Spleen there, done that.

Uncommon manifestations of a common virus

Ruby Goedsir and Dom Maberly

Part 1: The Case

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Broome/Kununurra RAPTOR Resident

Case Study– History

- 27 year old gentleman presented to KNX ED with one-week history of **headache, cough, fevers** and **sore throat** accompanied by **3 days of dark urine**
- **Systems review:** no dysuria, SoB, chest pain, palpitations, rashes, abdominal pain or vomiting
- Denied any recent sexual or sick contacts, overseas travel, excessive EtOH consumption, illicit drugs or recent tattoos

- **Medications:** zinc and vitamin C supplements
- Nil PMHx, NKDA
- SHx: Air conditioner/refrigerator mechanic, working in the Kimberley (from NSW)
- Binge drinks on weekends, vapes + occasional cigarettes, nil recreational drugs

Case Study– Examination

- **Vitals:** RR 18, sats 98% RA, HR 90 bpm, BP 120/70 mmHg and afebrile.
- No obvious rash
- HSD + nil added
- Chest was clear
- Abdomen was soft and non-tender with no flank tenderness or organomegaly
- Bilateral tonsillar swelling and erythema with exudate on the right tonsil.

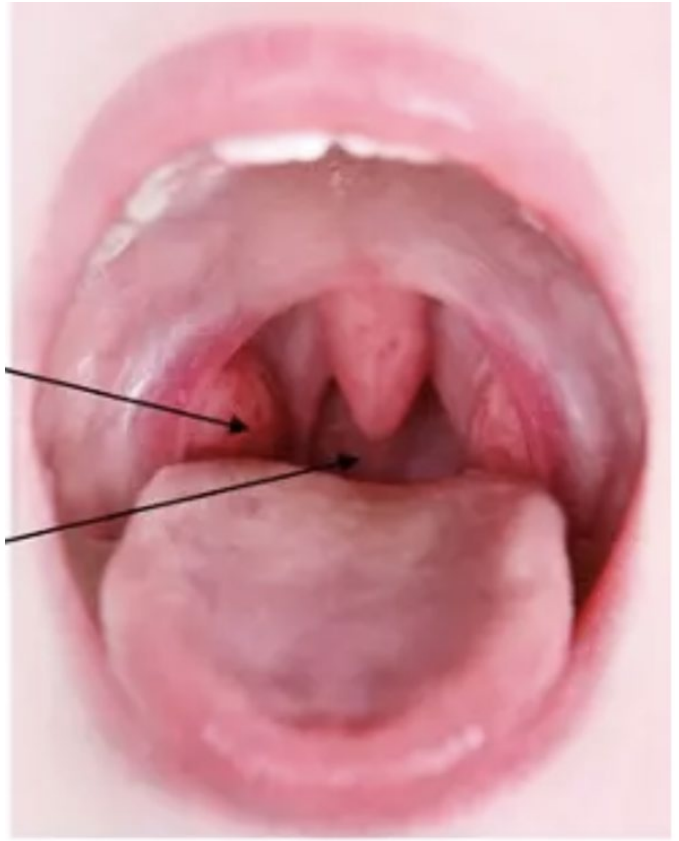


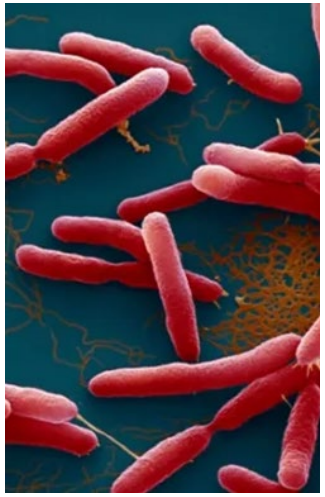
Image from: https://www.entkidsadults.com/pediatric-ent/tonsils-and-tonsillectomy/bacterial-tonsillitis-viral-tonsillitis/

Case Study– Investigations

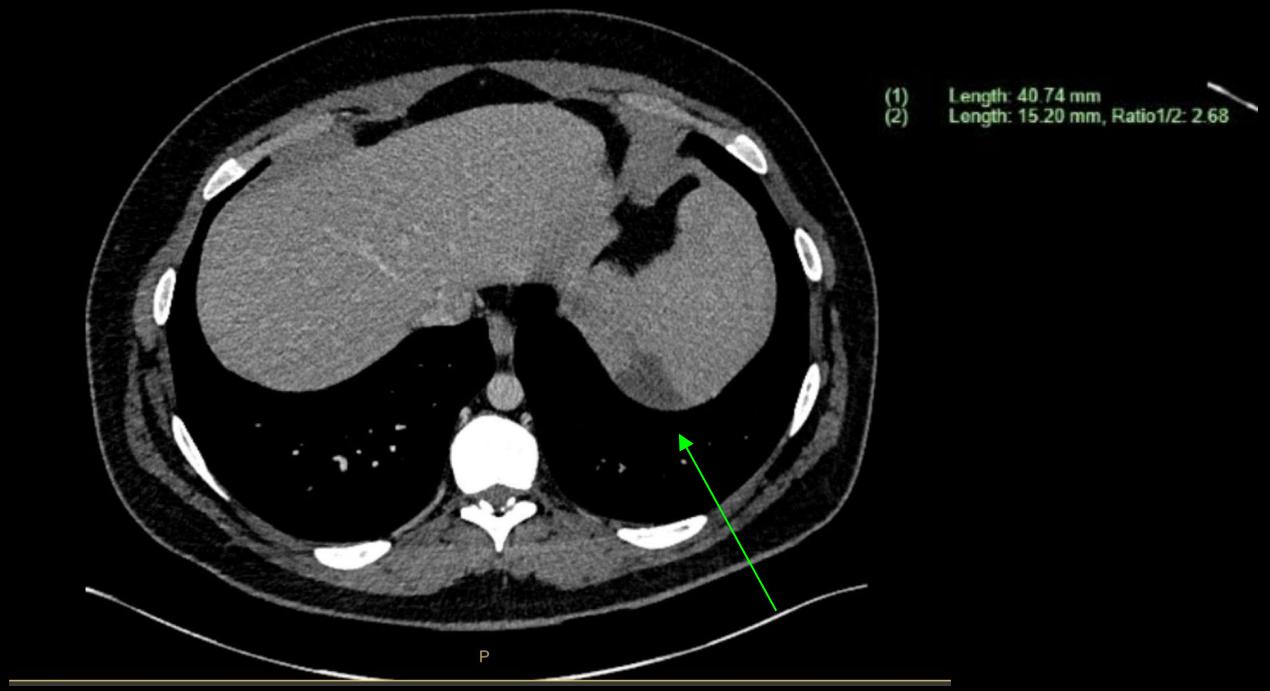
- Urinalysis: large bilirubin, moderate blood, protein and urobilinogen
- Full blood count: Hb 135, WCC 5.10 (neutrophils 1.60, lymphocytes 2.96) Plt 170
- CRP **45**
- LFTs: **total bilirubin 69**, conjugated bilirubin 55, **ALT 294, ALP 559, GGT 453,** albumin 38, protein 80, globulins 42
- UEC: Na 136, K 4.2, bicarb 23, urea 4.0, creatinine 83, eGFR >90
- VBG: lactate 1.0
- Coagulation Profile: PT 13.0, INR 0.8, APTT 29.5 and fibrinogen 3.9
- Urine albumin creatinine ratio was 2.9

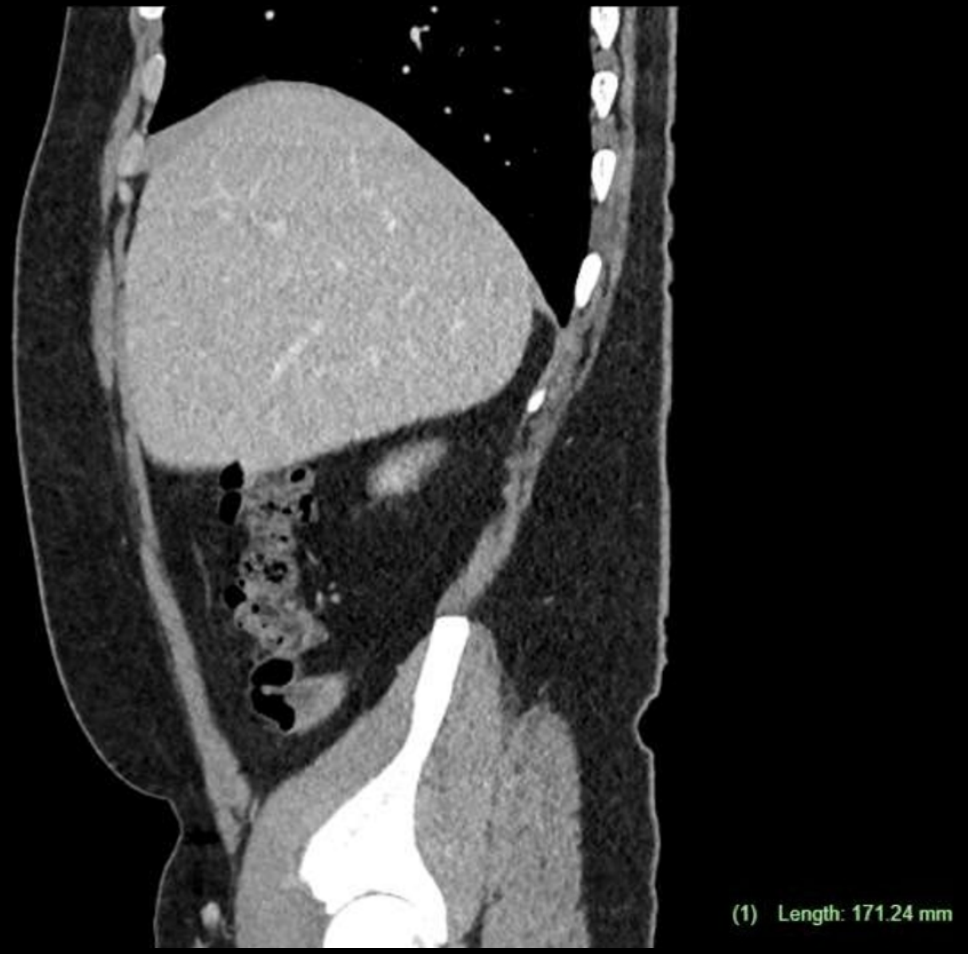
Case Study- Differential Diagnoses

- Biliary obstruction incl ascending cholangitis
- Infectious hepatitis (broad screen due to tropical region)
  - Viral including arboviral
  - Zoonotic including tick borne illness
- Melioidosis also considered



Case Study– Imaging





CT abdomen showed mild-moderate splenomegaly with a triangular shaped hypoattenuation in the upper pole of the spleen, no hepatomegaly, no hepatic lesion, no biliary lesion and no peribiliary fat stranding. There was a non-obstructing right renal calculi. **Impression: possible splenic infarct.**

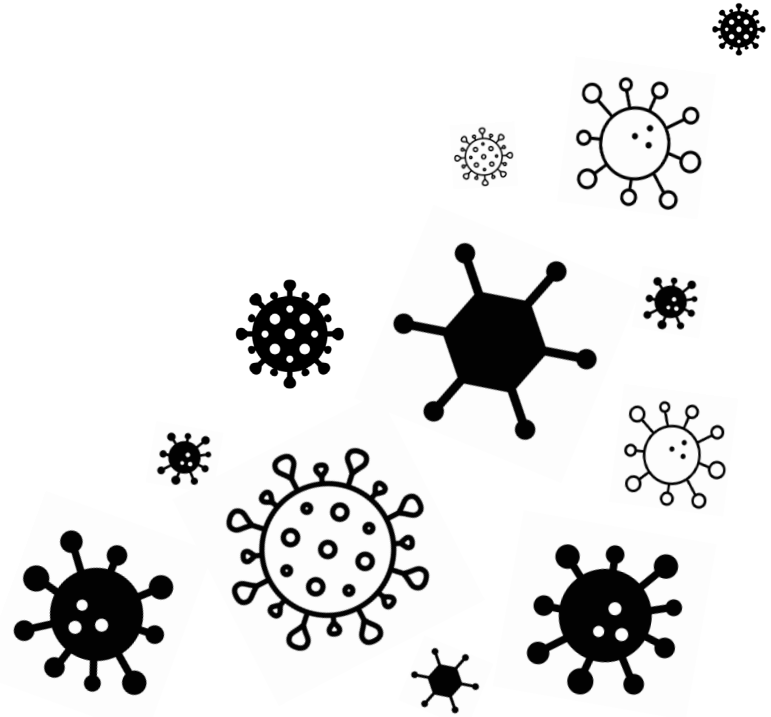
USS abdomen: normal appearance of liver and kidneys, gallbladder partially contracted (CBD 3.7mm appears sonographically normal), splenomegaly (162mm, patchy hypoechoic areas – 11x6x8mm). **Likely splenic infarct**.

Case Study– Hepatitis Screening

- **EBV IgG negative, IgM positive, Heterophile antibody positive**, anti-EBV nuclear Ag negative (**suggests primary EBV infection)**
- **Inf mononucleosis screen positive**

→ **Consistent with acute EBV infection**

- CMV IgG 217.8 IgM negative (consistent with past CMV infection)
- Hep B surface antigen not detected, Hep B surface antibody <10 (no evidence of past infection or immunity)
- Alphavirus and Flavivirus serology negative
- **Legionella pneumophila serogroup 1 64 (positive)**
- **Legionella longbeache 256 (positive)**
- Burkholderia pseudomallei <10
- Typhus group, Spotted Fever Group and Orientia tsutsugamushi (non-specific reaction)



Case Study- Progress (Day 4)

- **Progress:** ongoing myalgias, lethargy, 1x vomit, ongoing dark urine, **scleral icterus.** No abdominal pain.
- **Vitals:** HR 97 bpm, temperature 36.8, BP 134/80 mmHg
- **Investigations**
  - FBC Hb 137 WCC 10.04 (neutrophils 1.72, **lymphocytes 7.65**, Plt 204)
  - UEC unremarkable (Na 137, K 4.3, bicarb 28, urea 3.3 creatinine 92 eGFR >90)
  - LFTs: **bilirubin 100**, **ALT 556, ALP 662, GGT 363,** albumin 38, protein 83, globulins 45

Imp: Mixed liver injury consistent with cholestatic hepatitis and jaundice plus splenic infarct in setting of EBV Infectious Mononucleosis (IM)

In light of the above, patient was encouraged to consider early return to NSW

Questions

1. Significance of positive legionella serology?
2. Usual course of cholestatic hepatitis in EBV IM?
3. Is splenic infarct a known EBV complication or does it warrant investigation for another cause?

Literature Review

Dom Maberly

General Medicine Advanced Trainee, Kimberley Region

1. Significance of positive legionella serology?

- False positive serological results a known occurrence with EBV, often due to cross-reactivity[1-4]
  - Syphilis, Cytomegalovirus, Hepatitis A
- Legionella serological results in our case did not meet threshold to be considered likely for infection, clinical picture less concerning for Legionellosis[5]
- Supported by RPH ID colleagues in deciding not to treat for Legionella or investigate further in absence of suggestive symptoms

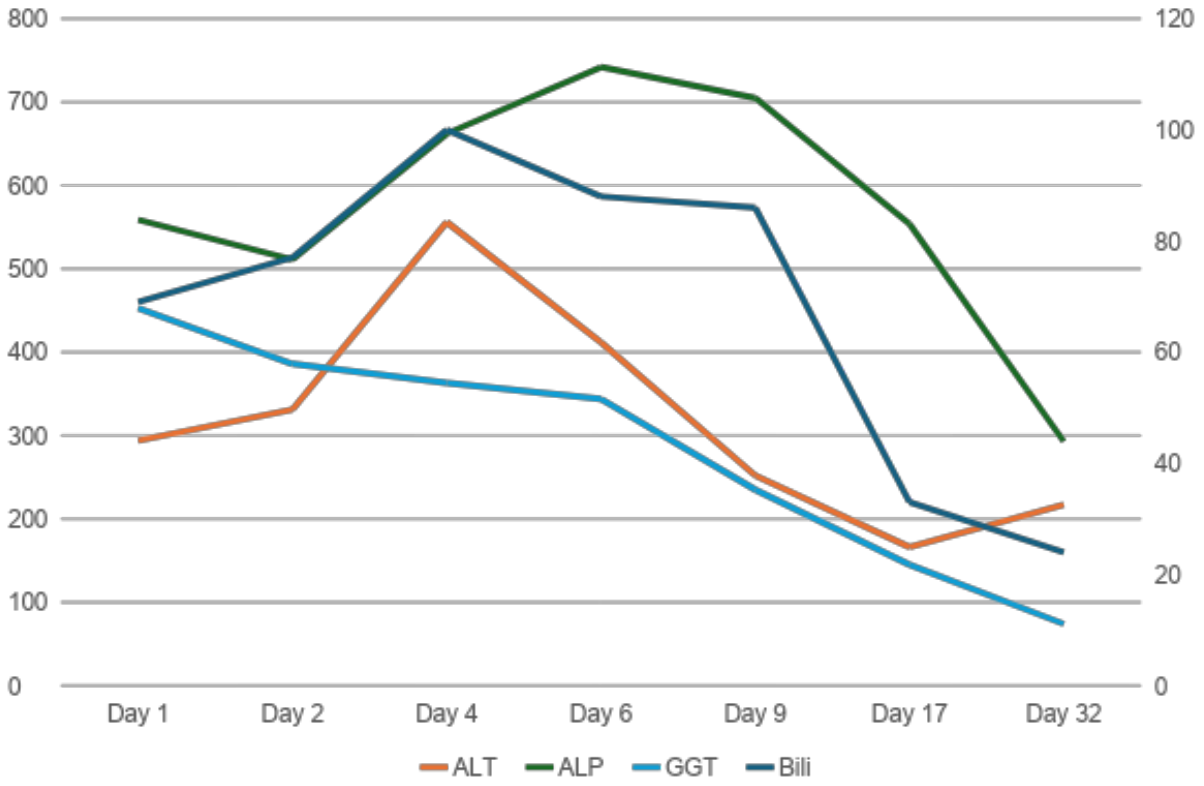
2. Cholestatic hepatitis in EBV IM

- Occurs in around 5% or less of EBV cases[5]
- Vast majority recover fully with supportive care only[6-14] – 1 death reported in an older adult[15]
- Treatments used: cholestyramine, ursodeoxycholic acid, steroids[9,12]
- Mechanism for cholestatic hepatitis in EBV unknown:
  - Cytokine related inflammation
  - Antibody mediated direct hepatotoxicity[9,12]
- Mechanisms for hyperbilirubinaemia in EBV include cholestatic hepatitis as well as haemolytic anaemia[16]
- Can co-occur with Haemophagocytic Lymphohistiocytosis (HLH)[17]

3. Splenic infarct and EBV IM

- 2023 systematic review identified **29 patients** with splenic infarct and acute EBV between 1970 and 2022[18]
  - Underlying haematological disease noted in 6 cases (21%)
  - Splenectomy performed in 3 patients
  - Transiently positive antiphospholipid antibodies identified in 1 case in the systematic review[18]
- Six further cases identified transient changes to thrombophilia markers[19-25]
- 2 cases had splenic infarction then splenic rupture[19]
- Anticoagulation used short term for a patient with splenic infarct in one case[23]
- Possible mechanisms - transient hypercoagulable state, perfusion mismatch
- **Vast majority recovered with supportive care[18-25]**

Back to case: LFT progress



	Day 1	Day 2	Day 4	Day 6	Day 9	Day 17	Day 32
Bili	69	77	100	88	86	33	24
ALT	294	331	556	412	252	166	217
ALP	559	511	662	742	705	554	293
GGT	453	386	363	344	235	145	74

Follow-up

- Ongoing Broome clinician review until return to NSW/handed over to usual GP
- Follow-up abdominal ultrasound one month later showed hepatomegaly (18cm), splenomegaly (16cm) – homogenous **without** infarct, no biliary dilatation
- Advised could return to contact sport cautiously 6-8 weeks following acute illness
- Recommended thrombophilia screen and echocardiogram which did not occur (patient did not proceed with these and given improvement we did not push for these to occur - discussed this decision with Royal Perth Hospital Hepatology and Haematology)

Summary

1. Beware false positive results in EBV!
2. Cholestatic hepatitis is uncommon and can usually be managed supportively
3. Splenic infarct is an uncommonly reported and likely under-recognised complication which can usually be managed supportively
4. Monitoring and management are context dependent, especially in a rural setting

Acknowledgements

- Patient: AW
- Kimberley Regional Physician Team
- Royal Perth Hospital Infectious Diseases, Hepatology and Haematology Teams

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