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CASE REPORT

Management of non-alcoholic fatty liver disease incidentally detected during other medical assessments

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Abstract

Elevated liver enzyme levels are a frequent incidental finding in primary care, and non-alcoholic fatty liver disease is the main cause of incidental elevation of liver enzymes worldwide. The features of the disease vary from simple steatosis, characterized by a benign prognosis, to non-alcoholic steatohepatitis and cirrhosis, increasing morbidity and mortality. In this case report, abnormal liver activity was incidentally detected during other medical assessments. The patient was treated with silymarin 140 mg three times daily, resulting in decreased serum liver enzyme levels over treatment with a good safety profile.

This article is part of the *Current clinical use of silymarin in the treatment of toxic liver diseases: a case series* Special Issue: https://www.drugsincontext.com/special_issues/current-clinical-use-of-silymarin-in-the-treatment-of-toxic-liver-diseases-a-case-series

Keywords: case report, elevated liver enzymes levels, herb-induced liver injury, non-alcoholic fatty liver disease, silymarin.

Citation

Lee YY, Tee V. Management of non-alcoholic fatty liver disease incidentally detected during other medical assessments. *Drugs Context*. 2023;12:2023-1-3. https://doi.org/10.7573/dic.2023-1-3

Introduction

Elevations in liver enzyme levels are a common incidental finding in primary health care settings and are associated with higher rates of mortality and comorbidity.[1] The main causes of deranged liver activity are alcohol and medication abuse, non-alcoholic fatty liver disease (NAFLD) and viral infections.[1]

Silymarin, a milk thistle extract, is the botanical medication most used for the management of liver disorders owing to its presumed hepatoprotective and antioxidant properties.[2]

In this case report, a patient planning surgery due to lumbar stenosis was recommended for silymarin treatment, as increased liver enzyme levels were incidentally found during the examination.

Ethics statement

No information is reported that could enable the patient to be identified; therefore, no patient consent to report this case was required. This manuscript was prepared according to CARE guidelines.

Case report

On 18 December 2016, a 56-year-old woman was referred to our department for planned surgery due to lumbar stenosis, but deranged liver enzyme levels were noted during the visit.

The liver disease behind the increased liver enzymes was unclear, but the hepatobiliary system ultrasound imaging noted mild liver infiltration, suggesting NAFLD.

The patient was also known for taking traditional medicines, with herbal medications, such as *Habbatus Sauda* and garlic pills, raising the hypothesis of herbal toxicity (herb-induced liver injuries; HILI).

The patient had a family history of thyroidectomy. Fine-needle aspiration cytology and a neck ultrasound were performed 5 years prior to the physician's examination (21/9/2011 and 3/10/2011, respectively), showing a thyroid suggestive of colloid goitre and a solitary right thyroid nodule, respectively. Moreover, the patient has a degenerative spine disease with lumbar stenosis L4/L5 and L5/S1, and she underwent open laminotomy of left L4 and right L5 and discectomy of left L5/S1 on 20 January 2017.

At the physician's examination (18 December 2016), the liver was one fingerbreadth palpable, and no jaundice was observed. The liver function tests (used to support diagnosis and monitoring of a liver disease or damage) revealed abnormal increases in the levels of some enzymes, particularly of alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) (Table 1).

Table 1. Liver function test at physician's examination.

Liver function test	18/12/2016 – Physician's examination
ALT (U/L)	318
AST (U/L)	149
ALP (U/L)	173
Total bilirubin (µmol/L)	86
Total protein (g/L)	73
Albumin (g/L)	42

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase.

The patient also underwent abdominal ultrasound assessment: the liver was smooth in outline, and no focal lesions were observed, but a patchy area of increased echogenicity emerged in both lobes (15 cm in craniocaudal diameter). The gallbladder was well distended, no calculus and wall thickening were observed, the bile duct was common and the rest of the biliary tree was not dilated. Pancreas and spleen evaluation were ordinary, and both kidneys were normal in echogenicity. In addition, the urinary bladder was well distended and had no calculus or mass within.

The complete patient clinical picture, along with the absence of positive serology for hepatitis B virus (HBV) or hepatitis C virus (HCV) and the apparent absence of excessive alcohol use, suggested the presence of early-stage NAFLD, the most common cause of elevated liver enzyme levels, characterized by mild liver steatosis (infiltration of extra fat). Furthermore, it cannot be excluded that liver damage could also be favoured by the hypothesis of HILI.

However, to manage the increased liver enzyme activity, the patient was prescribed treatment with silymarin (Legalon®) 140 mg three times daily (TDS) (18/12/16 to 20/3/17), because no other treatment-suitable options were available, and the patient was not eligible for clinical trials due to her medical conditions.

During different follow-up examinations (on 19/1/17, 13/3/17, 04/03/2021 and 18/07/2021), ALT, AST and ALP levels were significantly reduced and comparable to physiological levels (Table 2), suggesting a beneficial effect of silymarin treatment on the liver biochemical parameters.

The patient's clinical history is summarized in Table 3.

Table 2. Liver function test at different follow-up examinations.

Liver function test	19/01/2017	13/03/2017	04/03/2021	18/07/2021
ALT (U/L)	16	17	20	22
AST (U/L)	18	18	18	16
ALP (U/L)	99	91	110	116
Total bilirubin (µmol/L)	120	120	103	120
Total protein (g/L)	75	72	70	69
Albumin (g/L)	44	41	43	42

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase.

Table 3. Relevant data organized as a timeline.

Date	Events
21/09/2011	Fine-needle aspiration cytology showed a thyroid suggestive of colloid goitre
03/10/2011	Neck ultrasound highlighted a solitary right thyroid nodule
18/12/2016	1. Physician's examination: liver one fingerbreadth palpable and no jaundice; abnormal liver enzyme activity 2. Abdominal ultrasound 3. Diagnosis of non-alcoholic fatty liver disease, with the hypothesis of herb-induced liver injury
18/12/2016–20/03/2017	Silymarin 140 mg three times daily treatment
19/01/2017	Follow-up with significant reduction of liver activity
13/03/2017	Follow-up with normal liver activity
04/03/2021	Follow-up with normal liver activity
18/07/2021	Follow-up with normal liver activity

Discussion

In North America and Europe, NAFLD is the most common cause of incidentally elevated liver enzymes.[3] Type II diabetes, insulin resistance, hyperlipidaemia and obesity are well-known conventional risk factors for the development of NAFLD.[3] Drugs and polytherapies also represent an alternative cause of the fatty liver disease (drug-induced liver injury; DILI), characterized by intracellular lipid accumulation and steatosis in hepatocytes as a histopathological pattern.[4]

Particularly, during the last decades, the use of herbal supplements and alternative and traditional therapies has substantially increased worldwide.[5,6] Moreover, these drugs are easily obtained without a specific prescription, and their safety and efficacy are not always well defined. Indeed, worldwide studies highlighted the increased incidence of HILI in recent years,[6,7] and traditional medicine or herbal and dietary supplements are now one of the leading causes of DILI.[7]

Different liver function markers are usually used in clinical settings to assess and monitor patients with liver diseases. Commonly, patients with NAFLD may present with elevated concentrations of aminotransferases, particularly ALT and AST levels.[8] ALP can also be increased in parallel to other liver function markers. Furthermore, low levels of total protein in the blood can also occur because of impaired liver function; however, bilirubin and albumin levels are rarely altered.[8]

The management of HILI and DILI first involves interrupting all suspected traditional medicines, and liver function should be carefully monitored.[9] As a second line, supportive therapy with hepatoprotective drugs (N-acetylcysteine, antioxidants and corticosteroids) may be suggested to patients with DILI or other forms of liver injury.[9]

In this case report, after carefully evaluating the whole clinical picture, we recommended silymarin 140 mg TDS treatment for 4 months (18/12/16–20/3/17) to manage the increased liver enzyme activity and normalize liver function test outcomes.

This therapeutic choice was supported and based on several studies performed in patients with liver diseases, showing hepatoprotective and antioxidant properties of silymarin treatment. Specifically, silymarin significantly decreased ALT and AST levels[2,10] and reduced hepatic fat accumulation, as demonstrated by changes in hepatorenal brightness index at the ultrasonography imaging.[10]

At the follow-up visits (19/1/17, 13/3/17, 4/3/2021 and 18/7/2021), serum ALT, AST and ALP levels were notably decreased (Table 2). Additionally, there were no significant adverse effects during this period, and long-term treatment adherence was good. This demonstrated the efficacy of long-term maintenance and safety of silymarin in benign HILI and early-stage fatty liver disease.

Conclusion

NAFLD is the most common incidental cause of liver disease worldwide, marked by fat accumulation in the liver and alterations in liver biochemical tests. Medicinals represent a plausible cause of fatty liver disease. In

recent years, the use of herbal or traditional drugs has risen considerably worldwide, increasing at the same time the incidence of HILI.

In this case report, abnormal serum levels of liver enzymes were incidentally detected during other medical assessments. The patient was treated with silymarin 140 mg TDS, resulting in decreased serum ALT, AST and ALP levels over treatment with a good safety profile.

Thus, silymarin may be accepted as a safe, supportive therapy for the management of HILI and to maintain disease stability of NAFLD because the designed therapeutic dosage is known to be well tolerated, with only a few minor adverse events reported.[11] Therefore, its use in the management of NAFLD (or HILI) should be considered, if feasible.

Contributions: All authors contributed equally to the preparation of this manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosure and potential conflicts of interest: The authors declare that they have no conflicts of interest relevant to this manuscript. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2023/04/dic.2023-1-3-COI.pdf

Acknowledgements: Editorial assistance was provided by Francesca Cappellini, PhD, Mattia Zamboni, and Aashni Shah (Polistudium SRL Milan, Italy). This assistance was supported by Viatris Inc.

Funding declaration: This project was conducted with the non-conditioning assistance of Viatris Inc.

Article URL: https://www.drugsincontext.com/management-of-non-alcoholic-fatty-liver-disease-incidentally-detected-during-other-medical-assessments

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Provenance: Submitted; externally peer reviewed.

Submitted: 10 January 2023; **Accepted:** 29 March 2023; **Published:** 11 May 2023.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: 6 Green Lane Business Park, 238 Green Lane, New Eltham, London, SE9 3TL, UK.

BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252 7720 07.

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