Insight ... ADAMTS13 has a role in the formation of microthrombi in the liver but seems not to contribute to the development of NASH

What ADAMTS13 does in the liver...

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A disintegrin-like and metalloprotease with thrombospondin type I repeats 13 (ADAMTS13), a member of the ADAMTS-family comprising 19 members, is a protease that cleaves ultra-large multimeric von Willebrand Factor (VWF) into small fragments. Through this activity, ADAMTS 13 acts antithrombotic, as it prevents the formation of platelet-rich microthrombi. Besides endothelial cells, liver cells are thought to be the main source of ADAMTS13 (for review please see [1]). The latter finding and several studies support the notion that the protease beyond being involved in preventing thrombotic events could also play a role in modulating the pathogenesis of liver diseases (2). In their manuscript published in this issue of *Thrombosis and Haemostasis*, Geys et al. asked the question whether ADAMTS13 has a role in the formation of microthrombi in the liver and in addition might contribute to the development of non-alcoholic steatohepatitis (NASH) (3). To that end, the authors employed a murine model of high-fat diet-induced obesity and liver steatosis in ADAMTS13−/− mice. Indeed, the authors could show that obese ADAMTS13−/− mice developed more hepatic microthrombi than obese wild-type mice. Interestingly, plasmin-alpha2-antiplasmin levels were similar in both groups of mice, ruling out a compensatory activation of the fibrinolytic system to remove the microthrombi formed. In addition and as to be expected, ADAMTS13−/− mice showed higher levels of ultra large VWF multimers and lower platelet counts than their wild-type counterparts. However, markers of inflammation, oxidation and liver steatosis and fibrosis, albeit being increased in obese animals under high-fat diet compared with lean mice fed normal chow, were not affected by ADAMTS13 deficiency. Thus, the authors conclude that NASH is triggered by obesity, whereas ADAMTS13 does not seem to be involved in the development of this condition. However, ADAMTS13 deficiency leads to the formation of microthrombi in the liver in obese mice. Taken together, albeit being an experimental study using a mouse model only, this investigation provides important and relevant information as it thoroughly characterizes the role of ADAMTS13 in the pathogenesis of NASH.

Conflicts of interest
None declared.

References

Insights on ➤Geys et al. Thromb Haemost 2017; 117: 19-26