

Primary immune deficiency screening in patients with biopsy proven autoimmune liver diseases

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INTRODUCTION: Autoimmune liver diseases (ALD) includes autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC) which are chronic auto-inflammatory diseases of the liver with complex and heterogeneous pathogenesis. Malfunctioning immune system is the sine qua non of ALD, and affects liver and other organs. We aimed to delineate the frequency of primary immune deficiency (PID) in patients with biopsy proven ALD.

METHODS: Single-institutional liver biopsy database, along with chart data was retrospectively evaluated between January 2007 and January 2018. The cases with a designated diagnosis of AIH, PBC, PSC and overlap syndrome (OS) were included. Data collection included age, sex, liver tests, autoantibody profiles, leukocyte and thrombocyte counts, immunoglobulin levels and biopsy parameters (hepatic activity index (HAI) and METAVIR fibrosis score (FS)). Leukopenia, neutropenia, lymphopenia and thrombocytopenia were defined as smaller than 4,4x10³ cells/microL, 1,5x10³ cells/microL, 1,0x10³ cells/microL, and 1,5x10⁶ cells respectively. PID was screened by presence of lymphopenia (<1000/ml) and serum immunoglobulin levels evaluated by using standard deviations from age matched values.

RESULTS: ALD was confirmed in 60 cases out of 104 liver biopsy. The distribution of ALD was 37 (61.6%) AIH, 18 (30.0%) PBC, 3 (5%) PSC, and 2 (3.3%) OS. The median age was 47 years and 80.3% was woman. FS F1, F2, F3 and F4 were reported in 7 (11.6%), 18 (30.0%), 19 (31.6%), and 16 (26.8%) patients. Basal thrombocytopenia was reported in 15% of patients, and was not related to FS as 4/10 thrombocytopenic patients had F0 and F1 FS. The lymphopenia was detected 5 (8.3%) of ALD (8.1% in AIH, 5.6% in PBC, 50% in PSC, and 33.3% in OS). Leukopenia, neutropenia, and lymphopenia were respectively present in 13%, 8%, and 22% of patients. The lymphopenia was not associated with type of ALD, leukopenia, thrombocytopenia, HAI or FS. IgA levels were >70 mg/dL in all cases, however 6% were below 90 mg/dL. IgG and IgM levels were above lower limit in all cases. Leukopenia was seen in 13%, neutropenia in 8% and lymphopenia in 22%.

CONCLUSION: Although most of patients (88.4%) advanced fibrosis, leukopenia (13%) or thrombocytopenia (15%) was not frequent in this ALD cohort. Basal lymphopenia was present in approximately one-fifth of patients before immunosuppressive treatment. Lymphopenia was not associated with neither clinical or histological parameters. The immune dysregulation accompanying ALD warrants further investigation because of their well-known clinical and prognostic implications

Keywords: autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, primary immune deficiency