

Reversal of non-alcoholic fatty liver disease complicated with cirrhosis by traditional Chinese medicine: a case report and experience

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Author contributions

All authors read and approved the final manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; TCM, traditional Chinese medicine; AST, aspartate transaminase; ALT, alanine transaminase; CAP, controlled attenuation parameter.

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Abstract

Non-alcoholic fatty liver disease (NAFLD) has become the world's most common chronic liver disease and is considered one of the main causes of occult liver cirrhosis. To date, major guidelines in China and abroad have not recommended any drugs with precise efficacy and safety for NAFLD, especially for NAFLD-related liver fibrosis or cirrhosis, which lack effective drugs. Traditional Chinese medicine has significant curative effects and advantages in preventing and treating NAFLD. We retrospectively analyzed a case of liver cirrhosis due to NAFLD that was treated solely with traditional Chinese medicine for nearly one year at the Diagnosis and Treatment Center of Advantage Specific Diseases for Fatty Liver in our hospital to provide a reference for the prevention and treatment of non-alcoholic liver fibrosis and liver cirrhosis by traditional Chinese medicine.

Keywords: traditional Chinese medicine; non-alcoholic fatty liver disease; liver cirrhosis

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a metabolic stress-induced liver injury closely related to insulin resistance (IR) and genetic susceptibilities. Its disease spectrum includes non-alcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), liver cirrhosis (LC), and hepatocellular carcinoma (HCC) [1]. Recent studies have shown that NAFLD, especially NASH, is the most common cause of cryptogenic cirrhosis (CC) [2–4]. At present, according to the major guidelines both in China and abroad, there is no effective and safe drug for treating NAFLD. However, traditional Chinese medicine (TCM) has definite efficacy and substantial advantages in preventing and treating NAFLD. It even has certain efficacy in blocking and reversing fibrosis and early cirrhosis. In recent years, the TCM diagnosis and treatment center for fatty liver and obesity in our hospital has adopted pure TCM for the dialectical treatment of more than 6,000 cases of NAFLD; the treatment has shown significant effects, including in some patients with NAFLD cirrhosis. The details of the treatment and follow-up for one year of a well-documented patient with early-stage cirrhosis due to NAFLD are summarized below.

Case profile

The patient is a 57-year-old middle-aged woman. On June 1, 2020, she felt distending pain and discomfort in the liver region, and an upper abdominal CT scan was performed in a local hospital (Figure 1). The results suggested liver cirrhosis, thick spleen, and fatty liver (severe). On June 18, 2020, she visited the TCM Advantage Special Disease Diagnosis and Treatment Center for Fatty Liver and Obesity at our hospital, complaining of “liver pain and discomfort for more than one month.” The physical examination results were: height 154 cm, weight 60 kg, and body mass index (BMI) 25.3 kg/m² (slightly obese); yellow staining of the skin and sclera were absent, and she was negative for the cardiopulmonary abdomen. Her tongue was pale with a white coating, with obvious tooth marks, and she had a wiry and thin pulse. Accessory examination included liver function: aspartate transaminase (AST) 57 U/L, alanine transaminase (ALT) 54 U/L; and FibroScan: controlled attenuation parameter (CAP) 323 dB/m, E 27.4 kPa. Western medicine diagnosis: NAFLD liver cirrhosis (compensatory stage). TCM diagnosis: liver accumulation (spleen deficiency, stagnation of phlegm, and blood stasis). The treatment used was based on the principles of the invigorating spleen, assisting transportation, elevating yang, and eliminating turbidity. To apply the modified Jianpi Huazhuo Xiaozhi Prescription: *Rhizoma atracylodes macrocephalae* 15g, vinegar *Radix bupleuri* 6 g, *Poria cocos* 10 g, *Radix salviae miltiorrhizae* 15 g, *Alismatis rhizoma* 10 g, *Fructus Crataegi* 10 g, *Seaweed* 10 g, fried *Semen cassia* 10 g, *Folium nelumbinis* 12 g, and *Herba artemisiae scopariae* 10 g were used to decoct 15 doses of the Chinese medicinal decoction. One dose per day consisted of 400 ml of the decoction (200 ml, twice daily at a suitable temperature). The patient was asked to adjust her dietary structure, and a balanced diet of moderate fat and carbohydrate was recommended. Sugar-containing beverages, cakes, and deep-processed refined foods were limited. Her three meals a day were timed and consisted of moderate amounts, and the calorie of each supper and her eating behavior after supper were strictly controlled. To avoid sitting for a long time and moving less, she was recommended a moderate aerobic exercise regime of 30 min a day five times a week.

On July 22, 2020, the patient had her second visit. After taking 15 doses of the TCM decoction, her liver region discomfort was obviously relieved, with her tongue and pulse unaltered from her first visit. Re-examination found the following: liver function: AST 45 U/L, ALT 43 U/L; fasting blood sugar: 6.85 mmol/L; FibroScan: CAP 356 dB/m, E 22.1 kPa. The treatment plan thereafter consisted of the continuation of the Chinese medicine decoction, on the above-mentioned basis, with 10 g of *Eupatorium fortunei* added to remove the dampness and turbidity with an aromatic odor, and the

dose of vinegar *Radix bupleuri* was adjusted to 9 g. Altogether she has prescribed 30 doses of the Chinese medicinal decoction. She was instructed to take one dose orally daily, decocted in 400 ml of water, 200 ml in the morning, and 200 ml in the evening, at a moderate temperature.

On September 3, 2020, the patient had her third visit. The right hypochondriac discomfort disappeared, no new discomfort occurred, and the tongue and pulse were as before. Re-examination found normal liver function and blood sugar. The treatment has achieved apparent results, so the original treatment plan was continued, and she was prescribed another 30 doses as before.

On October 4, 2020, the patient had her fourth visit. The patient showed no discomfort, pale tongue with white coating, teeth marks, and wiry and thin pulse. Re-examination found normal liver function and blood glucose. The same decoction was prescribed for another 30 doses and was taken consecutively, decocted in water, at one daily dose.

On December 5, 2020, the patient had her fifth visit. She exhibited no discomfort, pale tongue with white fur, fewer teeth marks, and thin pulse. Re-examination found normal fasting blood sugar is normal. Based on the last prescription, to remove the *Eupatorium fortunei*, 20 g of *Phyllanthus urinaria* and 3 g of *Red yeast rice* were added, and 30 doses of traditional Chinese medicine decoction were taken continuously.

On February 1, 2021, the patient had her sixth visit. She showed no obvious discomfort. The tongue was pale with white coating, slightly tooth-marked, and the thin pulse persisted. She weighed 52 kg, with a height of 154 cm and a BMI of 21.9 kg/m². Re-examination found normal liver and kidney functions and normal blood glucose levels. Alpha-fetoprotein tumor marker (AFP): 1.86 ng/ml; FibroScan: CAP 252 dB/m, E 17.5 kPa. B-scan ultrasonography of the abdomen showed fatty liver, cholecystitis, and calculi. The treatment scheme was as follows: based on the previous treatment plan, *Herba artemisiae scopariae* was removed, and 20 g of *Herba sedi* and 10 g of *Rhizoma polygoni cuspidati* were added to clear heat and promote diuresis. The dose of *Semen cassia* was adjusted to 10 g, vinegar *Radix Bupleuri* was adjusted to 6 g, and 15 doses of Chinese medicinal decoction were administered consecutively.

On February 20, 2021, the patient had her seventh visit. She had no complaints. The tongue was pale, with a thin and white tongue coating, obvious reduction of tooth marks as before, and persisting thin pulse. Based on the last treatment, the dose of *Folium nelumbinis* was adjusted to 20 g, and 30 oral doses of Chinese medicinal decoction were administered.

On May 1, 2021, the patient had her eighth visit. The family members of the patient came to the hospital in her stead and reported that there was nothing wrong with the patient. Re-examination done in another hospital found normal liver function, kidney function and blood glucose level. Blood lipid series: CHO 5.47 mmol/L. Repeated at another hospital on April 25, 2021, FibroScan: CAP 244 dB/m and E 9.9 kPa. Based on the last prescription, 3 g of broken pieces of *Herba rabdosiae cirrhosae* was added, and the dose of *Folium nelumbinis* was adjusted to 15 g, and 15 doses were taken continuously.

On May 31, 2021, the patient had her ninth visit. There was no discomfort. Her height was 154 cm, her weight was 48 kg, and her BMI was 20.2 kg/m². The tongue was pale and dark, with a thin and white tongue coating, slight tooth marks, and her thin pulse persisted. Re-examination found normal liver function and fasting blood glucose. FibroScan: CAP 237 dB/m and E 9.4 kPa (Table 1). CT of the liver uncovered no obvious abnormality (Figure 2).

Table 1 Changes of fibroscan value in patients during treatment

Time	CAP (unit: dB/m)	E (unit: kPa)
2020.06.18	323	27.4
2020.07.22	356	22.1
2021.02.01	252	17.5
2021.04.25	244	9.9
2021.05.31	237	9.4

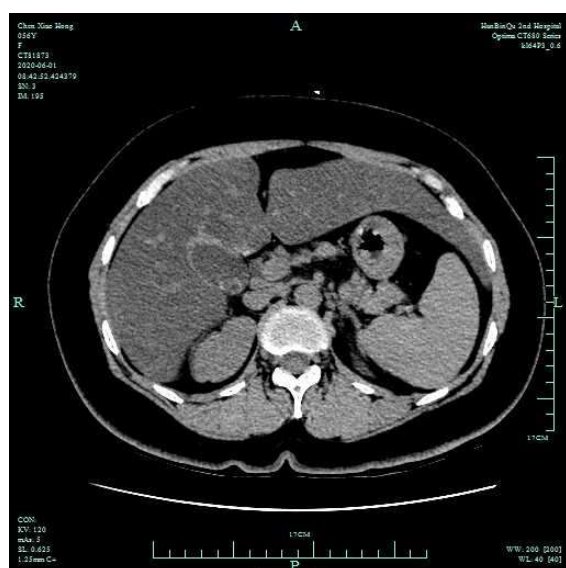


Figure 1 Image before treatment

After nearly one year of treatment with Chinese medicine, the liver hardness value E (< 17.5 kPa), the CAP value (< 238 dB/m), and the liver density value (CT value: liver/spleen > 1.0) were all restored to normal, thus suggesting that the severe fatty liver and early cirrhosis were reversed [5]. Requesting patients to have a proper diet and regular exercise, control their BMI, and have regular follow-ups after drug discontinuation are recommended

Discussion

The global incidence of NAFLD is between 10%–40%, and about 20% of patients will develop cirrhosis. The incidence of NAFLD in China is between 6%–45%, of which about one-third of patients have NASH, and the incidence of cirrhosis based on NASH is between 15%–25% [1]. Patients with NAFLD-related cirrhosis in the compensatory phase have a long disease course. They often have no apparent clinical manifestation in the early phase, showing occult progression that is difficult to detect. Once the disease progresses to the decompensated cirrhosis stage or HCC stage, the prognosis becomes poor.

The primary goals of treatment for NAFLD are improving IR and preventing and treating metabolic syndrome and its associated end-stage organ lesions, thereby improving the patient's quality of life and prolonging survival time. The second is anti-hepatic fibrosis treatment. Patients with NASH need to suspend the progression of liver disease and reduce or prevent the occurrence of end-stage liver diseases such as liver cirrhosis and liver cancer. However, it is regrettable that there are no safe and effective recommended drugs in all the major guidelines for NAFLD in China or abroad, and no medicine is available for liver fibrosis or cirrhosis [5–7].

As is known to all, liver protection and anti-inflammation are one of the most significant advantages of TCM in the prevention and treatment of chronic liver disease. Several clinical practices in our previous experience have confirmed that TCM compounds have specific efficacy in improving liver function and metabolic disorders [8, 9]. TCM has shown remarkable efficacy in preventing and treating chronic hepatitis B liver fibrosis or early cirrhosis, but clinical reports on NAFLD cirrhosis are relatively sparse [10, 11].

NAFLD can be classified into such disease categories as “hypochondriac pain”, “Fei Qi”, and “accumulation” in TCM. The occurrence of this disease is often associated with improper diet, loss of balance between work and rest, emotional disorders, and deficiency and decline of zang-fu organs, which lead to the failure of the spleen to maintain good health and transport, as well as phlegm-dampness stagnation. The disease is in the liver, and the basic pathogenesis is spleen deficiency and loss of transport. Based on the view of NAFLD

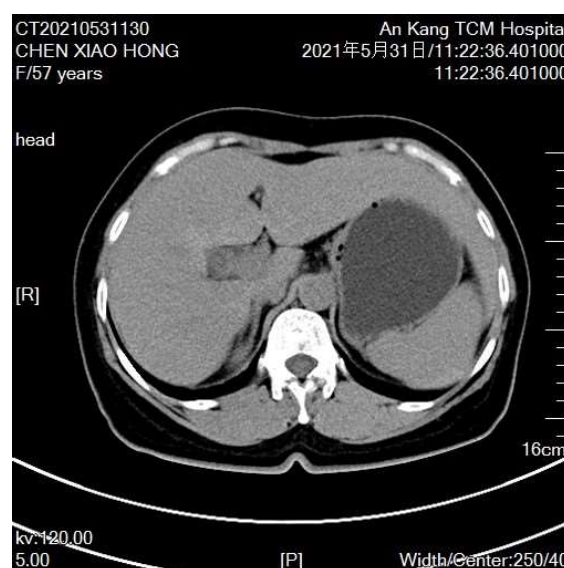


Figure 2 Image after treatment

from the perspective of “treatment based on spleen”, we have created the Jianpi Huazhuo Xiaozhi Decoction, which is prepared using *Rhizoma atractylodis macrocephalae*, *Radix bupleuri*, *Poria cocos*, *Radix salviae miltiorrhizae*, *Seaweed*, *Alismatis rhizoma*, *Fructus Crataegi*, *Massa medicata fermentata*, *Folium nelumbinis*, *Semen cassiae*, etc. And modified in the clinic for the treatment of NAFLD and related metabolic diseases, each to good effect.

Transient elastography (TE) is an ultrasonic elastography technique that measures the liver stiffness measurement (LSM) to assess the staging of liver fibrosis. It is non-invasive and rapid and has been widely used for the diagnosis and efficacy evaluation of liver fibrosis [12, 13]. Combined with the initial CT morphology and LSM values of her liver, the clinical diagnosis of our patient was NAFLD cirrhosis (early). Chinese medicine was used throughout the treatment for nearly one year. During the multiple reviews, the CAP and E values showed downward trends. At the end of the treatment, the CT value of the patient returned to normal, and the liver morphology improved (Figure 2). The CAP value returned to normal, and the E value was close to normal. Based on the comparison of the CT findings and FibroScan test data before and after the treatment, we believe that the combination of Chinese medicine treatment with behavioral therapy not only reversed the steatosis in the patient's liver but also improved the early stage of liver cirrhosis to a large extent, indicating that the recipe has significant efficacy in the treatment of NAFLD-related liver cirrhosis. As a research case, the lack of pre-and post-control of liver puncture biopsy before and after treatment is a shortcoming of this case study.

This case is not isolated, and several similar cases are still undergoing follow-up and need to be further summarized. Based on the clinical experience of more than 6,000 patients for whom TCM was used to prevent and treat NAFLD in the early stage in the Center for Diagnosis and Treatment of Fatty Liver and Obesity, as well as early relevant clinical research and experimental research, we proposed the goal and concept of “three standards” in the treatment of NAFLD with TCM on three levels, namely, protecting the liver, anti-inflammation treatment, reducing enzyme, improving metabolic disorders (blood glucose, blood lipid, uric acid, etc.), and reversing pathological liver changes (liver steatosis, liver fibrosis/early cirrhosis) [10, 11, 14]. Based on the concept of holism in TCM and from the perspective of integrating metabolic diseases, TCM has the characteristics and advantages of multi-directional and multi-target effects, which are worthy of further exploration and research in clinical practice to provide a safe and effective scheme using TCM for the prevention and treatment against this disease.

References

1. Xue R, Fan JG. Brief introduction of an international expert consensus statement: A new definition of metabolic associated fatty liver disease. *J Clin Hepatol* 2020;36(6):1224–1227. (Chinese) Available at: <http://125.221.83.226:18/rwt/CNKI/https/NNYHGLUDN3WX TLUPMW4A/kcms/detail/detail.aspx?FileName=LCGD202006010&DbName=CJFQ2020>
2. Lai J, Wang HL, Zhang X, Wang H, Liu X. Pathologic Diagnosis of Nonalcoholic Fatty Liver Disease. *Arch Pathol Lab Med* 2022;146(8):940–946. Available at: <https://doi.org/10.5858/arpa.2021-0339-RA>
3. Kang JH, Matsui T. Changing Etiology in Liver Cirrhosis in Sapporo, Japan. *Euroasian J Hepatogastroenterol* 2018;8(1):77–80. Available at: <https://doi.org/10.5005/jp-journals-10018-1266>
4. Wang TY, Shao CP, Xu YQ. Clinical diagnosis of 42 case of cryptogenic cirrhosis. *Chin J Med* 2022;57(01):88–91. (Chinese) Available at: <https://doi.org/10.3969/j.issn.1008-1070.2022.01.024>
5. National Workshop on Fatty Liver and Alcoholic Liver Disease, Chinese Society of Hepatology, Chinese Medical Association; Fatty Liver Expert Committee, Chinese Medical Doctor Association. Guidelines of prevention and treatment for nonalcoholic fatty liver disease: a 2018 update. *J Clin Hepatol* 2018;34(5):947–957. (Chinese) Available at: <http://125.221.83.226:18/rwt/CNKI/https/NNYHGLUDN3WX TLUPMW4A/kcms/detail/detail.aspx?FileName=XYWS201805003&DbName=CJFQ2018>
6. Eslam M, Sarin SK, Wong VW, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Hepatol Int* 2020;14(6):889–919. Available at: <https://doi.org/10.1007/s12072-020-10094-2>
7. Review Team, LaBrecque DR, Abbas Z, et al. World Gastroenterology Organisation global guidelines: Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. *J Clin Gastroenterol* 2014;48(6):467–73. Available at: <https://doi.org/10.1097/MCG.0000000000000116>
8. Hua P, Guo W, Xue JD, Li FP, Cui X. Evaluation the Clinic Effect for Treatment of Non-alcoholic Steatohepatitis by Jianpi Huazhuo Xiaozhi Prescription. *Chin J Integr Tradit West Med Liver Dis* 2020;30(05):408–410. (Chinese) Available at: <http://125.221.83.226:18/rwt/CNKI/https/NNYHGLUDN3WX TLUPMW4A/kcms/detail/detail.aspx?FileName=ZXGB202005008&DbName=CJFQ2020>
9. Cui X, Zang FY, Li L, et al. Experience of successfully treating a child with severe metabolic-associated fatty liver disease in 12 weeks using traditional Chinese medicine alone. *J Gastroenterol Hepatol Res* 2021;3(2):9. Available at: <https://doi.org/10.53388/ghr2021-06-035>
10. Li H. Advances in anti hepatic fibrotic therapy with Traditional Chinese Medicine herbal formula. *J Ethnopharmacol* 2020;251:112442. Available at: <https://doi.org/10.1016/j.jep.2019.112442>
11. Song YN, Chen J, Cai FF, et al. A metabolic mechanism analysis of Fuzheng-Huayu formula for improving liver cirrhosis with traditional Chinese medicine syndromes. *Acta Pharmacol Sin* 2018;39(6):942–951. Available at: <https://doi.org/10.1038/aps.2017.101>
12. Xu XY, Ding HG, Li WG, et al. Guidelines for diagnosis and treatment of liver cirrhosis. *J Clin Hepatol* 2019;35(11):2408–2425. (Chinese) Available at: <http://125.221.83.226:18/rwt/CNKI/https/NNYHGLUDN3WX TLUPMW4A/kcms/detail/detail.aspx?FileName=LCGD201911006&DbName=CJFQ2019>
13. Expert consensu on diagnosis of hepatic fibrosis with transient elastography (2018 update). *Chin J Hepatol* 2019;(03):182–191. (Chinese) Available at: <https://doi.org/10.3760/cma.j.issn.1007-3418.2019.03.004>
14. Cui X, Sheng GG, Xing YF, et al. Preventive and therapeutic effect and mechanism of Jianpi Huazhuo Xiaozhi Formula on non-alcoholic steatohepatitis in rats induced by high-fat diet. *J Tradit Chin Med* 2021;36(05):2555–2559. (Chinese) Available at: <https://kns.cnki.net/kcms/detail/detail.aspx?FileName=BXYY202105027&DbName=CJFQ2021>