Metabolic dysfunction-associated steatotic liver disease : the tree that hides the forest ?

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To the Editor,

The world of hepatology has been recently shaken by a much-needed change of nomenclature validated by a large expert consensus (1). This consensus finally adopts positive diagnostic criteria for the recently renamed metabolic dysfunction-associated steatotic liver disease (MASLD) (Table 1) (1). This change in nomenclature is supported by scientific arguments published in the *Acta Gastro-Enterologica Belgica* (2). However, making the diagnosis of MASLD easy on the basis of the coexistence of hepatic steatosis (by imaging or histology) and just one cardiometabolic criterion (Table 1) (1) instead of a diagnosis of exclusion must not relegate other causes of chronic liver diseases to second place (3,4). Here is a case study to illustrate the point. A 56-year-old man was referred to the hepatology outpatient clinic for mild elevation in ALT serum level (50 U/L, nl < 40 U/L). His medical history includes hypereosinophilic asthma, dyslipidaemia treated with a statin and overweight (body mass index measured at 29.9 kg/m²). Blood tests also showed abnormal triglyceride levels (236 mg/dL, nl < 150 mg/dL), an increased HOMA-IR index (4.6), and a significant elevation of serum eosinophilic count (1240/µl, nl < 500/µl). Screening for hepatitis B and C, iron overload, auto-immune hepatitis and alpha-1 antitrypsin deficiency returned negative. Liver ultrasound showed a hyperechoic liver. Transient elastography (XL probe) was compatible with severe steatosis (controlled-attenuation parameter measured at 344 dB/m) and advanced fibrosis (elasticity measured at 10.3 kPa) (Figure 1A). Based on the new definition (1), the diagnosis of MASLD can now be made. A percutaneous liver biopsy was nevertheless proposed to histologically confirm the diagnosis and its severity for inclusion in an interventional trial because of the suspected fibrosis and the lack of weight reduction and elasticity following dietary measures. Surprisingly, liver histology showed only focal steatosis (<5%) (S0 according to the Beaujon score) (Figure 1B), a stage two fibrosis (Figure 1C) and an eosinophilic portal hepatitis (Figure 1D). Eosinophilic hepatitis can be observed in several conditions including parasitic infections, drug hypersensitivities, vasculitis, hypereosinophilic syndroms or neoplasms (Table 2) (5). However, the cause remains unindentified in up to 60% of cases (5). Parasite serology tests including *Toxocara canis*, *Strongyloides stercoralis*, *Trichinella spiralis* and *Schistosoma* were performed. *Schistosoma* serology returned positive confirming the diagnosis of schistosomiasis. The treatment consisted in one dose of praziquantel 40 mg/kg and induced a drop in serum eosinophilic count. Taking a detailed history, the patient reported a long stay in sub-Saharan Africa in 2021 where he used to swim in freshwater, explaining the parasite transmission. Schistosomiasis is a frequent tropical condition affecting more than 230 million people worldwide, but data on its epidemiology in Caucasian travellers are scarce (6). The most frequent specie in sub-Saharan Africa is *Schistosoma mansoni* and the transmission occurs though skin contact with freshwater containing infective cercariae (6). Cercariae then pass though the intestinal wall to grow in mesenteric

Table 1. — **New diagnostic criteria for metabolic dysfunction-associated steatotic liver disease (MASLD)**

MASLD diagnostic criteria
Liver steatosis (confirmed by imaging or liver biopsy)
+ ≥ 1 cardiometabolic criteria: **BMI** ≥ 25 kg/m² (23 Asia) OR WC > 94 cm for men, > 80 cm for women OR ethnicity adjusted equivalent **Fasting serum glucose** ≥ 100 mg/dL OR 2-hour post-load glucose levels ≥ ≥ 140 mg/dL OR HbA1c ≥ 5.7% OR type 2 diabetes OR treatment for type 2 diabetes **Blood pressure** ≥ 130/85 mmHg OR antihypertensive drug treatment **Plasma triglycerides** ≥ 150 mg/dL OR lipid lowering treatment **Plasma HDL-cholesterol** ≤ 40 mg/dL for men, ≤ 50 mg/dL for women OR lipid lowering treatment

Table 2. — **Potential differential diagnosis for eosinophilic liver infiltration**

Differential diagnosis of eosinophilic liver infiltration	**Reported prevalence (%)**
Parasitic infections	25
Drug hypersensitivities	2
Vasculitis	2
Hypereosinophilic syndroms	9
Neoplasms	*undetermined*
Unindentified cause	62

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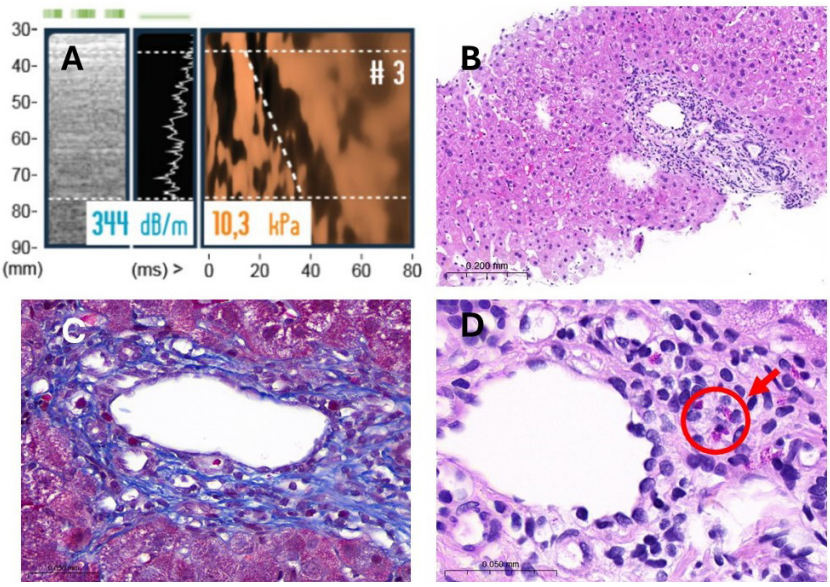

Figure 1. — Results of non-invasive evaluation by transient elastography and liver biopsy. Controlled attenuation parameter and elasticity are consistent with fibrosing steatotic disease (A). However, haematoxylin eosin staining at low magnification shows only discrete focal steatosis (B), Masson's trichrome staining evidences periportal fibrosis and haematoxylin eosin staining at high magnification reveals portal hepatitis containing eosinophils (red arrow) (C, D).

veines. Adult females release eggs in the intestine and the mesenteric veines which will end up in small portal branches, transported by the portal flow (6). These eggs induce a pro-fibrotic chronic eosinophilic inflammation promoting potentially severe portal hypertension (6). This case illustrates how important it is for hepatologists to remain vigilant in the face of an easy diagnosis of MASLD, which can be the tree hiding the forest. It is therefore important to keep a critical eye, a detailed medical history and perform a scrupulous analysis of laboratory data. Not all disturbances of the liver tests are MASLD, even though a hyperechoic liver is very frequently observed and more than 85% of people over 45 years have ≥1 cardiometabolic risk factor (4).

Keywords: MASLD, histology, hypereosinophilia, schistosomiasis, hepatitis, transient elastography.

Conflict of interest statement

The authors declare that they have no conflict of interest related to the content of this manuscript. The patient has given signed written consent for the publication of his case report.

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