Is there still room for liver biopsy in viral hepatitis?

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Topics
- Hepatitis B
- Hepatitis C
- Hepatitis E
- Viral hepatitis by non-hepatotrophic viruses
Basis for the discussion on liver biopsy in viral hepatitis

EASL-(ALEH) Clinical Practice Guidelines / Recommendations
- 2017 - Clinical Practice Guidelines on hepatitis B
- 2018 - Recommendations on treatment of hepatitis C
- 2018 - Clinical Practice Guidelines on hepatitis E
- 2015 - Clinical Practice Guidelines on non-invasive tests

Daily practice
- Interaction with hepatologist(s), Prof. Dr. Beat Müllhaupt, USZ
- Own cases
Two developments have changed the field

**Indications for liver biopsies decreased** mainly due to
- the availability of **direct-acting antiviral agents (DAA)**
- the availability of **non-invasive methods** to determine liver fibrosis

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Castera et al. (2005) Gastroenterology
Castera et al. (2008) Journal of Hepatology
HBV
Liver biopsy in hepatitis B

Natural history and assessment of patients with chronic HBV infection

- HBV markers
  - HBsAg
  - HBeAg/anti-HBe
  - HBV DNA

- Liver disease
  - Biochemical parameters: ALT
  - Fibrosis markers: non-invasive markers of fibrosis (elastography or biomarkers) or liver biopsy in selected cases

Assessment of patients with chronic HBV infection
- is based upon HBV markers, biochemical parameters and fibrosis markers
- including non-invasive markers or liver biopsy in selected cases

Li et al. (2016) Aliment Pharmacol Ther
Liver biopsy in hepatitis B

Patients without cirrhosis should be considered for treatment when
- they have HBV DNA levels above 2,000 IU/ml, serum ALT levels above the traditional ULN (40 IU/L)
- and severity of liver disease assessed traditionally by liver biopsy showing at least moderate necroinflammation (A2) and/or at least moderate fibrosis (F2)

Liver biopsy in hepatitis B

A liver biopsy or a non-invasive test should be performed to determine disease activity in cases where biochemical and HBV markers reveal inconclusive results.
A liver biopsy can be performed for treatment decision in hepatitis B

activity < A2 and fibrosis < F2
➢ no treatment

activity >/= A2 and/or fibrosis >/= F2
➢ treatment

figure adapted from Asselah et al. (2014) Journal of Hepatology
Liver biopsy in hepatitis C

In chronic hepatitis C, non-invasive methods should be used instead of liver biopsy to assess liver disease severity prior to therapy.

Fibrosis stage must be assessed by non-invasive methods initially, …

… with liver biopsy reserved for cases where there is uncertainty or potential additional aetiologies.
A liver biopsy may be performed in hepatitis C – mixed aetiologies

Liver biopsy may be required in cases of known or suspected mixed aetiologies (e.g. metabolic syndrome, alcoholism or autoimmunity).

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A liver biopsy may be performed in hepatitis C – uncertainty

**Liver biopsy** reserved for cases where there is uncertainty

In patients with advanced fibrosis and cirrhosis, **surveillance for HCC** must be continued because an SVR (sustained viral response) will reduce, but not abolish, the risk of HCC.
A liver biopsy may be performed for surveillance decision in hepatitis C

Surveillance for HCC:
- Patients with cirrhosis must be identified, as their treatment regimen must be adjusted and **post-treatment surveillance for HCC is mandatory**
- Post-treatment surveillance for HCC must also be performed in patients with **advanced fibrosis** (METAVIR score F3)
A liver biopsy may be performed for surveillance decision in hepatitis C

- fibrosis < F3 ➢ no surveillance for HCC
- fibrosis >= F3 ➢ surveillance for HCC: long term follow up by US

figure adapted from Asselah et al. (2014) Journal of Hepatology
HEV
Patients with acute or chronic **HEV infection** who develop new onset proteinuria may be considered for a **renal biopsy**.
Liver biopsy in hepatitis E

Immunohistochemistry for HEV ORF2 protein can be used to establish a histopathologic diagnosis of hepatitis E.
HEV can be visualized in the human liver

**HEV pORF2 IHC**
- HEV ORF 2 protein is detectable by IHC in FFPE human liver tissues
- IHC for HEV ORF 2 protein is a useful tool in daily practice

Debing Y et al. (2016) Journal of Hepatology
Liver biopsy – hepatitis of unknown etiology

Case, 67-y female patient
- Referral from GP to hepatologist because of recently elevated ALT, AST
- Suspected autoimmune hepatitis
- Lab values for autoantibodies not yet available at time of biopsy
Liver biopsy in hepatitis E

- On request: Travel history to South of France
Hepatitis E on pre-existing liver disease

**Case, 51-y male patient**
- Hx: IgA nephropathy, kidney transplantation
- Chronic liver disease / cirrhosis of unknown etiology
- Dramatic clinical worsening with icterus, ascites and pneumonia
Liver biopsy in viral hepatitis due to non-hepatotrophic viruses

Case, 26-y female patient

- Acute liver failure. Depressive mood since the age of 16.
- Liver failure of unclear origin.
- Suspected DILI.
Liver biopsy in viral hepatitis due to non-hepatotrophic viruses

Case, 52-y female patient

- Hx of rheumatoid arthritis.
- Elevated liver enzymes, suspected AIH.
Key message: Liver biopsy has still a role in viral hepatitis

Scenario: already established diagnosis of viral hepatitis (HBV or HCV infection):
- Selected indications for the assessment of disease activity and/or stage
  - for therapy decision (HBV infection)
  - for HCC surveillance decision (HCV infection)
- Search for competing factors
  - such as NAFLD or genetic metabolic diseases (iron, α1-AT)

Scenario: viral hepatitis among the differential diagnoses
- hepatitis E virus infection - value of HEV pORF2 IHC
- hepatitis by non-hepatotrophic viruses
References

- Li et al. (2016) The diagnostic accuracy of transient elastography for the staging of liver fibrosis in patients with chronic hepatitis B. Aliment Pharmacol Ther 43:458–469