Non-alcoholic fatty liver disease – Pathophysiology

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Nonalcoholic fatty liver disease (NAFLD) is the liver manifestation of the metabolic syndrome and one of the most common liver diseases in developed countries. NAFLD refers to a wide range of liver damage, ranging from pure steatosis to a more severe liver damage. Steatohepatitis (NASH) is characterized, in addition to steatosis, by an inflammatory process that can lead to fibrosis, cirrhosis and heaptocellular carcinoma. Recruitment and/or activation of inflammatory cells is a key issue in the progression of NAFLD. Only patients showing inflammation will develop advanced liver disease whereas patients without inflammation will remain at the steatosis stage.

The liver receives blood from the gastrointestinal tract and the systemic venous system and is constantly exposed to food antigens, bacterial products and potential pathogens. Consequently, a specific immune environment exists in the liver. Innate immunity is largely developed with an enrichment of innate lymphocytes, including both NK and NKT cells and a large amount of resident macrophages so called Kupffer cells. Lymphocytes homeostasy is disturbed in the fatty liver: NKT and T regulator lymphocytes are decrease, steatosis induced a higher recruitment of blood lymphocytes and Kupffer cells show a pro-inflammatory phenotype. Lipid accumulation in the liver is correlated to the immune tolerance disruption leading to the initiation of NASH.

Overall, decrease of liver immune tolerance by modulation of innate and adaptative immunity will lead to the progression from steatosis to severe liver damage.