

NAFLD-NASH-CIRRHOSIS

AN EPIDEMIC OF OBESITY



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Some Facts About Fatty Liver

- The most common cause of elevated ALT worldwide
- NAFLD is the leading cause of chronic liver disease in the U.S.
- Hepatic “fat” accumulation is a consequence and a marker for chronic insulin resistance and cardiovascular risk known as “Metabolic Syndrome”



Some Facts About Fatty Liver, cont.

- Metabolic syndrome
 - Aberrant glucose levels Hypertension
 - Dislipidemia Abdominal obesity

- 30% of patients with NASH can progress to cirrhosis

- 5% of patients with NASH may develop hepatocellular carcinoma ?



Prevalence of Metabolic Syndrome

- 34% in American adults
- 53% in patients with NAFLD
- 88% in patients with NASH

- “NASH/Cirrhosis will become the *leading* indication for liver transplantation by *2020!*”

- Estimated that it takes 8-12 years NASH to cirrhosis



Pathogenesis of Fatty Liver

“Its Complicated”

The “Two Hit Theory” of NAFLD

Hepatic lipid accrues by fatty acid transport *faster* than the rate of hepatic lipid clearance

- ▣ Increased ingestion of dietary fat
- ▣ Increased influx of free fatty acids
- ▣ Increased “de novo” lipogenesis
- ▣ Impaired hepatic beta-oxidation of fatty acids
- ▣ Impaired triglyceride export



Who needs to be worked up for NAFLD?

- In 2006 Chicago was named the “fattest” city in America!
- Consider with:
 - Elevated ALT
 - BMI over 30
 - Metabolic syndrome
- Remember – *ALWAYS* establish alcohol intake *AND* Hepatitis C status



Imaging

- “The liver should be imaged at least once!”
 - Ultrasound
 - CT scan / Tri-phasic CT scan
 - MRI scan

- Imaging *only* beneficial to rule out other significant liver lesions. The degree of fibrosis or inflammation *can not* be assessed with imaging



Liver Biopsy

- Does everybody require a liver biopsy?
- “At some point as the suspicion of increasing liver dysfunction progresses – a biopsy will be needed”
- Biopsy points
 - Samples only 1/50,000th of the liver
 - Cirrhosis missed in 10-20% of cases
 - Probably need to send specimen to hepatic pathologist for review



Liver Biopsy, continued

- Score
 - 1 to 3 Steatosis
 - 1 to 3 Inflammation
 - 1 to 2 Ballooning
 - Score 5 for NASH

- Fibrosis is scored 0 to 4



Now What to Do?

- So you have made the diagnosis of NASH in your obese patient with metabolic syndrome – now what to do?
- Weight loss, weight loss, weight loss
- “There is *no proven* benefit from any pharmacologic therapy”
- 10-20% reduction in baseline weight can normalize ALT in *some* patients



Vigorous Exercise

- “Vigorous” exercise (75 min/wk) improves NASH but *not* fibrosis
- *Doubling* “vigorous” exercise (150 min/wk) improves NASH *and* fibrosis
- “Vigorous” defined as heart rate over 141 minus age



Aggressively treat the Metabolic Syndrome!

- Hypertension
 - Insulin resistance
 - Cardiovascular disease
 - Dyslipidemia
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- It is ok and recommended to treat these patients with Statins, in spite of the elevated ALT
 - “These patients are more likely to die from cardiovascular disease than their liver disease”



What About Bariatric Surgery to “Save the Liver”

- Study – 180 morbidly obese – BMI 40 or over
- All had Bariatric Surgery
- All had NASH
- Followed for five years
- All had significant improvement ($p < 0.001$) in cholesterol, triglycerides, insulin resistance *and* hepatic steatosis score
- *No* progression of hepatic fibrosis occurred 5 years after Bariatric Surgery



Referral for O.L.T.

- “Difficult and Frustrating”
- Only *some* patients will actually become listed in spite of severe liver disease
- Most of these patients have *severe co-morbidities* that prevent OLT
- Most of these patients die from a combination of their co-morbidities and their liver disease *before* listing



Final – Therapy for NASH 2011

- Avoid exacerbating liver injury
 - Alcohol
 - Drugs that can contribute to steatohepatitis
- Treat clinically-indicated underlying co-morbidities aggressively
 - Lipid lowering agents
 - Insulin sensitizers in diabetes
- *Weight loss* – the *cornerstone* of treatment!



Questions

