

Experience of successfully treating a child with severe metabolic-associated fatty liver disease in 12 weeks using traditional Chinese medicine alone

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Abstract:

In recent years, the prevalence of non-alcoholic fatty liver disease combined with metabolic dysfunction in children has increased rapidly. Current international guidelines for the management of metabolic-associated fatty liver disease do not recommend any specific drug therapy or its exact effect and safety margin. Appropriate drug therapies for children are even more scarce. Traditional Chinese medicine has good advantages in the prevention and treatment of metabolic-associated fatty liver disease. The author reviewed and analyzed a case with complete clinical data treated in our hospital using traditional Chinese medicine alone and discussed the diagnosis and treatment process. This report aimed to provide a reference for clinical practice.

Keywords: metabolism associated fatty liver disease, non-alcoholic steatohepatitis, traditional Chinese medicine.

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Abbreviations: NAFLD, Non-alcoholic fatty liver disease; MAFLD, metabolic-associated fatty liver disease; TCM, Traditional Chinese Medicine; NASH, Non-alcoholic steatohepatitis.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) in children and adolescents under 18 years of age is a clinicopathological syndrome characterized by chronic steatosis of the liver that is not associated with chronic fatty deposits in the liver caused by drinking and other pathogenic factors. It is a metabolic stress liver injury closely related to insulin resistance and genetic susceptibility [1]. At the beginning of 2020, the International Expert Consensus Statement [2] published the new definition of metabolic-associated fatty liver disease (MAFLD) based on the consensus of an international panel of 30 experts from 22 countries. They also proposed that the diagnostic criteria of MAFLD should include histology from a liver biopsy, imaging results of the liver, or blood biomarker test results to confirm the presence of fatty liver. In addition, one of the following three conditions must be met at the same time: overweight/obesity, type 2 diabetes, or metabolic dysfunction. Modern western medicine lacks safe and effective drugs for this disease and appropriate medicine for children is even more scarce. The Fatty Liver and Obesity Traditional Chinese Medicine (TCM) Advantageous Specialist Clinic of our hospital has used syndrome differentiation of TCM alone to treat more than 200 cases of MAFLD with remarkable results. Among them, one child was cured after 12 weeks of treatment with traditional Chinese medicine alone. The report is as follows.

Case profile

The patient was a 13-year-old male. His routine physical examination on July 23, 2020, showed abnormal results including AST 259 U/L and ALT 494 U/L. He was hospitalized in the Pediatrics Department of our hospital. A liver CT examination conducted after admission showed severe fatty liver (liver/spleen 0.32) (figure 1). Kidney function was noted as UA 520 $\mu\text{mol/L}$. The blood lipids, blood glucose, myocardial enzyme spectrum, coagulation function, routine blood, urine, and stool tests, C-reactive protein, erythrocyte sedimentation rate were all normal. The results of the 9 items of the respiratory tract, Epstein-Barr virus, and TORCH tests were also all negative, as were hepatitis A, B, C, and E infection markers. Furthermore, the antinuclear antibody spectrum was negative. The patient has been healthy to date. He preferred to eat high-calorie food and drank carbonated beverages regularly. He lacked routine physical exercise. The patient had not taken any medication in the past six months. There was no family history of hereditary diseases. The diagnoses at admission were: 1. non-alcoholic steatohepatitis and 2. hyperuricemia. During his hospitalization, the patient was given

creatinine and vitamin C intravenously. He also took liver-protecting drugs including oral glucucrolactone, bifendate, silibinin, etc. successively.

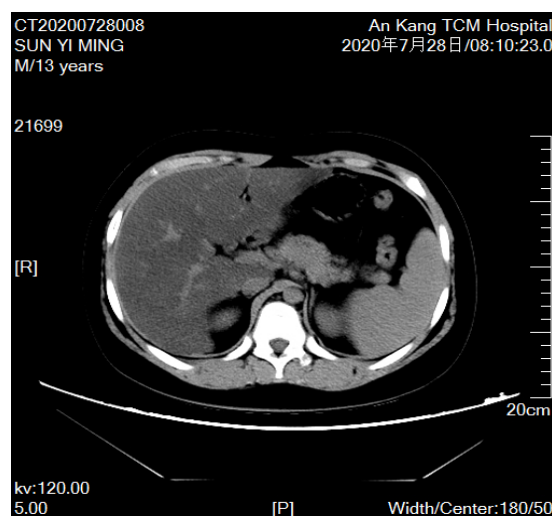


Figure 1. Image before treatment

The liver function test was performed again on August 15, 2020. The results showed AST of 91 U/L and ALT of 58 UL. Hence, the patient was discharged. After discharge, he continued to take oral silybin for liver protection treatment. The transaminase was tested again 3 times following discharge and the results fluctuated (table 1).

Table 1. Liver function during treatment with Western medicine (unit U/L)

Time	AST	ALT	AST/ALT
2020.07.28	228	444	0.5
2020.08.15	91	58	1.6
2020.08.24	107	135	0.8
2020.09.12	49	41	1.2
2020.11.14	58	103	0.56

On November 16, 2020, the child presented our department with a chief complaint of “abnormal liver function for 4 months.” Physical examination revealed the following: weight 62 kg, height 160 cm, BMI 24.2 kg/m^2 , and abdominal circumference 92 cm. His body shape was assessed as overweight. The patient’s skin and sclera had no yellow stains and examination results of the heart, lungs, and abdomen were negative. According to the four diagnostic methods of traditional Chinese medicine, the patient had a clear mind, obesity, dull tongue color, tooth marks, white and greasy moss, and slippery pulse string. The results of the liver function test showed: AST 58 U/L and ALT 103 U/L. The FibroScan scan indicated CAP 306 dB/m and E 7.1 kPa. The western medicine diagnoses were as follows: 1. severe MAFLD and 2. hyperuricemia. The TCM diagnoses were: fatty liver, spleen deficiency and dysfunction, mutual obstruction of phlegm, and blood stasis. He was treated by invigorating the spleen to

facilitate transportation, resolving the phlegm, =promoting blood circulation, raising Yang, and resolving turbidity. The patient was prescribed with a modified Jianpi Huazhuo Xiaozhi treatment recipe (for invigorating the spleen, dissolving turbidity, and removing fat) containing: atractylodes 15 g, bupleurum 8 g, poria 10 g, salvia 10 g, fried alisma 10 g, parched hawthorn fruit 10 g, seaweed 10 g, cassia seed 8 g, lotus leaf 10 g, Phyllostachys cuspidatum 15 g, Sedum sarmentosum 15 g, and Polygonum cuspidatum 10 g. The patient consumed 15 doses of traditional Chinese medicine decoction-free granules. The granules were mixed with 250 ml of boiling water and taken at 1 dose per day, at two separate times (in the morning and evening). Other liver-protecting drugs were stopped. Dietary guidance was given. The patient was instructed to increase physical exercise, record his weight and abdominal circumference every week, and attend a follow-up appointment every fortnightly (twice a month).

At the second visit, on December 05, 2020, after taking traditional Chinese medicine for half a month, the patient had no complaint. His tongue was dull, with tooth marks and white and slightly greasy fur. He also showed a slippery pulse string. Liver function and uric acid tests were performed again and showed: AST 45 U/L, ALT 75 UL, and UA 479 umol/L. The feedback was that dietary calorie intake should be strictly controlled, and exercise should be strengthened. Based on TCM, 10 g of pseudo-ginseng was added to the existing treatment recipe to promote blood circulation and dissipate blood stasis, and the medication would be continued with 15 doses.

At the third visit on December 22, 2020, the patient reported no discomfort. He had a dim tongue, with reduced tooth marks, and white fur. He also had a slippery pulse. The feedback was that compliance had been good and the medication should be continued for another 15 doses using the original prescription.

At the fourth visit on January 9, 2021, the patient had no complaints. He had a pale tongue, lessened tooth marks, and thin white fur. A slippery pulse was also noted. Liver function and uric acid tests were performed again and showed: AST 31 U/L, ALT 35 UL, and UA 388 umol/L. He was instructed to continue the medication for another 15 doses using the previous prescription.

At the fifth visit on January 25, 2021, the patient had no discomfort. His tongue was pale with thin white fur but the tooth marks disappeared. A flat pulse was noted. Liver ultrasound was conducted and the liver showed dense echoes. The FibroScan test indicated CAP 202 dB/m and E 6.0 kPa. The patient's weight was 58 kg, height 161 cm, BMI 22.4 kg/m², and abdominal circumference 88 cm. The medication was continued with another 15 doses of the above-mentioned prescription for consolidation.

At the sixth visit on February 08, 2021, the liver

function, blood lipids, kidney function, and other tests were performed again. The various indicators were normal. A plain CT scan of the upper abdomen was performed and no abnormality was seen (liver/spleen 1.04) (figure 2).

The patient met the recovery criteria in terms of three curative effect evaluation indicators, including liver fat content (CAP value < 238), liver imaging (CT value: liver/spleen > 1.0), and serum transaminase (see Table 2) [3]. He was instructed to eat rationally and continue regular exercises to control his BMI. The medication was stopped. Further follow-up appointments were scheduled to monitor his progress.

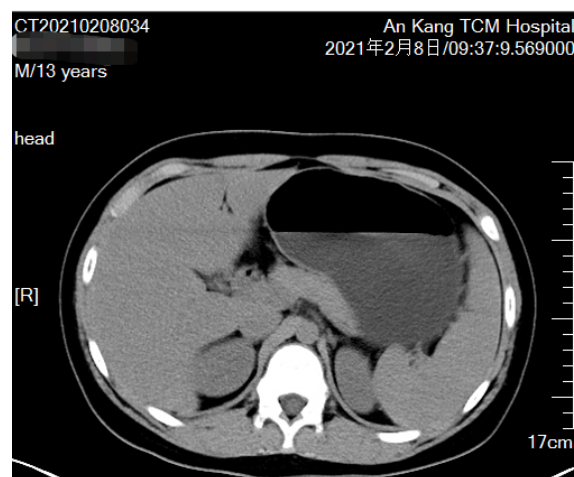


Figure 2. Image after treatment

Table 2. Transaminase levels after treatment with traditional Chinese medicine in the Department of Hepatology outpatient clinic (unit: U/L)

Time	AST	ALT	AST/ALT
11/14/2020	58	103	0.56
12/05/2020	45	75	0.6
01/09/2021	31	35	0.89
02/08/2021	26	26	1.0
Time	AST	ALT	AST/ALT

Experience

In recent years, the prevalence of NAFLD with metabolic dysfunction in children has increased rapidly in China. This is of concern as NAFLD seriously affects children's development, and physical and mental health [4]. Due to the particularity of children's physical development and the lack of large-scale cohort research data, the natural history of children's NAFLD is still not very clear. Non-alcoholic steatohepatitis (NASH) is generally considered to be a state of NAFLD progression that significantly increases the incidence of cirrhosis and hepatocellular carcinoma. The rate of disease progression in children with NAFLD mainly depends on the severity of the steatosis, obesity, higher ALT levels (> 80 U/L),

splenomegaly and AST/ALT ratio > 1 [1, 5]. Studies have shown that the lifespan of children with NAFLD is significantly shorter than normal controls. In one study, 66 children with NAFLD were followed up for 20 years, 2 cases (3.03%) underwent liver transplantation due to end-stage liver disease, and 4 out of the 13 cases who received liver biopsy again had liver fibrosis progression (30.8%) [6].

Unfortunately, none of the treatment guidelines have recommendations of safe and effective drugs for NAFLD in adults or children [1, 7, 8]. The primary goal of treatment is to control body weight, improve insulin resistance, and prevent or treat the metabolic syndrome and its related end-stage diseases. The secondary goals are to reduce liver steatosis, avoid the occurrence of NASH and the progression of liver disease, and prevent or reduce the occurrence of liver cirrhosis and liver cancer, etc. The alternative drugs recommended by the 2018 “Expert Consensus on the Diagnosis and Treatment of Non-alcoholic Fatty Liver Disease in Children” in China [9] include metformin, vitamin E, weight-loss drugs (orlistat, sibutramine), lipid-lowering drugs, and probiotics, but they all have safety and efficacy limitations. It is customary to use liver-protecting drugs in China. China’s 2018 updated version of the “Guidelines of Prevention and Treatment of Non-alcoholic Fatty Liver Disease” [10] highlighted that for patients with serum ALT higher than the upper limit of normal, a liver-protecting drug should be orally administered for 6 months and if the serum transaminase does not decrease significantly, the patient should switch to other liver-protecting drugs.

For this child, his body mass index exceeded the standard. There was no discomfort during treatment. He was referred to the hospital primarily due to elevated transaminase. The patient’s serum uric acid level exceeded the standard in multiple tests. His liver CT value significantly declined. The FibroScan test indicated that CAP was greater than 300 dB/m, E 7.1 kPa. Therefore, the diagnosis at the initial visit was severe NASH with obesity and hyperuricemia. The patient’s condition also met the newly established MAFLD diagnostic criteria. Although the E value was high, liver puncture and biopsy were not performed, so it is debatable whether it was complicated by fibrosis. Liver-protecting drugs were given during hospitalization. During hospitalization, the transaminase decreased, but the level fluctuated repeatedly, indicating that the use of liver-protecting and enzyme-lowering drugs alone did not improve liver steatosis and may sometimes cover up the condition.

In recent years, our hospital’s Fatty Liver and Obesity Specialist Advantageous Clinic has developed a “four-in-one” integrated model of treatment with syndrome differentiation that is in line with the concept of MAFLD, that is, a “western medical diagnosis + risk factor identification + traditional

Chinese medicine syndrome differentiation + physical constitution differentiation” model [11]. In Chinese medicine, we classify the “hyperglycemia, hyperlipidemia, blood uric acid, and intestinal endotoxin” that occur in metabolic disorders into the category of “turbid toxins.” The adhesion and bonding between “water dampness,” “phlegm stasis,” and other pathological products are the cause of “turbid toxins.” Based on the perspective of spleen and stomach movement and qi transformation, we proposed that the basic pathogenesis of MAFLD is “deficiency and dysfunction of the spleen, endogenous turbid toxins, dissipation of essence and loss of strength, and disturbance of qi transformation.” Hence, the basic treatment principle in the management of metabolic diseases was established to “invigorate the spleen, assist in transportation, promote Yang, and resolve turbidity (toxin)”. It is advocated that the treatment should be based on the spleen, and the prescription of Jianpi Huazhuo Xiaozhi treatment recipe (for invigorating the spleen, dissolving turbidity, and removing fat) is proposed. Treatment of adult MAFLD with abnormal transaminase using a modified recipe of this prescription has obtained good effects [12, 13]. The prescription utilizes raw atractylodes to invigorate the spleen, promote Yang, mobilize the spleen, promote bowel movement, promote clearness, and lower turbidity. Bupleurum is used to relieve stagnation of the liver and promote clear Yang. Poria and alisma are included to invigorate the spleen and remove dampness to eradicate the source of phlegm accumulation. Salvia and seaweed promote blood circulation and reduce phlegm. Hawthorn, medicated leaven, and lotus leaves revitalize the spleen and assist in transport, resolve turbidity, and promote clearness. Cassia seeds clear the liver, moisturize the intestines, and lower and discharge turbid qi. All the medicines are introduced into the liver meridian and large intestine meridian. Together, the complete prescription has the effects of invigorating the spleen, assisting in transportation, regulating the liver and intestines, promoting clearness, and reducing turbidity. MAFLD in children usually lacks typical clinical symptoms, but the cause is simpler than that of adults. It is mostly related to improper diet and a preference for fatty food and sweet food. During development, one of the physiological characteristics of children is that “the shapes are not mature, and the spleen is often insufficient.” Therefore, based on the idea of examining the causes for targeted treatment, this prescription was suitable for our patient. Coupled with a high degree of self-discipline from the child and diligent parental cooperation, the effect was outstanding in the short term. The recovery criteria were reached in 12 weeks.

This case is not an isolated case. Other and subsequent cases need to be collected and further accumulated. Based on the overall concept, TCM has a

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good treatment effect for MAFLD. Not only does TCM protect the liver and lower the enzymes, regulate the glucose and lipid disorders, and reduce the blood uric acid levels, but it also relieves liver steatosis with outstanding efficacy. Therefore, further research is warranted.

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