The Utility of Liver Elastography in the Evaluation of Nodular Regenerative Hyperplasia (NRH) in Patients with Common Variable Immune Deficiency (CVID)

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**BACKGROUND**
- Common variable immunodeficiency (CVID) is the most common, symptomatic primary immunodeficiency world-wide.\(^1\)
- A subset of CVID patients are susceptible to benign end-organ lymphoproliferative manifestations, including nodular regenerative hyperplasia (NRH) of the liver, characterized by remodeling of hepatic parenchyma with diffuse replicating/regenerating nodules resulting in cirrhotic physiology.\(^2\)
- Liver biopsy is the current gold standard for NRH diagnosis; however, implementation of liver elastography (FibroScan), a quick, noninvasive ultrasound test, in the diagnosis and monitoring of NRH has yet to be investigated in patients with CVID.

**OBJECTIVES**
- We sought to further evaluate the utility of FibroScan in the diagnostic scheme and monitoring of NRH in CVID patients.

**METHODS**
- We identified CVID patients with biopsy-confirmed NRH (n=8) from a retrospective CVID cohort followed at the Massachusetts General Hospital.\(^3\)
- We identified CVID patients without NRH (n=4) based on normal serial liver biochemistries and/or biopsy-confirmed non-NRH.
- We evaluated baseline patient characteristics, liver biochemistries, full clinical immunophenotypes, and autoinflammatory comorbidities.
- FibroScan reads (in kPa) for CVID patients with NRH were compared with prospective research FibroScan reads in CVID controls without NRH.

**RESULTS**

**Patient Demographics, Immunophenotypes, and Autoinflammation.**

***Fig. 1: CVID without vs. with NRH - Patient Demographics, Immunophenotypes, and Autoinflammation.***

- **(A) Patient Demographics:** Age [median 62 vs. 41 years; \(p=0.09\)], sex [male vs. female; \(p=0.07\)], and BMI [median 28 vs. 24 kg/m\(^2\); \(p=0.53\)] were not statistically different when comparing CVID patients without vs. with NRH. (B) Immunophenotypes: Naïve (CD45RA\(^+\)) T cell percentages [median 51.4% vs. 14.3%; \(p=0.0061\)] and IgA values [median 75 vs. 7 mg/dL; \(p=0.045\)] were significantly lower in CVID patients with NRH, indicating a worse clinical immunophenotype. A trend towards lower CD27\(^+\)CD8\(^+\) class-switched memory (SM) B cells was also observed. There were no significant differences in the other immunoglobulin levels (IgG and IgM) or flow cytometric markers (including CD3\(^+\), CD4\(^+\), CD8\(^+\), and CD19\(^+\) cells) evaluated.
- **(C) Autoinflammation:** Prevalence of autoinflammatory comorbidities (including autoimmune cytopenias and extraneous end-organ benign lymphoproliferation) was not significantly different when comparing CVID patients without vs. with NRH (\(p=0.15\)).

**Liver Biochemistries.**

***Fig. 2: CVID without vs. with NRH - Liver Diagnostics.***

- **(A) Liver Biochemistries:** AST values were higher [median 25 vs. 43 U/L; \(p=0.022\)] in CVID patients with NRH. ALT [median 22 vs. 32 U/L; \(p=0.17\)] and ALKP [median 90.5 vs. 160 U/L; \(p=0.15\)] trended towards higher in CVID patients with NRH but did not reach statistical significance.
- **(B) FibroScan Results:** FibroScan-obtained liver stiffness (kPa) was significantly elevated [median 46.4 vs. 11.0 kPa; \(p=0.0040\)] in CVID patients with NRH.

**CONCLUSIONS**
- Demographic parameters, (age, sex, and BMI) and prevalence of other autoinflammatory comorbidities were not significantly different for CVID patients without vs. with NRH.
- Naïve (CD45RA\(^+\)) T cell percentages and IgA values were significantly lower in CVID patients with NRH, indicating a worse clinical immunophenotype.
- AST values were significantly elevated in CVID patients with NRH.
- FibroScan-obtained liver stiffness (kPa) was significantly elevated [median 46.4 vs. 11.0 kPa; \(p=0.0040\)] in CVID patients with NRH.
- These preliminary data suggest the diagnostic utility of FibroScan in CVID patients with NRH. Elevated liver biochemistries and liver stiffness measurement by FibroScan may prompt earlier consideration for liver biopsy. Further studies will extend these findings to the full CVID cohort, correlate FibroScan reads with NRH disease severity on biopsy, and correlate serial reads of liver stiffness with NRH disease pathogenesis in the context of immunosuppressive therapy.

**CITATIONS**
