

PRESENCE OF IGA CLASS ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) IN CIRRHOSIS – POSSIBLE HINT TOWARDS THE INVOLVEMENT OF GUT MUCOSAL IMMUNE SYSTEM?

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA) are a non-uniform family of antibodies recognizing diverse components of neutrophil granulocytes. ANCA formation might be induced by protracted bacterial infections or probably reflect an abnormal immune response to commensal microorganisms. Bacterial infections are common complications in cirrhosis with high incidence of episodes caused by enteric organisms, therefore, we sought to study the presence and clinical importance of ANCA in cirrhosis.

Methods: Sera of 385 patients with cirrhosis of different etiologies were assayed for ANCA of IgG, IgA, IgA1, IgA2 and secretory IgA subtypes by indirect immunofluorescence and ELISAs. Control group comprised of 202 patients with chronic liver diseases without cirrhosis and 100 healthy subjects. In cirrhosis, a 2-year follow-up, observational study was conducted to assess possible association between presence of ANCA and clinically significant bacterial infections.

Results: Prevalence of ANCA IgA was significantly higher in cirrhosis (52.2%) compared to chronic liver diseases (18.6%) or healthy controls (0%, $p < 0.001$ for both). ANCA IgA subtyping assays revealed marked increase in the proportion of IgA2 subtype (46% of total ANCA IgA) and presence of the secretory component concurrently. Presence of ANCA IgA was associated to disease-specific clinical characteristics (Child-Pugh stage and presence of ascites, $p < 0.001$). During a 2-year follow-up period, risk of infections was higher among patients with ANCA IgA compared to those without (41.8% vs. 23.4%, $p < 0.001$). ANCA IgA positivity was associated with a shorter time to the first infectious complication ($pLogRank < 0.001$) in Kaplan–Meier analysis and was identified as an independent predictor in multivariate Cox-regression analysis (HR:1.74, 95%CI:1.18–2.56, $p = 0.006$).

Conclusions: Presence of IgA type ANCA is common in cirrhosis. Involvement of gut mucosal immune system is in center of the formation and probably reflects sustained exposure to bacterial constituents.