Did you know neutrophils can help to form gallstones?

Cholelithiasis, also known as gallstones, are hard masses of cholesterol and calcium crystals that get lodged in the gall bladder and can cause extreme pain. Gallstones is a very prevalent disease, causing high morbidity and hospitalisation. Despite the high morbidity, the mechanism of gallstones development, specifically factors that contribute to cholesterol and calcium aggregation is not well understand. Recent research published in Immunity by Muñoz *et., al* 2019 demonstrated the role of neutrophils in the development of gallstones.

Examination of “sludge” and gallstones extracted from individuals undergoing hepatobiliary stents (metal tube to keep the bile duct open), showed that gallstones contain extracellular DNA (ecDNA) and elastase derived from neutrophils. This finding was further confirmed by in vitro tests, where gallstones in the presence of neutrophils had deposits of ecDNA and neutrophil elastase on its surface.

Additionally, using a murine model with abrogated reactive oxygen species (ROS) driven NET formation, they demonstrated that NET is required for gallstone development. These findings suggested that dampening NET formation could inhibit gallstone growth. Thus, they showed that preventing NET formation by inhibiting of peptidyl arginine deiminase type 4 or abrogation of reactive oxygen species (ROS) production and damping of neutrophils by metoprolol prevents the growth of gallstone.

In summary, Muñoz *et.,* demonstrated that after crystal formation, NET foster their assembly into larger aggregates and finally gallstones. The discovery of NETs role in gallstone formation may offer areas of treatment and prevention of gallstones.

Journal Article: Muñoz, L.E. et., al 2019. Neutrophil Extracellular Traps Initiate Gallstone Formation. Immunity

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