

# Beyond the gut

Liver enzyme and electrolyte abnormalities in inflammatory bowel disease

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# Case Presentation

- 37F with ulcerative colitis (UC), on 5-ASA
- Two month history of migrating polyarthralgias, profound weakness, polyuria, polydipsia. No GI symptoms.
- Presented to hospital due to abnormal blood work suggesting dysfunction of two organ systems:

## 1. Liver:

- ALT 888, AST 555, ALP 263 U/L
  - Previously normal 6 months ago
- Total bilirubin 8 $\mu$ mol/L, Albumin 40g/L, INR 1.0

## 2. Renal:

- K<sup>+</sup> 2.2mEq/L, HCO<sub>3</sub><sup>-</sup> 14mEq/L, AG 16
  - Previously normal 6 months ago
- Urea 8.2mmol/L, Cr 118 $\mu$ mol/L (baseline ~110 $\mu$ mol/L)

# Objective 1

- (1) Develop an approach to the investigation of elevated transaminases in patients with inflammatory bowel disease (IBD)

# Approach to Transaminitis in IBD

Raised transaminases

<3 x ULN

No worrisome features/risk factors

>3 x ULN

Synthetic dysfunction, patient unwell, significant risk factors

# Approach to Transaminitis in IBD

## Raised transaminases

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### No worrisome features/risk factors

- Generally transient
- Commonly IBD flare or drug-related (AZA, MTX)
- Address IBD flare, reduce dose of culprit drugs, exclude EtOH

## Repeat in 3 months

### Resolves

### Persistent

- Commonly fatty liver
- Rule out serious hepatobiliary disease

### Consider and investigate:

- Toxic: EtOH
- Infection: Hepatitides, liver abscess
- Immune: PSC, AIH, Overlap syndromes
- Metabolic: NAFLD
- Vascular: Portal vein thrombosis
- Structural: Hepatic cysts, cholelithiasis
- Malignancy: Metastases or HCC

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# Return to Case - Transaminitis

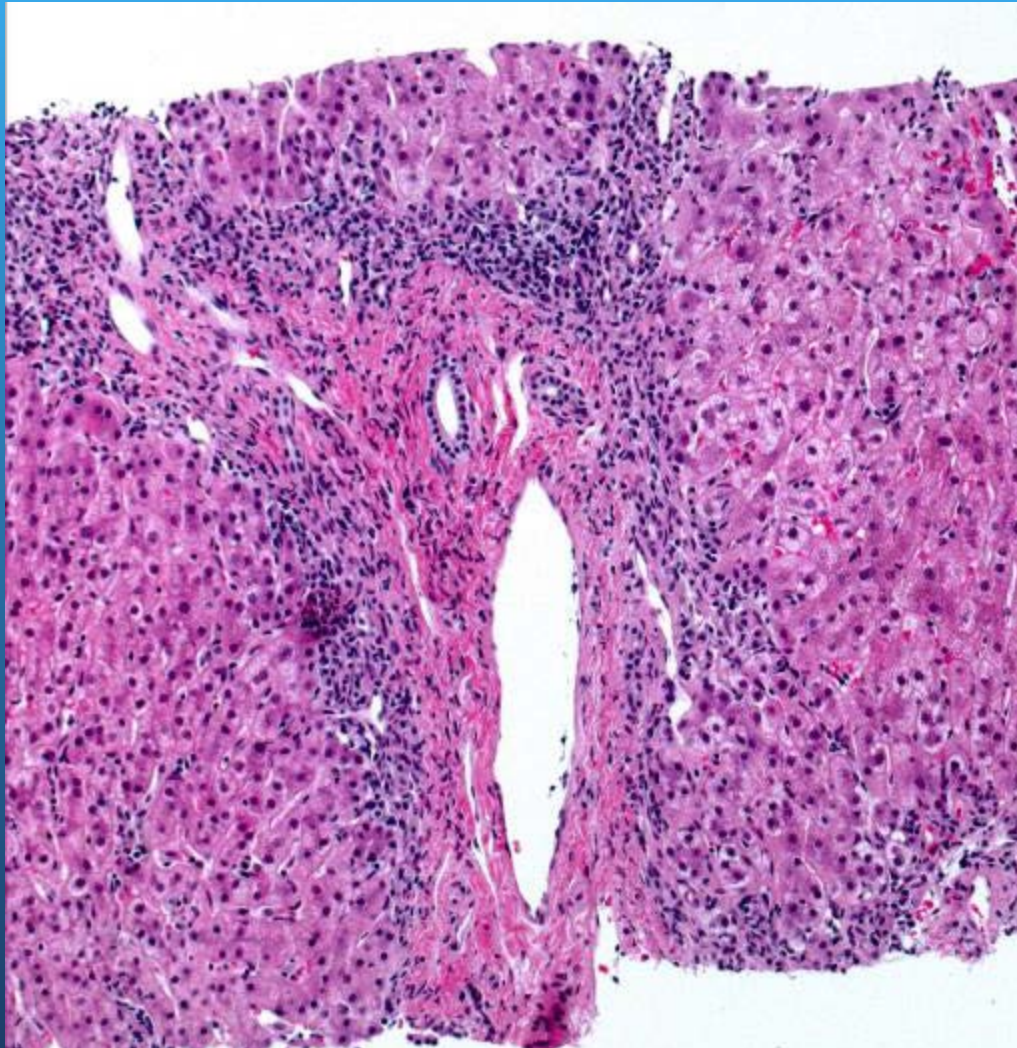
- 37F, UC on 5-ASA, migrating polyarthralgias
  - ALT 888, AST 555, ALP 263 U/L (previously normal)
  - Liver synthetic function normal
- 
- No history of alcohol abuse
  - Only medication is 5-ASA
  - Viral hepatitis panel: Negative
  - Abdominal ultrasound: No hepatic or biliary pathology
  - **Elevated IgG, positive ANA (1:160) and anti-smooth muscle antibodies (1:160)**



# Objective 2

- (2) Diagnose autoimmune hepatitis and understand the role of the liver biopsy

# Diagnosis of Autoimmune Hepatitis



2008 Simplified Criteria:  
Sens 88%, Spec 97% [Score  $\geq 6$ ]

<b>Elevated IgG</b>	
IgG above the normal limit	1 point
IgG 110 times above normal limit	2 points
<b>Autoantibodies</b>	
ANA or ASMA $\geq 1.40$	1 point
ANA or ASMA $\geq 1.80$	1 point
LKM $\geq 1.40$	2 points
SLA/LP positive	2 points
<b>Histology of Chronic Hepatitis</b>	
Compatible with AIH	1 point
Typical of AIH	2 points
<b>Absence of viral hepatitis</b>	2 points
Points $\geq 6$ : PROBABLE AIH	
Points $\geq 7$ : DEFINITE AIH	

IgG: serum level of immunoglobulin G. ANA: antinuclear antibodies. SMA: smooth muscle antibodies. SLA/LP: Anti-soluble liver antigen/liver-pancreas. LKM: Anti-liver kidney microsomes.

# Return to Case - Abnormal Lytes

- 37F, UC on 5-ASA, polyuria, polydipsia
  - $K^+$  2.2mEq/L,  $HCO_3^-$  14mEq/L (previously normal)
  - Cr 118 $\mu$ mol/L (baseline 100-110 $\mu$ mol/L)
- 
- Normal anion gap, no unmeasured anions
  - Urinalysis: pH = 7.0, trace +WBC, no glucosuria or proteinuria
  - Urine anion gap = +16 ( $U_{Na^+}$  20,  $U_{K^+}$  17,  $U_{Cl^-}$  21mEq/L)
  - Sterile urine culture
  - Diagnosis of **distal (Type I) renal tubular acidosis**

# Objective 3

- (3) Recognize distal renal tubular acidosis in the context of autoimmune disease and understand its clinical significance on patient outcomes

# Distal RTA (RTA-1)

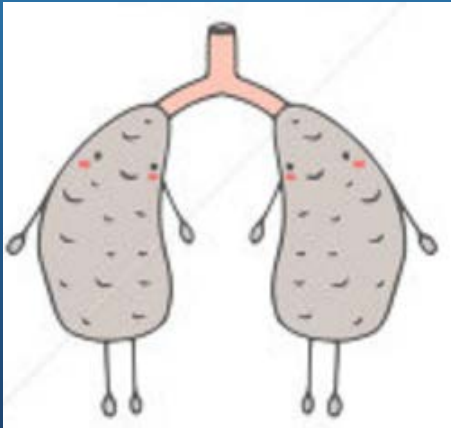
- Syndrome of impaired urine acidification
- Likely secondary to autoimmune hepatitis
- Untreated: Nephrolithiasis, nephrocalcinosis, osteoporosis, hypokalemic paralysis (rare)
- **Properly managed:  
no adverse long-term  
consequences**



# Case Resolution



- Autoimmune hepatitis:
  - Corticosteroids started in hospital followed by azathioprine
  - Rapid resolution of polyarthralgias and transaminitis



- Distal renal tubular acidosis:
  - Electrolytes initially supplemented
  - Resolution of RTA-1 with remission of autoimmune hepatitis

# Learning Points

- (1) Develop an approach to the investigation of elevated transaminases in patients with inflammatory bowel disease (IBD)
- (2) Diagnose autoimmune hepatitis and understand the role of the liver biopsy
- (3) Recognize distal renal tubular acidosis in the context of autoimmune disease and understand its clinical significance on patient outcomes

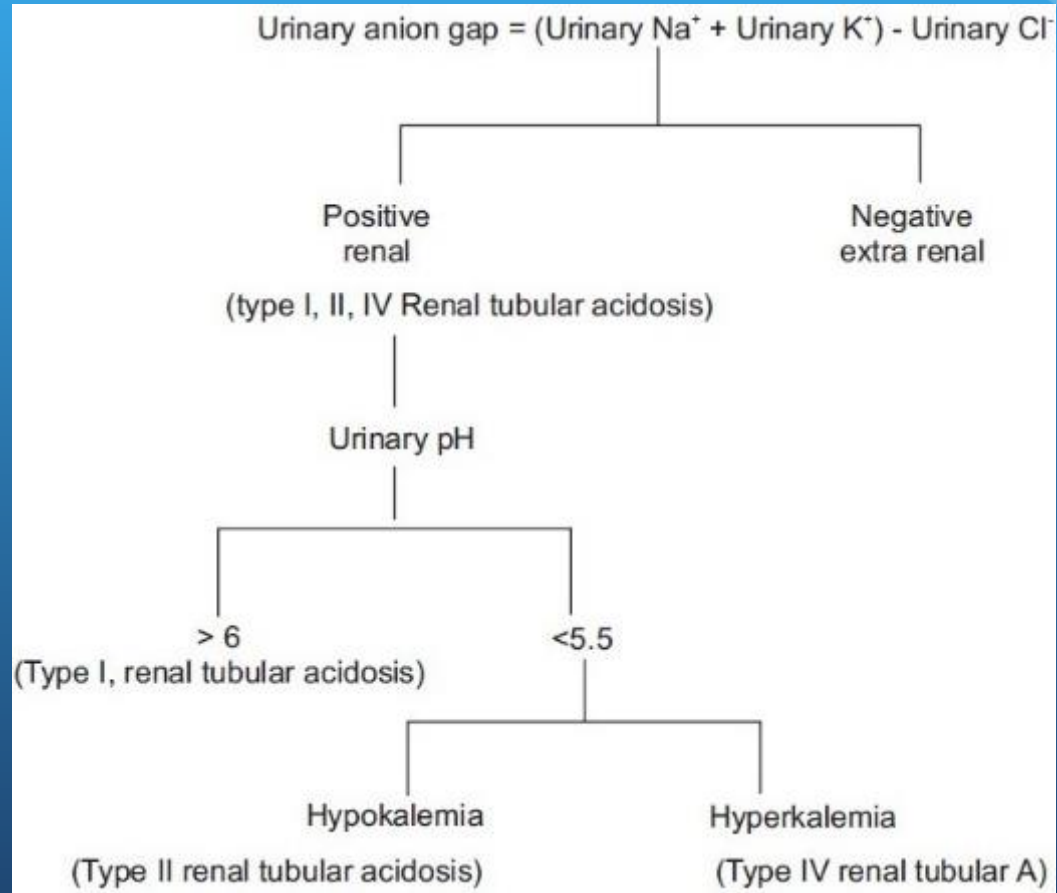
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- Dr. Janice Kwan, supervisor
- Drs. Asad Merchant and Mayur Brahmania for their invaluable input on the nephrology and hepatology content, respectively





# Normal Anion Gap Metabolic Acidosis



# Tubulointerstitial Nephritis (TIN)

- Chronic inflammatory process resulting in fibrosis of tubulointerstitial tissue
- Well known association between IBD and TIN
  - Direct nephrotoxicity due to granulomatous interstitial nephritis
  - Allergic reaction secondary to medications (e.g. 5-ASA)
- May present with pyuria, decreased GFR, and specific tubular disorders such as DI, RTA 1 or RTA 2 → presumptive diagnosis made in this case
- Accounts for patient's chronic kidney disease (Cr 100-110)