Case Study: NAFLD as A Cardiovascular Risk Factor

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A 48 years male obese patient complaining of generalized weakness, chronic fatigue, and right hypochondrial dull aching pain. His BMI is 31Kg/m2, WC is 112cm, and the hepatic transaminases are elevated more than three times upper normal level. He had a past history of hypertension and dyslipidemia (hypertriglyceridemia, low HDL-C). No history of alcoholic intake and had a negative viral marker. Ultra-sonography revealed increased echogenicity, Elastography study suggested fatty liver, significant fibrosis and liver biopsy shew steatosis, hepatocyte ballooning and lobular inflammation (components of NASH).

He received treatment for these risk factors, but after 4years he suffered from typical anginal chest pain and accidently discovered diabetes mellitus. He was admitted in CCU for urgent PCI, stented in the left anterior coronary artery and discharged on cardiological and antidiabetic medications.

Definition and causes of NAFLD (1)

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease affects approximately 25% of the adult population. Since NAFLD is frequently associated with further metabolic comorbidities such as obesity, type 2 diabetes mellitus, or dyslipidemia, it is generally considered as the hepatic manifestation of the metabolic syndrome.

NAFLD is also associated with subclinical and clinical cardiovascular disease (CVD) as hypertension, coronary heart disease, cardiomyopathy, and cardiac arrhythmias, which clinically result in increased cardiovascular morbidity and mortality especially those with progressive forms of NAFLD, including non-alcoholic steatohepatitis (NASH) and/or advanced fibrosis, as well as NAFLD patients with concomitant type 2 diabetes.

Differential Diagnosis of NAFLD (2)

Diseases other than the metabolic syndrome can be associated with hepatic fat, and these might enter into the differential diagnosis of fatty liver disease as uncommon causes of NAFLD: (Table)

• Disorders of lipid metabolism as: - Familial combined hyperlipidemia,
- Glycogen storage disease,
- Lipodystrophy.
• Total Parenteral Nutrition. • Wilsons Disease.
• Celiac Disease. • HCV infection.
• Severe surgical weight loss •Starvation.
•Medications: as Methotrexate, Amiodarone, Corticosteroids, etc.…
• Environmental Toxicity.

Clinical Impression

This obese patient had an elevated transaminase, negative viral markers, without history of alcohol intake, ultrasonography revealed increased echogenicity, and the liver biopsy shew steatosis, hepatocyte ballooning and lobular inflammation. So, he could be diagnosed as NASH. Another emerging term could be applied on this patient which is MAFLD (Metabolically Associated Fatty Liver Disease) since he had also some evidence of metabolic dysregulation as hypertension, diabetes dyslipidemia beside the fatty liver.

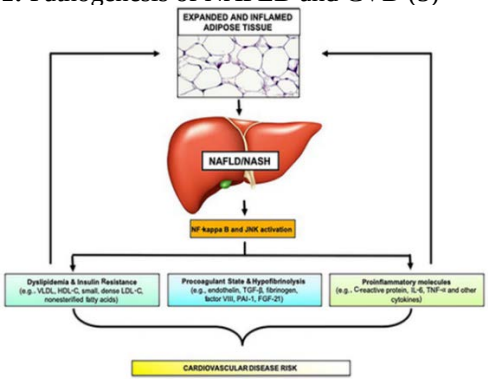
NASH and CVD

A number of studies have shown that NAFLD is a risk factor for CVD and in particular CHD, independent of traditional risk factors (as age, dyslipidemia, hypertension, etc.….) and accounts for at least 40% of total deaths (3).

As NAFLD progresses, expansion and inflammation of intra-abdominal visceral adipose tissue precipitate a proinflammatory cascade through the nuclear factor kappa B (NF-κB) and c-Jun N-terminal kinase (JNK) pathways.

The downstream sequelae are multiple and include systemic/hepatic insulin resistance caused by adipose tissue inflammation with accelerated hepatic steatosis; increased production of inflammatory cytokines by hepatocytes, Kupffer cells, and hepatic stellate cells; synthesis of procoagulant factors with hypo fibrinolysis; and disordered lipid metabolism (4).

Fig 1: Pathogenesis of NAFLD and CVD (5)



CVD Risk Management and Stratification in NAFLD

CVD in NAFLD is associated with traditional and nontraditional CVD risk factors. The Framingham Risk Score (FRS) estimates 10-year rates of CVD events has been validated in NAFLD and may be helpful to risk-stratify individuals and guide treatment of CVD risk factors. A subsequent prospective study in patients with biopsy-proved NAFLD showed that advanced fibrosis on biopsy and higher fibrosis scores were independent predictors of incident CVD. (6)

Of the traditional risk factors, plasma low-density lipoprotein cholesterol (LDL-C) level has shown inconsistent association with CVD in the NAFLD population that may reflect lipid-lowering therapy or advanced liver disease.

Management of our patient with NAFLD (7)

Management of NAFLD must extend beyond liver disease to include CVD risk modification to decrease CVD mortality.

• Healthy diet; in form of High intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, Minimize the intake of trans fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages.

• ≥150 min/week moderate-intensity or ≥75 min/week vigorous-intensity physical activity.

• Stop smoking.

• Nonpharmacological and/or pharmacological therapy with target blood pressure <130/80 mm Hg.

• Statin therapy as the first-line treatment for CVD primary prevention in patients with elevated LDL-C levels ≥190 mg/dL, established diabetes, age 40-75 years, and/or elevated ASCVD score.

• Glycemic control and individualized the target according to the case. Metformin is the first-line therapy, followed by consideration of a SGLT2 inhibitor or a GLP1 receptor agonist with proven CV protection.

Recently, a systematic review and meta-analysis of randomized controlled trials (RCTs) were studied. Besides, three large electronic databases were systematically searched (up to 15 December 2020) to assess the efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) for treatment of nonalcoholic fatty liver disease (NAFLD) or steatohepatitis (NASH). They concluded that treatment with GLP-1 RAs (mostly liraglutide and semaglutide) is a promising treatment option for NAFLD or NASH that warrants further investigation. (8)

References

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