Pregnancy-Induced Type 2 Autoimmune Hepatitis

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Introduction

- We report the first documented case of Type 2 Autoimmune Hepatitis (AIH) elicited by pregnancy.
- Type 2 AIH is similar clinically to Type 1 AIH, differentiated by the presence of anti-liver-kidney microsomal antibodies (anti-LKM).
- Pregnancy has been established as a risk factor for the development of autoimmune disease.
- The link between pregnancy and autoimmune disease is not yet well-established but thought to be a result of hormonal modulation and fetal microchimerism.

Admission and Initial Workup

19-year-old female with history of recent uncomplicated pregnancy with successful delivery 3 months prior, presented to the emergency department with 1 week of right upper quadrant pain, 2 days of worsening itching and yellowing of her skin.

Past Medical History:
Successful delivery of baby three months prior to admission.
Gravida 1, Para 1.

Social History:
Denies use of alcohol, tobacco, illicit drugs, herbal supplements.

Medications:
No current or recent new medications

Review of systems:
Positive for abdominal pain, pruritus, jaundice, and nausea. Negative for confusion or pale stools

Physical Exam:
Vitals: Within normal limits
BMI of 23kg/m^2
Eye: Scleral icterus present
Abd: Discomfort on palpation of right upper quadrant, no mass, no distention
Skin: Jaundice present
Neuro: Fully oriented, no asterixis present

Biochemical Testing:
AST 670
ALT 1107
ALP 329
Total Bilirubin 6.7
Conjugated Bilirubin 4.8
Unconjugated Bilirubin 1.9
INR of 1.3
Lipase 20

Acetaminophen negative
Ceruloplasmin 38
Ferritin 20
Alpha-1-antitrypsin 167
Hepatitis A/B/C/E negative
CMV/EBV/HSV negative

ANA negative
Antimitochondrial Ab negative
Soluble Liver Antigen Ab negative
Anti-Smooth Muscle Ab negative

Anti-Liver-Kidney Microsomal Antibody positive (titer of >1:2560)

Immunoglobulin levels normal

Histopathology

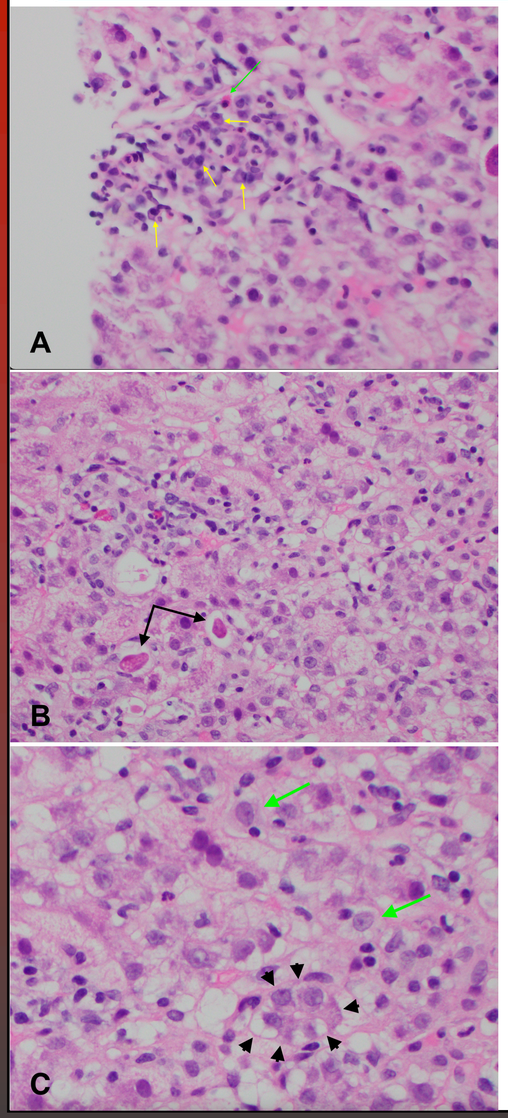

Figure A: H&E stain at 400x mag. Portal tract with lymphocytic infiltrate into surrounding hepatocytes consistent with mild interface hepatitis. Plasma cells present (yellow arrow). A lone eosinophil is present (green arrow).

Figure B: H&E stain at 400x mag. Acidophil bodies present (indicated by black arrows) which represent apoptotic hepatocytes, found in a background of lobular inflammation.

Figure C: H&E stain at 400x mag. Emperipolesis is present (green arrow) and is characterized by infiltration of lymphocytes into the cytoplasm of a hepatocyte. Rosette formation (black arrowheads) which represents small groups of hepatocytes arranged around a lumen, thought to be indicative of hepatocellular regeneration.

Treatment and Follow up

- High titer anti-LKM antibodies combined with the pathology findings confirmed a diagnosis of Type 2 Autoimmune Hepatitis. Chart review indicated that the patient did not receive methyldopa or hydralazine during pregnancy, medications which are known to cause drug-induced autoimmune hepatitis. Review also revealed that preconception and antepartum labs were normal, supporting that this was a new diagnosis.
- She was discharged on prednisone 60 mg daily with close follow up in liver clinic where she was started on azathioprine with subsequent improvement of her symptoms and laboratory markers.

Discussion

- The mechanism for initiation of autoimmune disease is unclear in the setting of pregnancy. It has been hypothesized that exchange of fetal and maternal cells occurs, known as fetal microchimerism, which may be a trigger for generation of autoimmune disease in pregnancy. This mechanism is proposed to be through immune sensitization by exposure to HLA-susceptibility alleles or a graft-vs-host type of mechanism.
- Another proposed mechanism suggests that hormonal fluctuations generate a shift between Th1 and Th2-mediated immunity during pregnancy. In the 3rd trimester and continuing into the postpartum period, there is a decrease in hCG which results in decreased expression of T-regulatory populations and resultant increase in inflammation. There is also an increase in prolactin which causes production of proinflammatory TNF-α, INF-γ, and IL-2 production.
- We believe our patient had a defect in allogeneic immune tolerance during pregnancy with resultant initial flare of AIH in the post-partum period.

References

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