Clinical Perspectives on Liver Biopsy and FNA

Ray Chung, M.D.
Director of Hepatology and Liver Center
Vice Chief, Gastroenterology Division
Kevin and Polly Maroni Research Scholar
Massachusetts General Hospital
Liver Biopsies and Clinical Trials

- Histologic endpoints have had relevance as primary endpoints in nonviral liver disease
  - NAFLD
- For HBV and HCV, virologic or serologic endpoints have been traditional primary endpoint
  - Histologic response as supportive secondary endpoint
  - Intrahepatic analysis generally a research rather than clinical tool
  - For HBV, liver tissue also important (and only reliable) source of cccDNA
The inexorable move to a noninvasive landscape

• Liver biopsies increasingly falling out of favor in clinical practice
• Improving performance of noninvasive fibrosis testing
  • Elastography
  • Serum markers
• With increased attention to functional cure of HBV, how best to assess correlates of immunologically directed anti-HBV therapy?
  • HBV specific T cell responses
• Sampling of PBMC compartment
  • Low yield for HBV-specific T cell responses
  • Fails to reflect critical intrahepatic responses
How to sample the intrahepatic immune environment in a minimally invasive manner?

• While liver biopsies much more accurately capture intrahepatic T cell responses, in general not clinically warranted

• Fine needle aspirations of the liver offer a viable alternative
Fine Needle Aspiration of the Liver

• Historically FNA used to sample focal lesions from a variety of tissues

• Typically yield enriched for mobilizable cell populations
  • Immune cells: lymphocytes, monocytes/macrophages, DCs, NK cells, MAIT cells

• Prior studies have demonstrated that they sample the breadth of immune cell landscape in liver

• Can be done with minimal blood contamination
  • Algorithms to normalize for peripheral blood
Procedural distinctions from liver biopsy

- Size of needle
  - 22-25g vs. 15-16g
- Risk limited compared with percutaneous core biopsy
- Up to 4 passes permissible using introducer needle
- US guidance or blind
- No requirement for sedation
- No absolute need for monitoring
- Can be performed in the office setting
Can FNAs be practically implemented as key exploratory endpoint?

• Need for standardized protocols (aspiration procedure)
• IR suite
• Technician in suite for sample processing
• Minimization of blood contamination (normalization)
• Adequacy of cell yield
• Viability of cells (flash freezing)
FNAs and clinical interventions

• Nuc stop studies
  • Define immune profiles of successful future containment/control

• Immunotherapy
  • Define effects of T cell, innate immune directed therapies on functional responses (e.g., anti-PD1)
  • scRNAseq

• RNAi and other DAAs
  • Assess indirect effect on T cell responses

• Development of biomarkers related to intrahepatic immune profiles
Summary

• FNA capable of reliably sampling the intrahepatic immune environment
• Safe, well tolerated
• Standardizable technique
• Holds promise as exploratory endpoint for HBV treatment trials directed at functional cure