Microvesicular Steatosis in NAFLD Not Rare

BY SHERRY BOSCHERT

SAN DIEGO — Microvesicular steatosis may be more common in patients with nonalcoholic fatty liver disease than previously thought and is associated with markers of severe disease, a study of 1,022 biopsies suggests.

Of the liver biopsies from adult patients with nonalcoholic fatty liver disease (NAFLD), 10% showed microvesicular steatosis when reviewed by a pathology committee for the study, Dr. Sweta R. Tandra and her associates reported at the annual meeting of the American College of Gastroenterology.

Previously, microvesicular steatosis was thought to be rare in patients with NAFLD, which is more typically associated with macrovesicular steatosis, said Dr. Tandra of Indiana University, Indianapolis. The significance of the presence of microvesicular steatosis has been unclear.

The investigators identified microvesicular steatosis in 102 (10%) of the biopsies, which came from patients who had an average age of 50 years and a mean body mass index of 35 kg/m^2. The patient cohort was 63% female and 82% white.

The presence of microvesicular steatosis was significantly associated with histologic indexes denoting severe disease, including higher grades of macrovesicular steatosis, advanced fibrosis, ballooned hepatocytes, megamitochondria, higher NAFLD activity scores, and a diagnosis of nonalcoholic steatohepatitis, she said.

The findings were based on a multivariate analysis that adjusted for the influence of age, sex, race, body mass index, and the presence of diabetes.

The presence of macrovesicular steatosis increased the likelihood of finding microvesicular steatosis two- to sixfold.

Also, patients with fibrosis were two to six times more likely to have microvesicular steatosis than were patients without fibrosis.

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Microvesicular steatosis was three to four times more likely in the presence of ballooning and five times more likely in the presence of megamitochondria, two markers of cell injury.

No associations were seen between microvesicular steatosis and lobular inflammation or levels of aspartate aminotransferase (AST) or alanine aminotransferase (ALT).

Biopsies for the study were obtained from a consortium of eight clinical research centers and one data coordinating center sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases.

On histology, macrovesicular steatosis is defined by a single, large vacuole of fat that fills up the hepatocyte and displaces the nucleus to the periphery of the cell.

In comparison, the presence of multiple small intracellular lipid droplets with an undisplaced nucleus generally defines microvesicular steatosis, which has been thought to result from impaired mitochondrial beta-oxidation of fatty acids, Dr. Tandra said.

The investigators defined microvesicular steatosis as the presence of "nonzonal contiguous patches of foamy hepatocytes with centrally placed nucleus" on hematoxylin and eosin staining under light microscopy, she added.

"As microvesicular steatosis generally indicates mitochondrial dysfunction, our data support a role for mitochondrial dysfunction in the pathogenesis of nonalcoholic steatohepatitis," Dr. Tandra said.

More research is needed to clarify the significance of microvesicular steatosis in patients with NAFLD, she added. ■

Disclosures: *Dr. Tandra reported having no conflicts of interest related to the study.*

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