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Postprint of a General Practice Case Analysis of a Patient with “Three Highs” Complicated by Fatty Liver Disease

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Abstract

Background Hypertension, diabetes, and dyslipidemia (“the three highs”) often coexist with metabolic-associated fatty liver disease, influencing each other and significantly increasing the risk of cardiovascular and hepatic adverse outcomes. Currently, the standardized diagnostic and treatment pathway for such comorbid patients in primary care settings is still under exploration. Objective To explore the general practice diagnostic thinking and practical workflow for patients with “the three highs” combined with fatty liver disease through a typical case report. Methods Report the general practice diagnostic and treatment process of screening, identification, risk assessment, two-way referral, and comprehensive management for one patient with “the three highs” combined with fatty liver disease, demonstrating an individualized comprehensive management plan and general practice pathway. Results After 8 months of whole-process, all-round comprehensive management led by general practitioners, the patient’s blood pressure and blood glucose reached target levels, low-density lipoprotein cholesterol decreased, body weight reduced, waist circumference decreased, hepatic steatosis and fibrosis improved significantly, medication adherence and self-management ability markedly improved. Conclusion Through comprehensive management led by general practitioners for patients with “the three highs” combined with fatty liver disease, metabolic indicators and liver condition can be significantly improved, demonstrating the core role of general practice in chronic disease comorbidity management and providing practical reference for optimizing the standardized primary care management pathway for such patients.

Full Text

Case Analysis of General Practice Diagnosis and Treatment in a Patient with “Three Highs” Comorbid with Fatty Liver Disease

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Abstract

Background: Hypertension, diabetes mellitus, and dyslipidemia (the “Three Highs”) frequently coexist with metabolic dysfunction-associated steatotic liver disease (MASLD), interacting synergistically to significantly elevate risks of adverse cardiovascular and hepatic outcomes. Currently, standardized diagnostic and treatment pathways for such comorbid patients in primary care settings remain under exploration.

Objective: Through a typical case report, this paper aims to explore the diagnostic reasoning and practical workflow of general practitioners managing patients with the “Three Highs” comorbid with MASLD.

Methods: We report the general practice process of screening, identification, risk assessment, two-way referral, and comprehensive management in a patient with the “Three Highs” and fatty liver disease, demonstrating an individualized comprehensive management plan and general practice care pathway.

Results: Following eight months of continuous, comprehensive management led by general practitioners, the patient achieved target blood pressure and glucose levels, reduced low-density lipoprotein cholesterol, experienced weight loss and decreased waist circumference, and showed significant improvement in hepatic steatosis and fibrosis. Medication adherence and self-management capabilities also improved markedly.

Conclusion: General practitioner-led comprehensive management of patients with the “Three Highs” and fatty liver disease can significantly improve metabolic

parameters and liver status, reflecting the central role of general practice in managing multiple chronic conditions and providing practical reference for optimizing standardized management pathways for such patients at the primary care level.

Keywords: Three Highs; Fatty Liver Disease; Hypertension; Diabetes Mellitus; Dyslipidemias; General Practice; Case Report

Case Presentation

Subjective Data (S) The patient is a 69-year-old male with junior high school education, retired, and a registered patient in our practice. He presented with a one-year history of intermittent abnormal liver function tests, which he had previously ignored. During his community follow-up visit, we recognized him as a high-risk individual for fatty liver disease (FLD) and completed blood work including complete blood count, liver function, and renal function panels. His fibrosis-4 (FIB-4) index was calculated at 7.40, indicating high risk for advanced liver fibrosis, prompting further evaluation with liver elastography. The patient denied nausea, vomiting, anorexia, diarrhea, abdominal pain, dizziness, headache, blurred vision, palpitations, heat intolerance, diaphoresis, limb pain or numbness, and hand tremors. He reported adequate diet and sleep, normal bowel movements and urination, and no significant weight changes.

His past medical history includes hypertension for 15 years (peak blood pressure 160/95 mmHg, currently controlled with nifedipine controlled-release tablets 30 mg once daily, with home self-measured blood pressure 130-140/80-90 mmHg); diabetes mellitus for 10 years (regularly taking dapagliflozin 10 mg once daily for the past year, with fasting glucose 4-7 mmol/L, 2-hour postprandial glucose 6-10 mmol/L, and HbA1c 6.5%); dyslipidemia and history of cerebral infarction for 15 years (self-discontinued aspirin enteric-coated tablets and atorvastatin calcium tablets for the past three years). He denied histories of tuberculosis, malaria, hepatitis B, or other viral hepatitis infections, and denied any tumor history.

His personal history includes iodinated contrast allergy, no long-term use of health supplements or traditional Chinese medicine, a 40-pack-year smoking history (20 cigarettes/day, quit within the past year), and a 30-year alcohol consumption history (predominantly spirits 42°, 200-250 g per occasion, 7 times/week, reduced to 50-100 g/day in the past year). He previously worked as an office clerk, is now retired, prefers salty foods, exercises little, has harmonious family relationships, and good economic status. Based on the Reason-Idea-Concern-Expectation (RICE) principle: the patient presented due to abnormal liver function, attributed it to alcohol consumption, expressed concern about liver function changes and fear of developing liver cancer, and desired definitive diagnosis and standardized treatment.

Family history: Parents, spouse, and one son are all healthy. No family history of hepatitis or other infectious diseases, tumors, or genetic disorders.

Objective Data (O) Physical Examination: Height 172 cm, weight 80 kg, BMI 27.0 kg/m², waist circumference 106 cm, blood pressure 137/88 mmHg. The patient appeared normally developed, well-nourished, conscious, with a chronic disease facies, comfortable expression, and voluntary position. Gait was normal and he cooperated with examination. No palmar erythema or spider nevi were observed. No obvious jaundice of skin or sclera. Thyroid was not enlarged. Lung breath sounds were clear without rales. Heart rhythm was regular at 72 beats/min without murmurs. Abdomen was soft without tenderness or rebound tenderness. Liver and spleen were not palpable below costal margins. Shifting dullness was negative. Muscle strength and tone were normal in all four limbs. No lower extremity edema was present. Bilateral dorsalis pedis pulses were diminished, but plantar temperature, tactile, and pressure sensations were normal. Asterixis and ankle clonus were negative.

Auxiliary examinations are shown in Table 1 .

Electrocardiogram: Sinus rhythm, normal ECG. **Abdominal ultrasound:** Severe FLD. **Body composition analysis:** Body fat percentage 24.3%, muscle mass 55.7 kg, basal metabolic rate 6,740 kJ/1,611 kcal; “standard” body type. **Liver elastography:** Controlled attenuation parameter (CAP) value 305 dB/m, liver stiffness measurement (LSM) 13.6 kPa, indicating severe hepatic steatosis and advanced liver fibrosis. **Carotid ultrasound:** Carotid plaques with bilateral stenosis, possible right-sided occlusion.

Assessment (A) Risk factors and health issues: The patient has multiple coexisting risk factors including hypertension, diabetes, dyslipidemia, and carotid stenosis, with health issues related to cardiovascular and cerebrovascular diseases. His overall risk assessment for atherosclerotic cardiovascular disease (ASCVD) in Chinese adults is classified as extremely high risk, requiring urgent control of metabolic components and active management of chronic diseases. Calculated alcohol consumption was 470.4 g/week (for the first 30 years) and 235.2 g/week (in the past 1-2 years), exceeding 210 g/week, indicating excessive alcohol use requiring intervention. He has successfully quit smoking and should be encouraged to maintain abstinence. Patient Health Questionnaire-9 (PHQ-9) score was 2 (normal); Generalized Anxiety Disorder-7 (GAD-7) score was 2 (normal); Morisky Medication Adherence Scale-8 (MMAS-8) score was 4 (low adherence); Chronic Disease Self-Management Study Measures (CDSMS) score was 21 (poor self-management), with irregular follow-up visits, requiring adherence intervention. **Family resources:** The patient has a harmonious family with good economic status, and family members are willing to supervise his treatment.

Based on auxiliary examination results, preliminary diagnoses include: FLD with high risk of liver fibrosis, Grade 3 hypertension (very high risk), type 2

diabetes mellitus, dyslipidemia, central obesity, hyperuricemia, metabolic syndrome, old cerebral infarction, and carotid artery stenosis.

Plan (P) Treatment: Aspirin enteric-coated tablets (100 mg once daily) for antiplatelet therapy; rosuvastatin calcium tablets (10 mg once daily) combined with ezetimibe tablets (10 mg once daily) for intensive lipid-lowering; nifedipine controlled-release tablets (60 mg/tablet, once daily) for blood pressure control; and dapagliflozin (10 mg once daily) for glycemic control, with home monitoring of blood pressure and glucose.

Referral: The patient has high risk of liver fibrosis meeting FLD referral criteria [10] (FIB-4 index >2.67 ; LSM 13.6 kPa >12 kPa) and should be referred to a tertiary hospital hepatology department for definitive diagnosis and treatment adjustment. Using knowledge-attitude-practice theory and motivational interviewing techniques, we aimed to enhance the patient's awareness of abnormal liver function and overall health status, strengthen his belief in actively intervening in his multiple conditions, and develop actionable intervention plans under the premise of his subjective willingness to address disease progression.

Referral Record

After referral to the tertiary hospital hepatology department, laboratory tests showed: C-reactive protein 11.3 mg/L; alanine aminotransferase 19 U/L, aspartate aminotransferase 34 U/L, total bilirubin 18.3 mol/L, direct bilirubin 6.7 mol/L, albumin 38.6 g/L; creatinine 78 mol/L, estimated glomerular filtration rate (eGFR) $87.6 \text{ mL} \cdot \text{min}^{-1} \cdot (1.73 \text{ m}^2)^{-1}$, potassium 4.15 mmol/L; triglycerides 2.52 mmol/L, total cholesterol 6.74 mmol/L, high-density lipoprotein cholesterol (HDL-C) 0.92 mmol/L, low-density lipoprotein cholesterol (LDL-C) 5.03 mmol/L; uric acid 436 mol/L. Liver elastography: CAP 331 dB/m, LSM 15.2 kPa. Magnetic resonance imaging for liver fat measurement showed a relatively smooth liver surface, heterogeneous signal reduction in liver parenchyma on out-of-phase T1 imaging, and magnetic resonance elastography (MRE) approximately 3.439 (3.182-3.767) kPa, suggesting FLD, hepatic iron overload, and liver fibrosis.

Liver biopsy pathology results (Figure 1 [Figure 1: see original paper]) showed steatohepatitis consistent with both alcoholic and metabolic etiologies. According to the non-alcoholic steatohepatitis scoring system: NAFLD Activity Score (NAS) = $2+3+2 = 7$ points, fibrosis stage F2-F3; Steatosis-Activity-Fibrosis (SAF) score: S2A4F2-3. Immunohistochemistry: hepatitis B surface antigen (-), hepatitis B core antigen (-), CK7 (bile duct +), CK19 (bile duct +), MUM1 (few plasma cells +), CD34 (vessels and some sinusoids +). Special stains: copper (rhodanine, -), iron (few hepatocytes and Kupffer cells +).

Comprehensive testing excluded viral and autoimmune hepatitis. The definitive diagnosis was "MAFLD combined with alcoholic liver disease, liver fibrosis, possible cirrhosis, steatohepatitis, grade 3 hypertension (extremely high risk), type

2 diabetes mellitus, dyslipidemia, central obesity, hyperuricemia, metabolic syndrome, old cerebral infarction, hypoalbuminemia, carotid artery stenosis, and arteriosclerosis.” Given the patient’s “Three Highs” comorbidity, priority was given to glucose-lowering medications with potential hepatic benefits and improved cardiovascular and renal outcomes. The medication regimen was adjusted to: pioglitazone (30 mg once daily), dapagliflozin (10 mg once daily), semaglutide (once weekly, starting at 0.25 mg and titrating up to 1 mg) [11], and telmisartan (40 mg once daily) [12-13], while maintaining antiplatelet and lipid-lowering therapy, with guidance on home blood pressure and glucose monitoring.

Follow-up Record

After returning to community care, active follow-up was conducted within two weeks (May 6, 2024). Through shared decision-making, personalized comprehensive treatment goals were established [14]: BMI 18.5-24 kg/m², waist circumference <90 cm; blood pressure <130/80 mmHg; fasting glucose 4.4-7.0 mmol/L, 2-hour postprandial glucose <10.0 mmol/L, HbA1c <6.5%; LDL-C <1.4 mmol/L, triglycerides <1.7 mmol/L, total cholesterol <4.5 mmol/L; normalized liver enzymes; and no significant increase in liver stiffness index. Management focused on lifestyle interventions including diet and exercise, plus comprehensive measures for weight and adherence.

Lifestyle Interventions Dietary Intervention: A calorie-restricted balanced diet was implemented, reducing total daily energy intake by 10-30% compared to weight maintenance requirements while ensuring adequate protein, fat, carbohydrates, vitamins, and minerals. Principles included choosing healthy fats (olive oil, fish oil) while limiting saturated fat; encouraging whole grains and fiber-rich carbohydrates while reducing refined sugars and white flour products; increasing dietary fiber for satiety; ensuring adequate hydration to support metabolism and reduce appetite; using portion control with smaller plates to avoid overeating; limiting salt to <5 g/day; and controlling daily energy intake to 1,200-1,400 kcal with protein 15-20% (84-112 g), fat 20-25% (44-55 g), and carbohydrates 50-60% (150-168 g) of total calories. A personalized dietary prescription is shown in Table 2 .

Exercise Intervention: Combined aerobic and resistance training was prescribed based on patient preferences (Table 3) to promote long-term exercise habit formation. The program followed FITT-VP principles (Frequency, Intensity, Time, Type, Volume, Progression), starting with 20-30 minutes daily and gradually extending to 1 hour, with 5-10 minutes each for warm-up and cool-down. Target heart rate during exercise was 90-110 beats/min (moderate intensity where talking is possible but singing is difficult). Resistance training used <40% 1RM, 10-15 repetitions \times \$1 set, progressing to 2 sets per session.

Alcohol Cessation Intervention: The dangers of alcohol consumption were emphasized using the “5A” technique (Ask, Advise, Assess, Assist, Arrange).

Sleep and Psychological Intervention: The patient was advised to ensure adequate sleep (7 hours/day) and avoid staying up late, with psychological support through cognitive behavioral therapy and relaxation training if anxiety or depression emerged.

Supportive Management Measures Health Education: Education covered MASLD and liver fibrosis (etiology, symptoms, complications, treatment), emphasizing the importance of lifestyle interventions and medication adherence, with guidance on self-monitoring and timely medical consultation.

Self-Management Enhancement: The patient was required to maintain records of lifestyle modifications with family support and supervision.

Efficacy Evaluation and Follow-up Plan Biochemical indicators (liver and kidney function, lipids, glucose) should be checked every 3-6 months; blood count and abdominal/carotid ultrasound every 6-12 months; body composition analysis annually; and FIB-4 index or transient elastography annually to monitor fibrosis progression. Follow-up visits were scheduled every 2 weeks initially, then monthly after stabilization, then every 3 months after achieving lipid and blood pressure targets, with annual comprehensive assessment.

Subsequent Follow-up Results

Based on the transtheoretical model of behavior change, phased intensive interventions were implemented: biweekly follow-ups initially, then monthly after 2 months of stable treatment, then every 3 months after 3 months of stable glycemic and blood pressure control. No significant symptoms or adverse drug reactions were reported during follow-up. Family resources were leveraged with full family participation throughout the intervention period.

At the 8th follow-up visit (after 8 months of comprehensive treatment), the patient maintained self-monitoring of blood pressure and glucose, performed aerobic combined with anaerobic exercise 3-5 times weekly for 20-30 minutes each session. MMAS-8 score improved to 7.5 (markedly improved adherence), and CDSMS score increased to 48 (significantly enhanced self-management). Clinic blood pressure was 125/71 mmHg (target achieved). Recent fasting glucose was 5.3 mmol/L, 2-hour postprandial glucose 7.6 mmol/L (target achieved), HbA1c 5.5%. Weight decreased to 73.9 kg, BMI 25.0 kg/m², waist circumference 94 cm (significantly decreased, not yet at target). Liver elastography showed CAP median 296 dB/m and LSM 10.1 kPa (significant improvement in FLD severity). The patient was very satisfied with treatment outcomes. Semaglutide was discontinued, maintaining dapagliflozin monotherapy for glycemic control, with unchanged antihypertensive, lipid-lowering, and antiplatelet therapy. He was advised to continue alcohol abstinence and current lifestyle modifications, further improve self-management, maintain regular community follow-up, and continue monitoring.

Discussion

Current Status of FLD Tiered Diagnosis and Treatment System Construction With the gradual improvement of medical consortiums and integrated healthcare systems, China has made significant progress in chronic disease tiered management. However, FLD has not yet been incorporated into the national primary chronic disease prevention and control framework, and a scientific, orderly two-way referral system remains incomplete [9,15]. Community health institutions serve as the primary venues for FLD screening and assessment, bearing core responsibilities for early diagnosis, risk stratification, and follow-up management. Domestic scholars have proposed constructing a “family-community-hospital” layered, whole-course management model, with multidisciplinary specialists participating in family doctor contract teams to co-manage FLD patients with general practitioners. Through staff training, two-way referral coordination, case discussions, and community specialist clinics, this model strengthens generalist-specialist collaboration, implementing “primary care first visit, initial screening, tiered referral, and convenient follow-up” for comprehensive health management, aiming to achieve a closed-loop pathway from health screening to multidisciplinary diagnosis and treatment to community follow-up [16].

Therapeutic Inertia in Managing the “Three Highs” and FLD Therapeutic inertia refers to the failure to initiate or adjust treatment in a timely manner, resulting in poor disease control [17]. Primary care physicians demonstrate significant therapeutic inertia in managing both FLD and the “Three Highs.” A 2021 Dutch cohort study of 6,400 hypertensive patients found therapeutic inertia in 87% of cases [18]. A 2023 systematic review of 575,067 patients with type 2 diabetes found over 50% of clinicians exhibited therapeutic inertia in diabetes management [19]. The situation is more severe in China, with one survey of 3,346 type 2 diabetes patients showing 93.96% therapeutic inertia among primary care physicians [20]. Interestingly, most primary care physicians are unfamiliar with the term “therapeutic inertia” and, after learning its definition, some deny responsibility and attribute it to poor patient adherence and missed follow-ups [21]. A US study suggested that specialty clinics managing type 2 diabetes had less therapeutic inertia than general internal medicine clinics, possibly due to more integrated and coordinated healthcare systems [22].

Compared with the “Three Highs,” therapeutic inertia in FLD management may be even more severe, with more pronounced deficiencies at physician, patient, and healthcare system levels. These include insufficient diagnostic tools and effective medications [6], low patient awareness and poor adherence, and lack of effective management systems and protocols [2]. Table 4 summarizes common causes and coping strategies for therapeutic inertia from these three perspectives [22-27].

Advantages and Diagnostic-Treatment Process of General Practitioners in FLD Management General practitioners' advantages in FLD management center on early identification and comprehensive management, effectively countering therapeutic inertia. Since FLD patients are often asymptomatic, identification depends on timely screening and assessment of high-risk populations, including those with obesity, type 2 diabetes, metabolic syndrome, excessive alcohol consumption, and asymptomatic transaminase elevation [2]. This patient, having the “Three Highs” and asymptomatic transaminase elevation, was identified as potentially having liver fibrosis through abdominal ultrasound and FIB-4 index. Liver elastography confirmed referral criteria for fatty liver disease, leading to tertiary hospital referral for definitive diagnosis. After comprehensive evaluation including MRI and liver biopsy, the diagnosis of “MAFLD combined with alcoholic liver disease” was confirmed, treatment was adjusted, and the patient was reintegrated into community management, demonstrating the advantages of tiered diagnosis and treatment.

FLD is characterized by long disease course and slow treatment response, with diet and exercise modification remaining first-line therapy requiring full general practitioner involvement to develop scientifically sound management protocols. Currently, general practitioners lack systematic, comprehensive protocols and integrated management models for complex cases like “Three Highs” combined with FLD, resulting in insensitivity, under-recognition, poor intervention, and inadequate follow-up. In this case, the general practitioner implemented comprehensive whole-course management including individualized treatment goal setting, two-way referral coordination, combination pharmacotherapy, lifestyle management, intensive alcohol cessation intervention, health education, self-management capacity building, family involvement, and close follow-up. Post-treatment outcomes showed significant improvement with multiple parameters reaching targets. The management process applied the RICE principle for history-taking, motivational interviewing to mobilize patient initiative, knowledge-attitude-practice theory to optimize adherence, and the transtheoretical model to strengthen execution, ensuring effective intervention. This case fully leveraged primary care initiative through community-upper level hospital coordination, whole-course management, and generalist-specialist collaboration (Figure 2 [Figure 2: see original paper]), demonstrating high patient satisfaction and effective management outcomes.

This case report provides a demonstration for primary care general practitioners managing “Three Highs” patients with fatty liver disease. It optimizes a standardized general practice pathway for screening, risk assessment, and two-way referral; explores a whole-course management framework for typical multimorbidity centered on general practitioners; and for the first time reveals therapeutic inertia in managing such patients through case analysis, addressing insufficient patient awareness and physician inertia through adherence intervention, family involvement, and shared decision-making.

Limitations: This is a single case report with limited sample representative-

ness. While it can enhance primary care physicians' awareness of fatty liver disease, its impact on improving disease prevention, screening, diagnosis, and treatment capabilities, as well as optimizing community management models and promoting whole-cycle health management for FLD patients, is limited through a single case. Future efforts will focus on broader promotion and validation of this protocol and pathway to construct a general practitioner-centered, whole-course, comprehensive management pathway for such patients.

In conclusion, early identification and assessment are crucial for outcomes in FLD patients with "Three Highs," and comprehensive management is an effective intervention. The integrated management model explored in this case proved effective, with significant improvement in FLD and "Three Highs" related parameters. This management model warrants further promotion and application.

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