findings, making diagnosis challenging. Among the implicated medications, letrozole-associated autoimmune hepatitis has been reported only rarely in the literature. Herein this case reports the case of a 64-year-old female receiving letrozole therapy for breast carcinoma who presented with features of hepatic encephalopathy and worsening liver dysfunction. Laboratory investigations demonstrated markedly elevated liver enzymes, raised immunoglobulin G (IgG) levels, and positive anti-smooth muscle antibodies (ASMA). Radiological evaluation suggested chronic liver disease, while liver biopsy revealed interface hepatitis with established cirrhotic changes, findings consistent with autoimmune hepatitis. After exclusion of other causes of liver injury, a diagnosis of letrozole-induced autoimmune hepatitis was considered. Early recognition, prompt withdrawal of the offending drug, and timely initiation of appropriate management are essential to prevent progression to advanced liver disease and liver failure.

Keywords: Letrozole, Autoimmune hepatitis, Hepatic encephalopathy, Drug-induced liver injury

INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic inflammatory immune-mediated liver disease characterized by elevated transaminases, increased IgG levels, circulating autoantibodies, and histological evidence of interface hepatitis. The pathogenesis involves genetic predisposition, environmental triggers, and immune dysregulation leading to loss of self-tolerance.¹⁻⁴

AIH is classified into type 1 AIH (ASMA and/or antinuclear antibody positive) and type 2 AIH (anti-liver kidney microsomal type 1 antibodies) with type 1 more common in adult females.^{3,4}

DIAIH is a recognized entity in which certain medications trigger an autoimmune-like hepatic injury resembling

idiopathic AIH.⁵ Several drugs have been implicated, including antimicrobials and immunomodulatory agents.^{6,7} Letrozole is widely used in hormone receptor-positive breast cancer and is generally well tolerated, with only occasional mild elevations in liver enzymes. Reports of letrozole-induced autoimmune hepatitis progressing to cirrhosis are extremely limited.^{5,8}

In this report, we describe a case of letrozole-associated AIH presenting with hepatic decompensation and cirrhosis in an elderly female.

CASE REPORT

A 64-year-old postmenopausal woman presented with 3 days of altered sensorium preceded by 2–3 weeks of weakness, progressive confusion, and altered behaviour.

There was no history of fever, headache, seizures, focal neurological deficits, vomiting, or recent head injury.

She also reported decreased appetite and a gradual onset of abdominal distension. There were no history of upper gastrointestinal bleeding and no significant unintentional weight loss. No cholestatic symptoms were reported. Her past medical history was significant for being treated for breast carcinoma with surgery followed by letrozole for 8 months. Her adherence to letrozole had been consistent.

She had no prior history of liver disease, jaundice, blood transfusions, or viral hepatitis. There was no history of alcohol use, intake of alternative or herbal medications, or exposure to other potentially hepatotoxic drugs. There was no personal or family history suggestive of autoimmune

disease. The patient was drowsy but arousable, disoriented to time and place. She was icteric with mild pallor and bilateral pedal edema. Vital signs were stable.

Neurological examination revealed altered sensorium with the presence of asterixis.

Abdominal examination showed mild distension with shifting dullness. The liver was not palpable, and there was no splenomegaly. There were no features of peritonitis. Systemic examination was otherwise unremarkable. Initial laboratory evaluation revealed cytopenias, coagulopathy, and elevated serum IgG levels. Autoimmune markers were consistent with autoimmune hepatitis (Table 1). Liver function tests were deranged (Table 2).

Table 1: Baseline laboratory investigations.

Parameters	Value	Reference range	Units
Hemoglobin	9.8	12–15	g/dl
Total leukocyte count	5320	4000–11000	/mm ³
Platelet count	1.1 × 10 ⁵	1.5–4 × 10 ⁵	/mm ³
Prothrombin time	17.3	11–14	sec
International normalised ratio (INR)	1.29	<1.2	-
Total protein	8.1	6–8	g/dl
Albumin	2.9	3.5–5	g/dl
Serum ammonia	198	15–45	µmol/l
Serum immunoglobulin G	2840	700–1600	mg/dl
Anti-smooth muscle antibody	Positive	Negative	-
Anti-nuclear antibody	Negative	Negative	-
Anti-liver kidney microsomal type 1 antibody	Negative	Negative	-

Table 2: Liver function test trends.

Parameters	Initial	Follow-up	Reference range	Units
Total bilirubin	2.1	1.2	0.3–1.2	mg/dl
Direct bilirubin	0.8	0.5	<0.3	mg/dl
Aspartate aminotransferase	98	111	<40	IU/l
Alanine aminotransferase	33	57	<40	IU/l
Alkaline phosphatase	145	157	44–147	IU/l



Figure 1: Contrast-enhanced CT abdomen showing irregular liver margins with ascites suggestive of cirrhosis and portal hypertension.

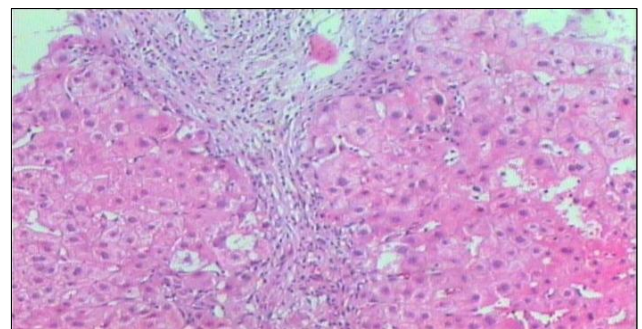


Figure 2: Liver biopsy H and E stain (x100) showing interface hepatitis with inflammatory infiltrates, suggestive of autoimmune hepatitis.

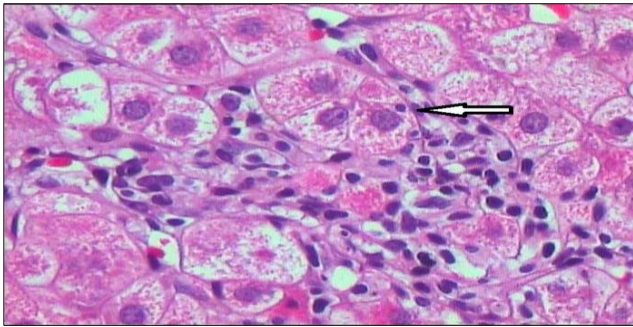


Figure 3: High-power view (x400) of liver biopsy demonstrating emperipolesis, a characteristic feature of autoimmune hepatitis.

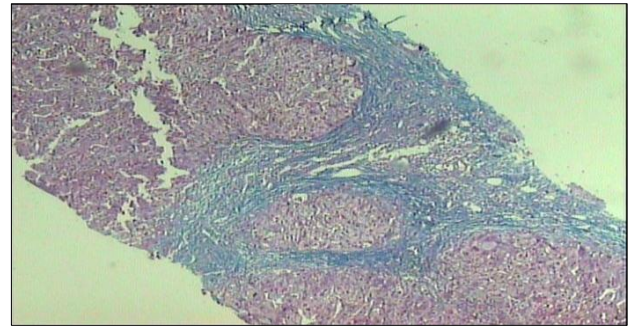


Figure 4: Liver biopsy (Masson's trichrome stain) showing fibrous septa with nodular architecture, consistent with cirrhosis.

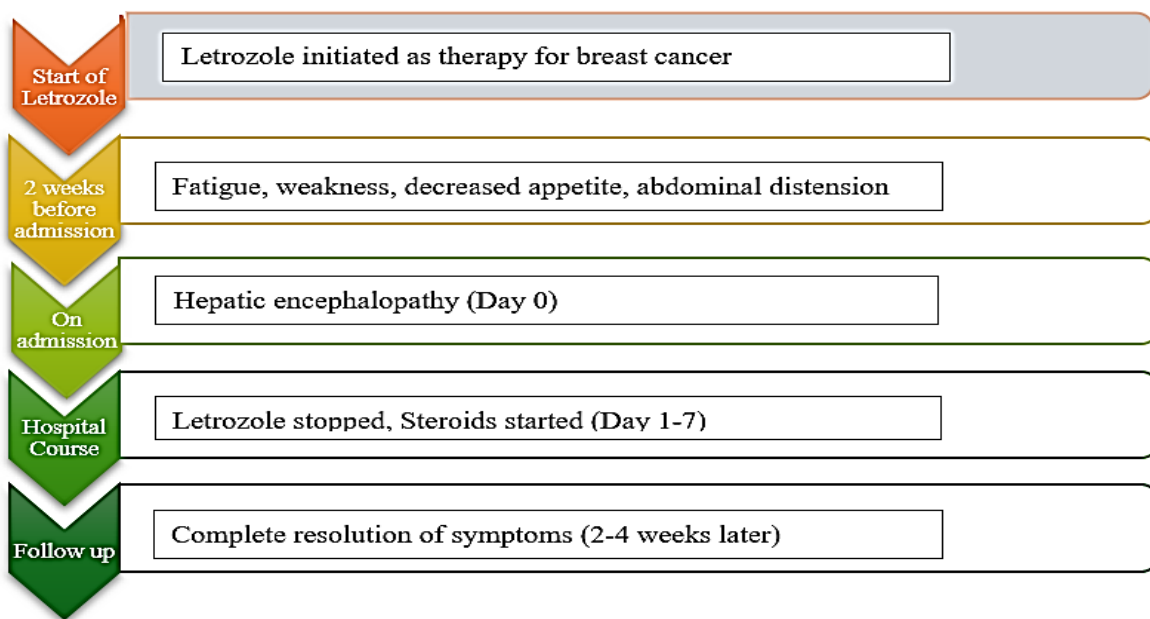


Figure 5: Clinical timeline of letrozole-induced autoimmune hepatitis.

Viral hepatitis markers including hepatitis B surface antigen and anti-HCV were negative. Contrast-enhanced computed tomography of the abdomen showed irregular liver margins, mild ascites, and splenic vein collaterals suggestive of cirrhosis with portal hypertension (Figure 1).

Liver biopsy demonstrated interface hepatitis with lymphoplasmacytic infiltrates along with established cirrhotic changes, consistent with AIH (Figures 2-4). The patient was initially managed with supportive care, which included diuretics, lactulose, rifaximin, and beta-blockers.

In view of suspected DIAIH, letrozole was discontinued. Corticosteroid therapy was initiated with prednisolone 40 mg/day (0.5-1 mg/kg), followed by gradual tapering.

The patient demonstrated marked clinical improvement following withdrawal of letrozole and initiation of corticosteroid therapy, with complete resolution of symptoms on follow-up.

The chronological sequence of clinical events, investigations, and management is summarised in Figure 5.

DISCUSSION

DIAIH is a condition that closely resembles idiopathic AIH in its clinical, serological, and histological features. Diagnosis is based on temporal drug association, exclusion of other causes, and improvement following withdrawal of the offending agent.^{5,6}

Letrozole is generally considered safe with minimal hepatic adverse effects. Progression to cirrhosis with hepatic encephalopathy is particularly rare.^{5,8} The pathogenesis is thought to involve immune dysregulation leading to classical AIH-like injury.^{2,4}

The diagnosis was supported by prolonged exposure to letrozole, exclusion of other causes, and characteristic

serological and histological findings. The presence of hepatic encephalopathy indicated advanced liver involvement.

Although alanine aminotransferase predominance is typical, atypical patterns including AST-predominant elevation may be seen in advanced disease or cirrhosis as seen in this case.

The diagnosis of AIH was supported using the simplified international autoimmune hepatitis group (IAIHG) scoring system. The cumulative score indicated a diagnosis of autoimmune hepatitis (Table 3).

To evaluate the likelihood of DIAIH, the Roussel Uclaf Causality Assessment Method (RUCAM) was applied. The calculated RUCAM score indicated a highly probable association between letrozole and the development of AIH (Table 4).

IAIHG and RUCAM scores strongly supported the diagnosis of letrozole-induced AIH in this patient. Management involves withdrawal of the offending drug and initiation of corticosteroid therapy. The marked improvement observed in our patient following discontinuation of letrozole and steroid therapy further supports the diagnosis and reversibility of this condition when treated early.⁹

Table 3: Simplified IAIHG score.

Parameter	Finding	Score
Autoantibodies	ASMA positive	+2
Immunoglobulin G level	>1.1 x upper limit of normal	+2
Liver histology	Typical of AIH (interface hepatitis with lymphoplasmacytic infiltrate)	+2
Absence of viral hepatitis	Yes	+2
Final score		8 (definite AIH)

Table 4: RUCAM score.

Parameter	Score
Time to onset of liver injury after starting letrozole (8 months)	+2
Course after drug withdrawal (improvement in liver function)	+3
Risk factors (age >55 years)	+1
Concomitant drugs	0
Exclusion of non-drug causes (viral, alcoholic, metabolic)	+2
Known hepatotoxicity of letrozole (rare but reported)	+1
Rechallenge	0
Total score	9 (highly probable causality)

This case emphasises considering DIAIH in unexplained liver dysfunction, particularly in the setting of long-term medication use. Early diagnosis and intervention are crucial to prevent progression to irreversible liver damage.

CONCLUSION

Letrozole-induced AIH is rare but can progress to cirrhosis. Early recognition, drug withdrawal, and corticosteroid therapy are crucial for favorable outcomes.

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REFERENCES

- Andrade RJ, Chalasani N, Björnsson ES, Suzuki A, Kullak-Ublick GA, Watkins, et al. Drug-induced liver injury. Nat Rev Dis Primers. 2019;5(1):58.
- Manns MP, Czaja AJ, Gorham JD, Krawitt EL, Mieli-Vergani G, Vergani D, et al. Diagnosis and management of autoimmune hepatitis. Hepatology. 2010;51(6):2193-213.
- European Association for the Study of the Liver. EASL clinical practice guidelines: autoimmune hepatitis. J Hepatol. 2015;63(4):971-1004.
- Jameson JL, Fauci AS, Kasper DL, Dennis L. Kasper. Harrison’s Principles of Internal Medicine. 21st edition. New York: McGraw-Hill. 2022.
- Björnsson E, Talwalkar J, Treeprasertsuk S, Kamath PS, Takahashi N, Sanderson S, et al. Drug-induced autoimmune hepatitis: clinical characteristics and prognosis. Hepatology. 2010;51(6):2040-8.

6. Chalasani NP, Hayashi PH, Bonkovsky HL, Navarro VJ, Lee WM, Fontana RJ. ACG clinical guideline: diagnosis and management of idiosyncratic drug-induced liver injury. *Am J Gastroenterol.* 2021;116(5):878-98.
7. Feldman M, Friedman LS, Brandt LJ, editors. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease.* 11th edition. Philadelphia: Elsevier. 2021.
8. de Boer YS, Kosinski AS, Urban TJ, Zhao Z, Long N, Chalasani N, et al. Features of autoimmune hepatitis in patients with drug-induced liver injury. *Clin Gastroenterol Hepatol.* 2017;15(1):103-12.
9. Gharia B, Seegobin K, Maharaj S, Marji N, Deutch A, Zuberi L. Letrozole-induced hepatitis with autoimmune features: a rare adverse drug reaction with review of the relevant literature. *Oxf Med Case Rep.* 2017;2017(11):omx074.

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