Myocardial infarction accelerates hepatic pathological progression of NASH by triggering immunoinflammatory response and induction of periostin

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SUMMARY

Patients with non-alcoholic fatty liver disease (NAFLD), especially advanced non-alcoholic steatohepatitis (NASH), have an increased risk of cardiovascular diseases (CVD). Whether CVD events will, in turn, influence the pathogenesis of NAFLD remains unknown. Here, we show that myocardial infarction (MI) accelerates hepatic pathological progression of NAFLD. Patients with NAFLD who experience CVD events after their diagnosis exhibit accelerated progression of liver fibrosis. MI promotes hepatic fibrosis in mice with NASH, accompanied by elevated circulating Ly6C^{hi} monocytes and their recruitment to the damaged liver tissues. These adverse effects are significantly abrogated when deleting these cells. Meanwhile, MI substantially increases circulating and cardiac periostin levels, which act on hepatocytes and stellate cells to promote hepatic lipid accumulation and fibrosis, finally exacerbating hepatic pathological progression of NASH. These preclinical and clinical results demonstrate that MI alternates systemic homeostasis and upregulates pro-fibrotic factor production, triggering cross-disease communication that accelerates hepatic pathological progression of NAFLD.

Graphical Abstract