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Case Report

A juvenile case with nonalcoholic steatohepatitis and traditional Korean medicine-based treatment

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) has become the common cause leading to chronic liver diseases recently. Unlikely past humankind history, NAFLD is like a new illness especially in developed countries due to decreased number of hepatic virus carriers and increased population with obesity. Among subjects with NAFLD, development of nonalcoholic steatohepatitis (NASH) is a key pathological step which determines the clinical progression. This study reports a case of a boy who has suffered from NASH for 2 years. This study aims to discuss the clinical feature, risk aspect, and treatment strategy of NASH as well as potential of traditional Korean medicine (TKM) therapies.

1. Introduction

Hepatic steatosis is a condition of the excessive accumulation of triglyceride fat in hepatocytes, and fatty liver disease refers the any liver disease with hepatic steatosis.[1] Alcohol consumption is a main cause of hepatic steatosis; however, recently many subjects are suffering from nonalcohol-related fatty liver, called as nonalcoholic fatty liver disease (NAFLD). In a recent meta-analysis, the global prevalence of NAFLD is known to rise by approximately 25% in especially developed countries.[2] Along to increase of population with obesity, the incidence and disease burden from NAFLD will continue to increase.[3,4]

NAFLD is now considered as a silent killer by a new epidemic of the Third Millennium.[5] NAFLD is known to show a strong association with diabetes mellitus, cardiovascular disease or cerebrovascular disease as well as high cancer incidence of 1.3 hazard ratio (HR), especially 16.7 HR for hepatocellular carcinoma respectively.[6–8] For Asian population including Korean, NAFLD appears as a medical issue in the past two decades, due to rapid urbanization, sedentary lifestyle, or over nutrition.[9] NAFLD also becomes a common in children and adolescents with prevalence of 7.6% for general population and 34.2% for obese children.[10]

In contrast, the clinical risk of NAFLD is defined by progression into non-alcoholic steatohepatitis (NASH), a pathologic condition characterized by inflammation and damage in

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hepatic tissue.[11] Both NAFLD and NASH have a complex pathology involving the imbalance between lipogenesis and lipolysis, leading to lipotoxicity.[12] In aspect of medicinal herbs composing multi-compounds and pathophysiological features of multi-targets of NAFLD and NASH, herbs-derived remedies are emerging as potential therapeutics recently.[13]

This report aimed to demonstrate a typical case of adolescent patient with NASH, and discuss the clinical feature, risk aspect, and treatment strategy by traditional Korean medicine (TKM)-based therapeutics.

2. Case report

2.1. Characteristics of patient and medical history

A 16-year-old boy visited a Korean medicine hospital with uncomfortable symptom in gastrointestinal function such as mild abdominal pain, diarrhea, as well as frequent fatigue since 12 months ago. He has visited frequently the nurse's office at school because of abdominal pain after entering high school. Several medical examinations found no abnormality in abdominal X-ray and colonoscopy at a Western hospital, but noticed the moderate fatty liver with the elevated serum level of alanine aminotransferase (ALT) by 100 IU/L. Based on the diagnosis of irritable bowel syndrome (IBS), the irregular medications were given to treat only IBS, but the long-term symptoms became worse. The boy neither drank alcoholic beverages nor smoked cigarettes earlier, but still prefers to eat fast foods and oily snack. His parents decided to receive TKM therapeutics against abdominal pain and hepatic inflammation.

2.2. Diagnosis, treatments, and course of symptom

After visiting the Korean medicine hospital, the patient had been examined using biochemistry, complete blood counts, urinalysis, and ultrasonography. Based on the finding of abnormality in only serum ALT (81 IU/L, normal range 0–40 IU/L) and moderate fatty liver in ultrasonography, he was diagnosed with NASH (Fig. 1A). The patient was a little fatty body (body mass index, BMI 26.0), but has a shape of central obesity as thin four limbs and tummy fat. The genomic analysis using his salivary contents was conducted by a company (Genoplan, Co.), and then the body's genome showed the vulnerable feature for fat and glucose metabolic problem (Fig. 1B).

Table 1 – Composition of *Chungganplus*

Weight each	Composition (10 mL syrup containing 2 g extract from 13 herbs)
5 g	Artemisia capillaris Herba, Carapax Trionycis, Semen Raphani
3 g	Rhizoma Atractylodis Macrocephalae, Poria, Alismatis Rhizoma, Atractylodis Rhizoma, Salviae Miltiorrhizae Radix
2 g	Polyporus, Amomi Fructus, Aurantii Fructus
1 g	Glycyrrhizae Radix, Helenii Radix

The patient complained physical lethargy and less motivation for everything including school life, with sudden and frequent abdominal pain at middle abdominal area. The status of the coat on his tongue was mild pink color, and pulsation was tender. No abnormal tense was in abdominal area. His symptom differentiation was diagnosed as "*disharmony between liver and spleen* (肝脾不和)". The patient was administrated with an herbal drug, *Chungganplus* (淸肝plus, Table 1) twice per day. In addition, Taeumin taegeuk acupuncture (helping HT4; 灵道 and LU9; 太渊, but reducing LR3; 太冲 for 20 min once a week for 3 months with 0.25 × 30 needles purchased from *DongBang Co.* Seoul), and indirect moxibustion on umbilical area were given to the patient. In particular, physical exercise and diet management were strongly recommended, and thus he had joined a boxing gym and regularly did the practice three times weekly. He had reduced body weight about 3 kg during 6 months and the general symptoms including abdominal pain as well as blood chemistry (ALT by 41 IU/L) were improved.

3. Discussion

According to the change of medical environments, such as less population of hepatitis B type virus carrier, increase of obese subjects and over calorie diet habit, NAFLD evolved as a serious public health problem in developed countries.[14] NAFLD increases liver-related morbidity and mortality, and also is linked to the extra-hepatic diseases such as metabolic syndrome, type 2 diabetes mellitus, dyslipidemia, hypertension, cardiovascular or cerebrovascular diseases, and even chronic kidney disease.[15,16] No currently available drug-based therapy

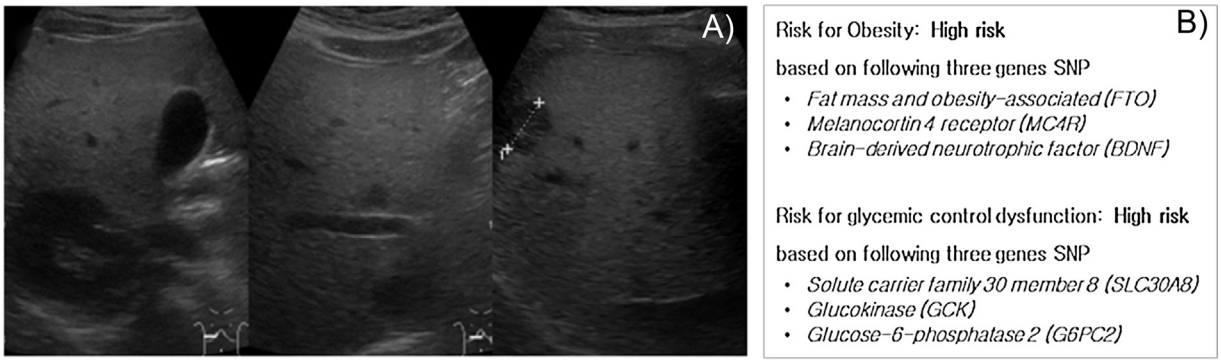

Fig. 1 – Sonographic finding in liver. The moderate fatty liver and a hemangioma and multiple cysts were found in abdominal nosography (A), and SNP analysis showed the vulnerable feature for fat and glucose metabolism (B).

has been approved yet, and then herbs have been attracted as potential therapeutics against NAFLD because of terms of multi-targets and multi-compounds.[17]

The present study reports a juvenile case suffering from NASH, a typical condition of hepatic inflammation and damage of NAFLD. In general, obesity is well known as an independent risk factor for NAFLD, which 21.7% increase of BMI is 3.4 odd ratios for development of NAFLD in a middle aged cohort study.[18] Age is another risk factor for NAFLD, but the present case is young boy and has a little fatty body as BMI 26.0. These facts suggested the presence of any other risk factors including genetic feature in the boy patient. Beside a high-fat diet and inactive lifestyles, the interplay between diet, gut microbiota, and genetic background is believed to be more important in the development and progression of NAFLD.[19] In fact, the boy had enjoyed the fast foods and oily snack with low physical activity; furthermore he had the SNP-based genetic feature presenting the low capacity in fat and glucose metabolism.

Regarding the hepatic risk of NAFLD, the development of NASH is a clinical key step determining the progress into hepatic fibrosis, cirrhosis and/or hepatocellular cancer, and then NASH is predicted to become the leading cause of liver transplantation in the USA by 2020.[20,21] In general, approximately 10% of subjects with NAFLD are known to present the NASH feature, of which 10–25% would progress into cirrhosis.[22] This case was hepatic inflammation, but not progressed into fibrotic change yet, however his uncontrolled NASH could progress into liver cirrhosis due to the early onset at very young age. Furthermore, recent evidence has suggested that NAFLD may directly promote hepatic carcinogenesis independent of cirrhosis.[23] The nosography of this patient showed a mass-like regions, but fortunately hemangioma and multiple cysts were proved via the computed tomography (data not shown). In addition, he might have comorbid of type 2 diabetes mellitus in the future, related to central obesity body shape and genetic analysis in the future. His Sasang constitutional type was judged as Taeumin-type, and then Taeumin-type individual was known to have the highest prevalence in metabolic syndrome and its associated disorders.[24]

Based on his gastrointestinal symptoms and physical features, the symptom differentiation was diagnosed as "*disharmony between liver and spleen* (肝脾不和)". Along with the acupunture, moxibustion, and herbal prescription (*Chunggan plus*), the boy had been strictly educated to practice the physical exercise and diet control for his NASH treatment. Although no therapeutics to cure the NAFLD or NASH is available in conventional medicine, lifestyle modifications with physical exercise and diet control showed the curative effects.[25] Weight reductions of >10% can resolve NASH and induce fibrosis improvement, and modest weight loss (>5%) can also produce important benefits on NAFLD management.[26] In this case, the regular boxing practice and diet control reduced his body weight 3 kg (about 4%, from 75 kg to 72 kg) during 6 months, which might attenuate the lipotoxic reaction in liver. *Chungganplus* was known to have hepatoprotective effects against hepatosteatosis and oxidative injury,[27,28] thus this prescribed herbal drug might work to improve the hepatic inflammation.

The pattern of diseases evolves according to the change of environments, and the therapeutic strategy also should be changed. NAFLD and NASH constitute a new epidemic hepatic disorder which could be an optimal target the disease of TKM-based integrative treatment. This study reported the important clinical information and potential of TKM-therapies through a juvenile NASH case, thus will be helpful for the development of TKM-derived treatments for NAFLD and NASH.

Conflict of interest

The author declares no conflict of interest.

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