A Case of Liver Failure Secondary to Chronic Intestinal Failure and Augmentin Use

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INTRODUCTION AND BACKGROUND

- We present a case of acute on chronic liver failure in a patient on chronic Augmentin and total parenteral nutrition (TPN). We highlight the mechanisms and key findings of liver injury associated with intestinal failure and Augmentin, which are relevant for evaluating the risks and benefits of such therapies.
- TPN is often used for patients with Crohn's disease, cancers, short bowel syndrome, or ischemic bowel disease. Critically ill patients who cannot receive nutrition orally for more than 4 days are candidates for TPN. Prolonged TPN use has been associated with liver disease.
- Intestinal Failure Associated Liver Disease (IFALD), also called parenteral nutrition-associated liver disease, is one of the main causes of death in patients with permanent intestinal failure.
- Drug Induced Liver Injury (DILI) can be caused by various mechanisms depending on the drug. Commonly identified drugs associated with DILI include Methotrexate, Amiodarone, HAART, Tamoxifen, and Corticosteroids. Antibiotics such as Augmentin are also known to be associated with DILI.

CASE DESCRIPTION

A 49-year-old woman with a history of cervical cancer treated with chemoradiation complicated by vaginal stenosis with reconstructive surgery complicated by short gut syndrome with chronic TPN dependency and chronic pelvic infections on Augmentin suppression therapy presented with hyperbilirubinemia and acute renal failure.

Initial Laboratory Results

- Bilirubin 29.4 (direct 18.9)
- Mild elevations in LFTs (AST 140, ALT 86)
- Normal Alkaline phosphatase
- INR 1.6
- Ammonia 145
- Creatinine 3.64
- Her labs three months ago had been at her baseline: Bilirubin 2.0, AST 40, INR 1.2, and Cr 2.0

Work Up

- Negative autoimmune hepatitis markers
- Negative acute viral hepatitis serologies
- Heterozygous C282Y mutation via genetic testing
- High urinary copper (401), low serum ceruloplasmin (17). Ophthalmology exam was not concerning for Wilson's disease
- Abdominopelvic non-contrast CT showed new abdominopelvic ascites
- Liver ultrasound and subsequent biopsy revealed cholestatic hepatitis and cirrhosis

Hospital Course

- Over her hospital stay, her bilirubin reached a peak of 47.9 despite ursodiol therapy, ultimately settling around 38.
- She was transferred for evaluation for multi-organ transplant)liver, small intestine, kidney) and ultimately expired due to septic shock
- Her overall presentation was likely secondary to acute Augmentin hepatotoxicity in the setting of chronic intestinal-failure associated liver disease (IFALD)

DISCUSSION

Intestinal Failure Associated Liver Disease (IFALD)

- Death in patients with chronic TPN use is often due to liver disease, sepsis, and primary disease.
- There are no standard diagnostic criteria for IFALD, and current literature utilizes varying objective measures for IFALD. Typically, these measures include an increase from baseline of LFTs, GGT, total or direct bilirubin compared to pre-parenteral nutrition levels.
- Several mechanisms have been described**,** including chronic cholestasis and changes in bile acid and free fatty acid metabolism, nutritional deficiencies.

Chronic Cholestasis	Bile Acid Metabolism	Nutritional Deficiencies
•Lack of enteral intake •Phytosterol accumulation	•Decreased FGF 19 •Patients with short bowel syndrome experience mucosal remodeling, microbiota alterations and interrupted of enterohepatic circulation	•Carnitine: necessary for FFA transfer •Choline: necessary for lipoprotein and hepatic VLDL secretion

Initial IFALD Management

- Ursodeoxycholic acid to reduce cholestasis and livery injury
- Termination of PRN if possible
- Utilization of Fish-oil and olive-oil lipid emulsification TPNs, which have emerged as less hepatotoxic options due to the decreased omega6 to omega3 polyunsaturated fatty acid ratio and reduction of phytosterol load

Severe IFALD Management

- Patients with ESLD and/or portal hypertension warrant intestinal transplant in addition to typical therapies

Emerging therapies

- FXR agonist chenodeoxycholic acid, which stimulates FGF 19 activity
- Pure n-3 fish oil-based lipid emulsion
- Carnitine, vitamin C and E supplementation

DISCUSSION CONTINUED

Augmentin Associated Drug Induced Liver Injury

- Augmentin is a well-established cause of DILI, with clavulanic acid found as the causative agent
- Onset occurs days to months following use, with a peak around 3-4 weeks after initiation
- Laboratory evaluation typically demonstrates a cholestatic pattern of injury with histology revealing cholestasis and bile duct injury with mild inflammation.
- Granulomas and/or eosinophils are also common, which is consistent with current thinking that the DILI is secondary to an immuno-allergic response.

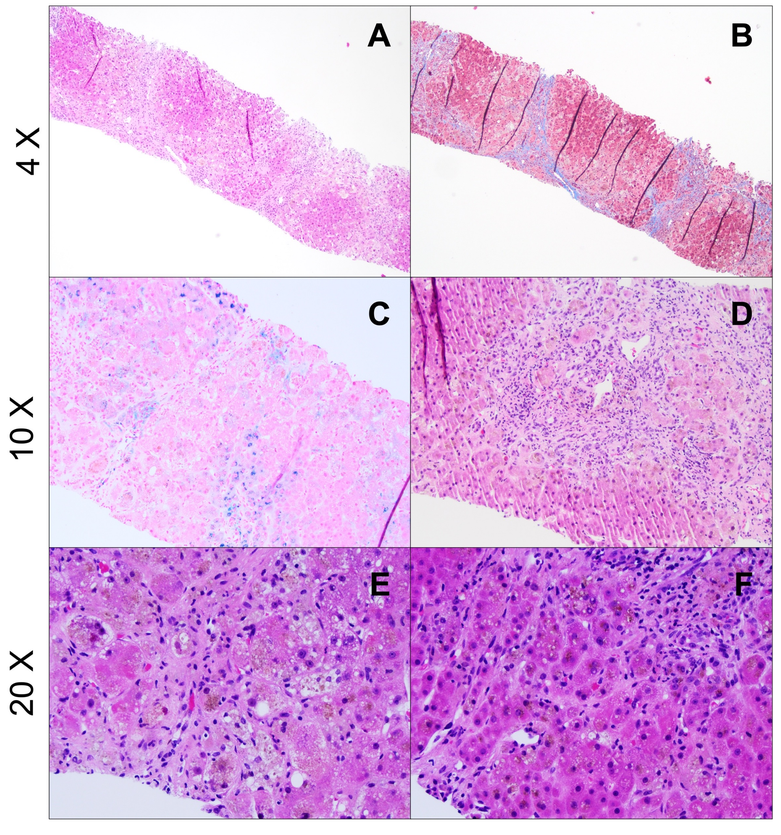

Figure 1. H&E (A) and trichrome stain (B) highlighting Cirrhosis and fibrosis at 4x magnification. Iron deposition (C), and periportal inflammation (D) and (F) at 10X and 20X respectively. Mallory bodies at 20X (E). Overall histology highlighting ballooning degeneration, focal Mallory bodies, and portal triads mildly expanded with mixed inflammation and ceroid laden macrophages.

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