Citywide Conference

HoJoonYou, MD PGY-5

HPI

50’s yo F presenting with abdominal pain for 1 week

- Intermittent, sharp and dull
- Lower quadrants and RUQ, worsening to involve the flanks and back
- Nausea + poor appetite. No vomiting
- Subjective fevers

Additional Hx

Presented to the ED 2 days prior

- Temp 38.1ºC
- CT abd/pelvis was unremarkable
- Labs were unrevealing
- UA: 0-5 wbc, no bacteria
- Urine culture: negative

She was diagnosed with “UTI,” given IV ceftriaxone x1, then discharged on cephalexin

PMHx

- HTN
- HLD
- DM
- Breast Ca (BRCA 2) s/p b/l mastectomy & chemotherapy in 2007, in remission
- Irritable bowel syndrome
- Hx of cholecystectomy
- B/l oophorectomy

Home Medications

- Aspirin
- Cephalexin
- Cymbalta
- Flonase
- Metformin
- HCTZ
- Atorvastatin
- Lisinopril
- Meloxicam

Social Hx

Former Tobacco user

Denies any alcohol or illicit drug use

Denies any recent travel

Denies any recent insect bites/tick exposure

Lives in transitional housing

Vitals

Temp: **38.0ºC**, Tmax **39.4ºC**

Heart Rate: **100 BPM**

BP: 110/55 mmHg

SaO2: 97% on room air

Physical Exam

Constitutional: Obese. Not in acute distress.

Eye: Conjunctivae clear, sclerae non-icteric; pupils 2-3 mm equally reactive to light

Mouth/Ear/Nose/Throat: No lip ulcers; oropharynx clear, no pharyngeal exudates; no sinus or mastoid tenderness

Neck: Supple without adenopathy or masses

Respiratory: Non-labored breathing; **decreased breath sounds R base**

Physical Exam (cont.)

Cardiovascular: S1/S2; no leg edema

GI: Abdomen soft, obese, **+tender RUQ. No rebound or guarding**

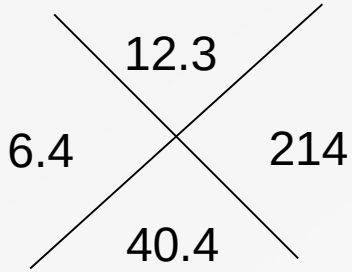
GU: No CVA or suprapubic tenderness

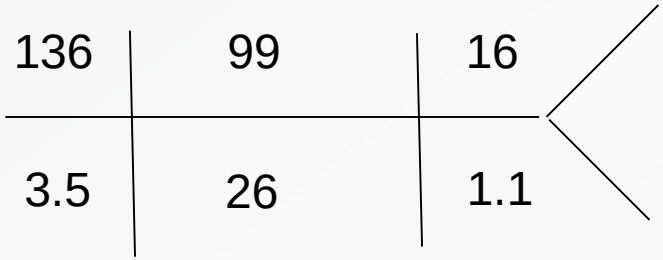
Lymphatic: no palpable cervical lymph nodes

Musculoskeletal: No joint tenderness/effusions; no cyanosis or clubbing

Neurologic: No focal deficits. Moves all extremities.

Labs





Neutrophils:	69.1
Lymphocytes:	19.4
Monocytes:	10.7
Eosinophils:	0

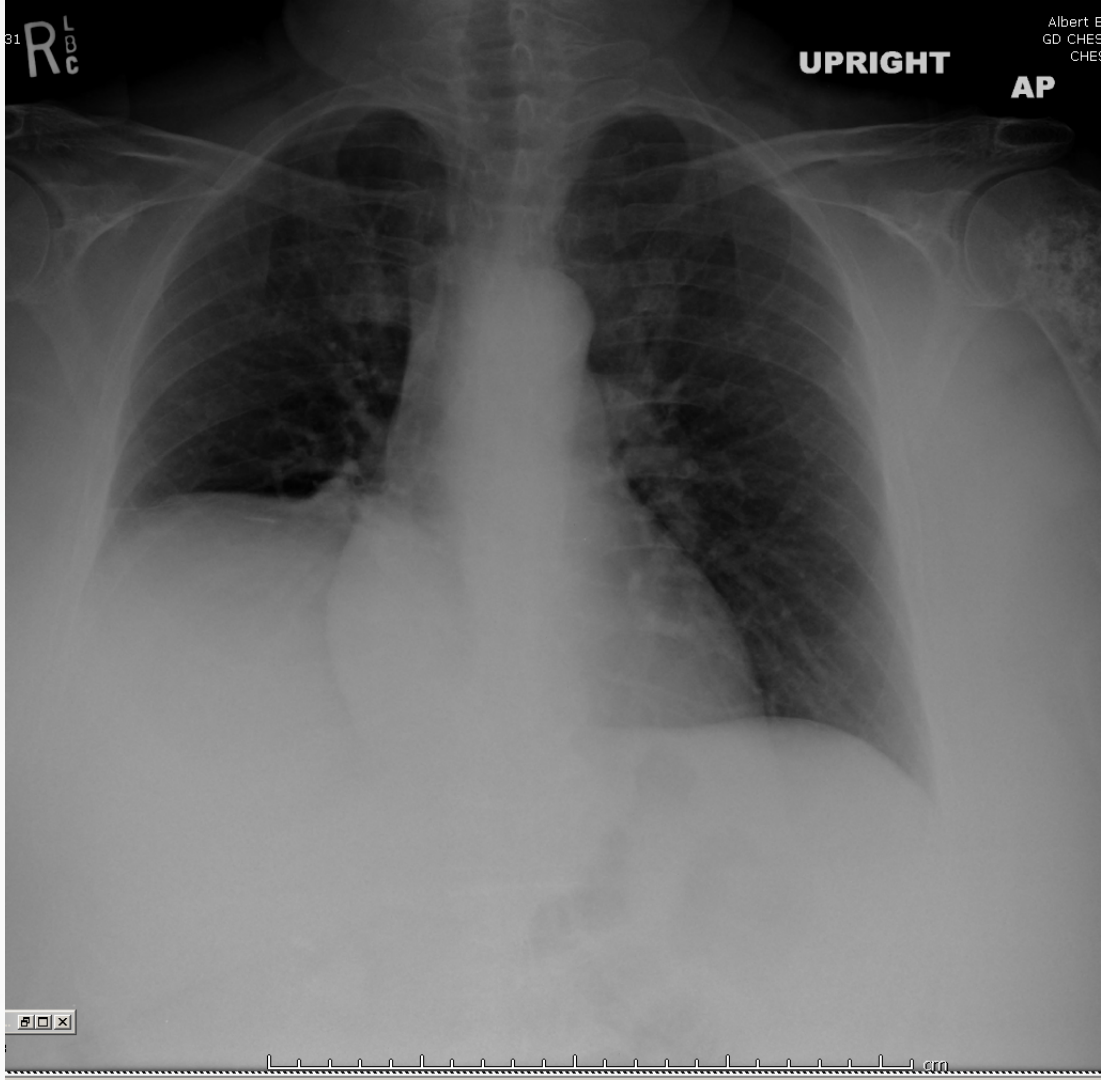
ALP: 73
ALT: **139**
AST: **172**
Total Bili: 0.5

Procalcitonin: 0.13
HIV negative
CRP **43.3**
ESR **59**

CXR

Elevation of the

right hemidiaphragm



CT abd/pelvis w/ contrast

- Hiatal hernia
- Sigmoid diverticulosis without diverticulitis
- Osteopenia, age indeterminate L1 compression deformity
- No lymphadenopathy

Differential

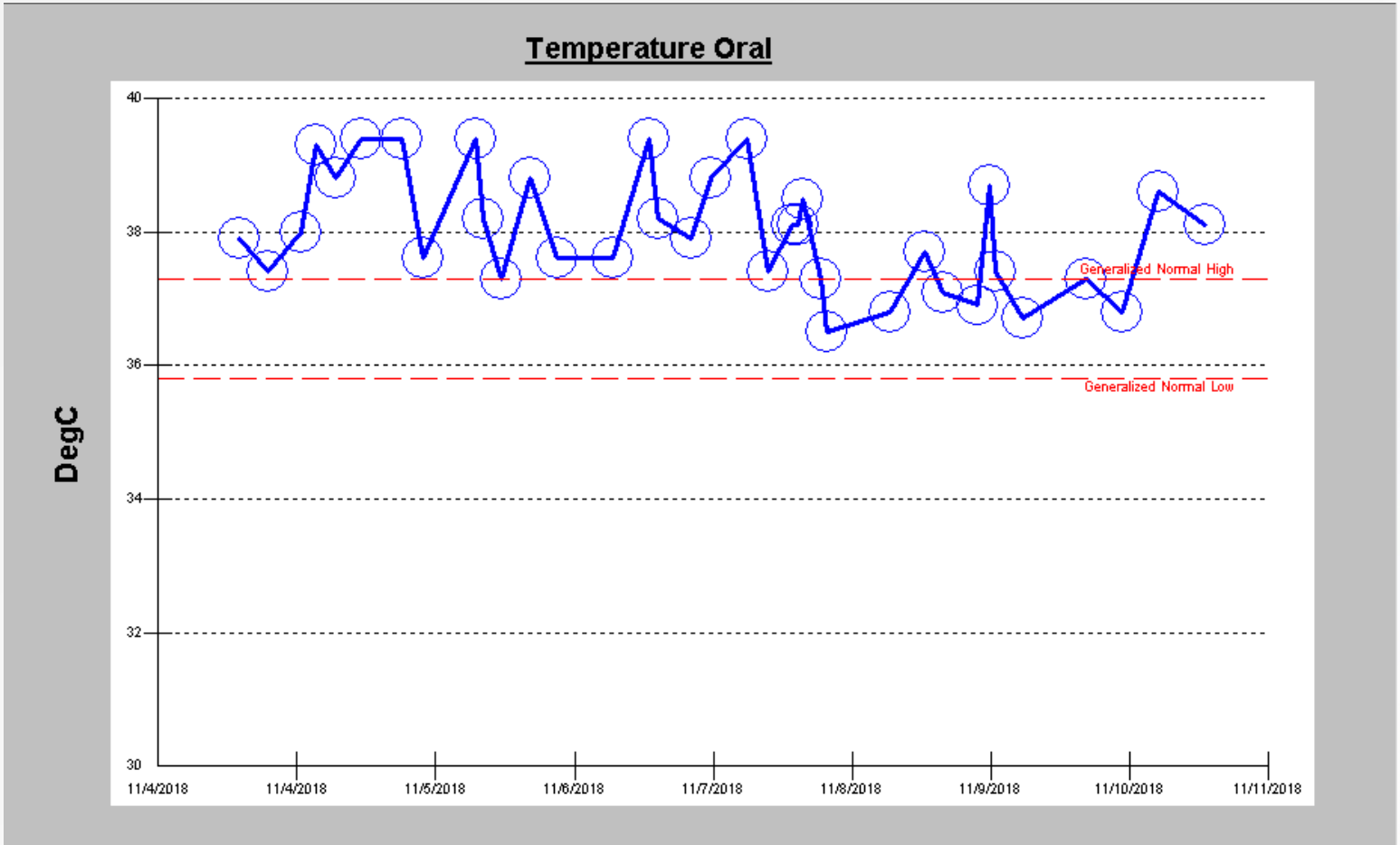
Thoughts?

Further tests?

Hospital Course

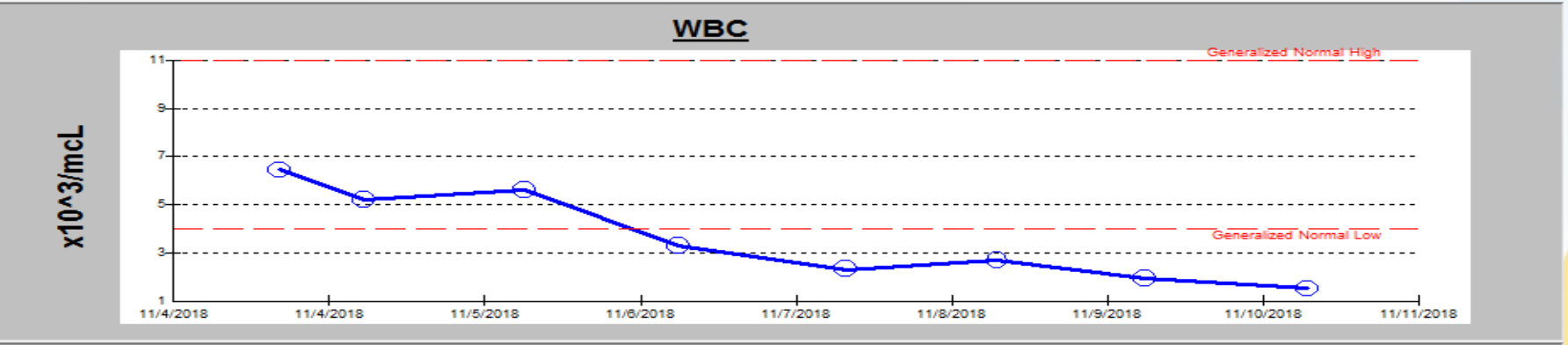
- Cefepime and Vancomycin x1 in ED
- Admitted for abdominal pain with fever
- Antibiotics were not continued

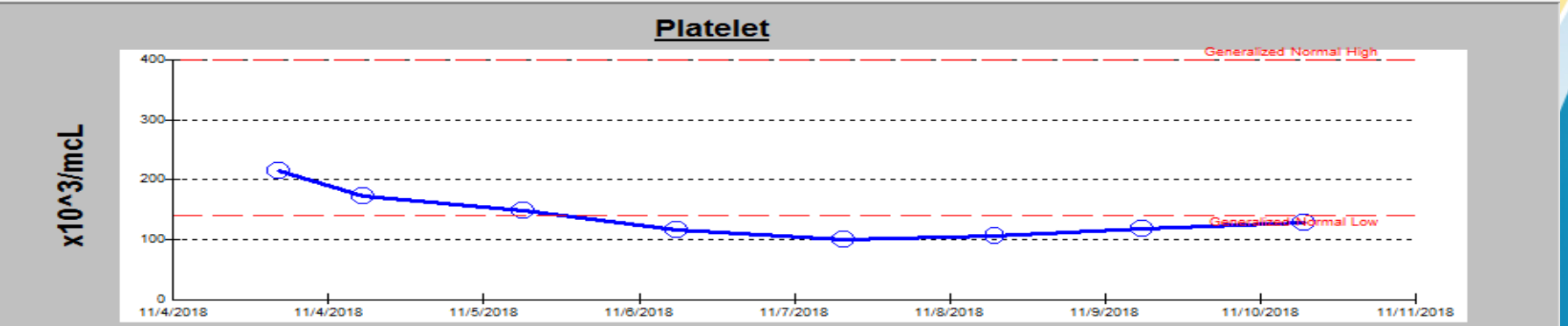
Hospital course



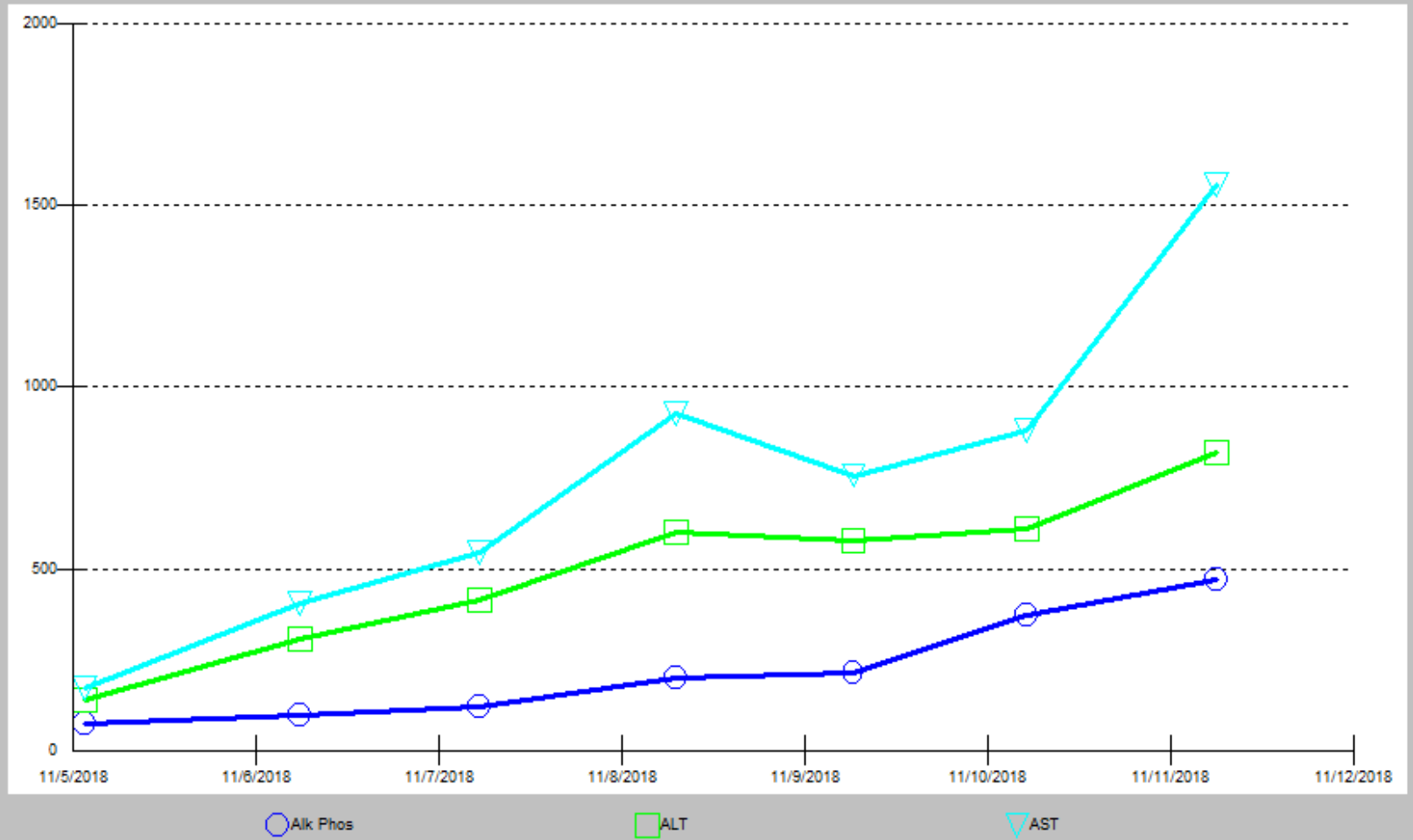
Hospital Course

WBC: 5.6 -> 3.3 -> 2.3 -> 1.9





Alk Phos, ALT, & AST



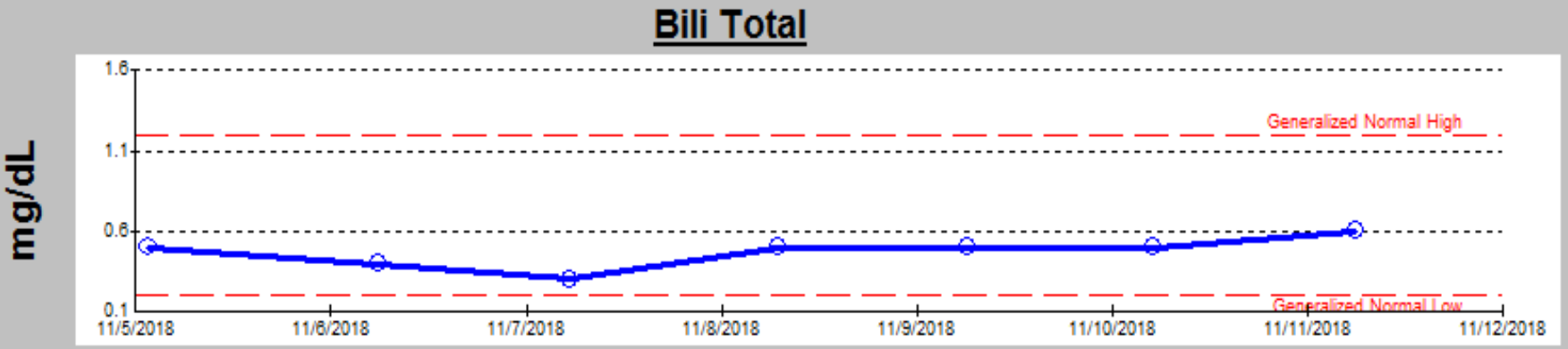
Hospital course

ALP: 99 ->201 ->215

ALT: 308 -> 599 ->578

AST: 405 ->927 -> 757

Total Bili: 0.4 ->0.5



Differential

Further thoughts?

Additional Testing

Hepatitis A IgM negative

Hepatitis BsAg negative

Hepatitis Bc IgM negative

Hepatitis C negative

CMV PCR negative

HCV PCR negative

HBV PCR negative

Hospital course

- Started on doxycycline for possible tick-borne illness, Anaplasma PCR sent

Hospital course

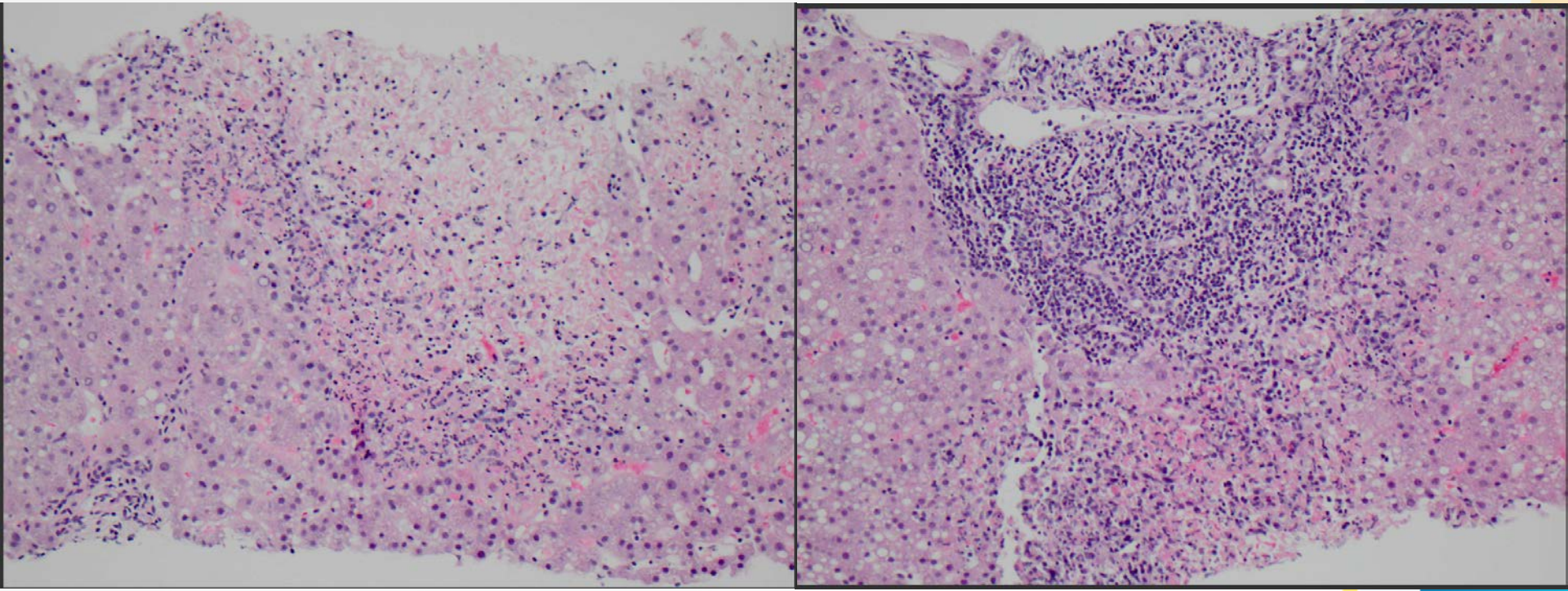
- US liver: Mild hepatic steatosis
- MRCP: Mild hepatomegaly with steatosis, no biliary pathology. New small volume ascites and retroperitoneal fat stranding

Further thoughts?

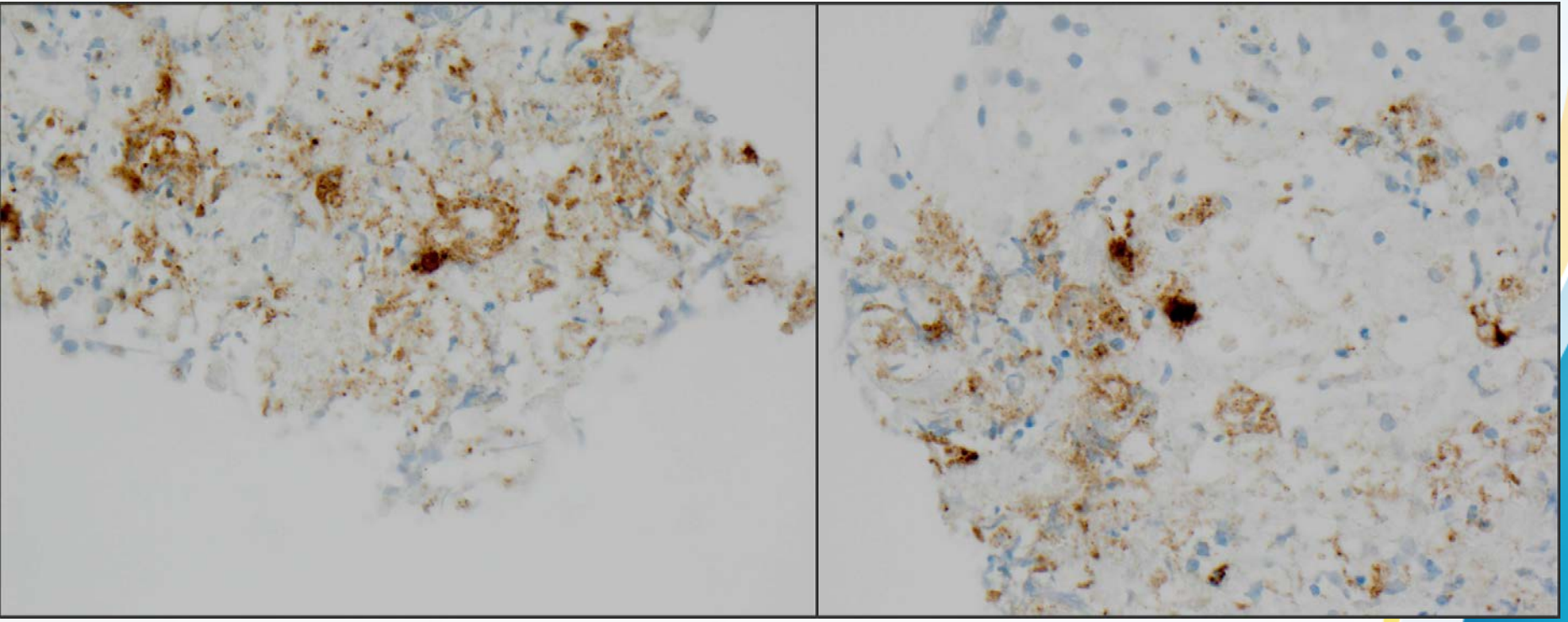
Hospital course

- Anaplasma PCR negative
- Liver biopsy performed (core needle biopsy)

Biopsy: H&E staining



Biopsy: HSV Immunostaining



Biopsy Results

- Hepatic necrosis in a random distribution (portal and intralobular)
- Positive HSV immunostain consistent with herpes simplex virus hepatitis.
- Mild macrovesicular steatosis
- Portal fibrosis

Degree of portal and interface chronic inflammation greater than that expected from HSV hepatitis alone, perhaps underlying autoimmune hepatitis or drug-induced liver injury

Lab results

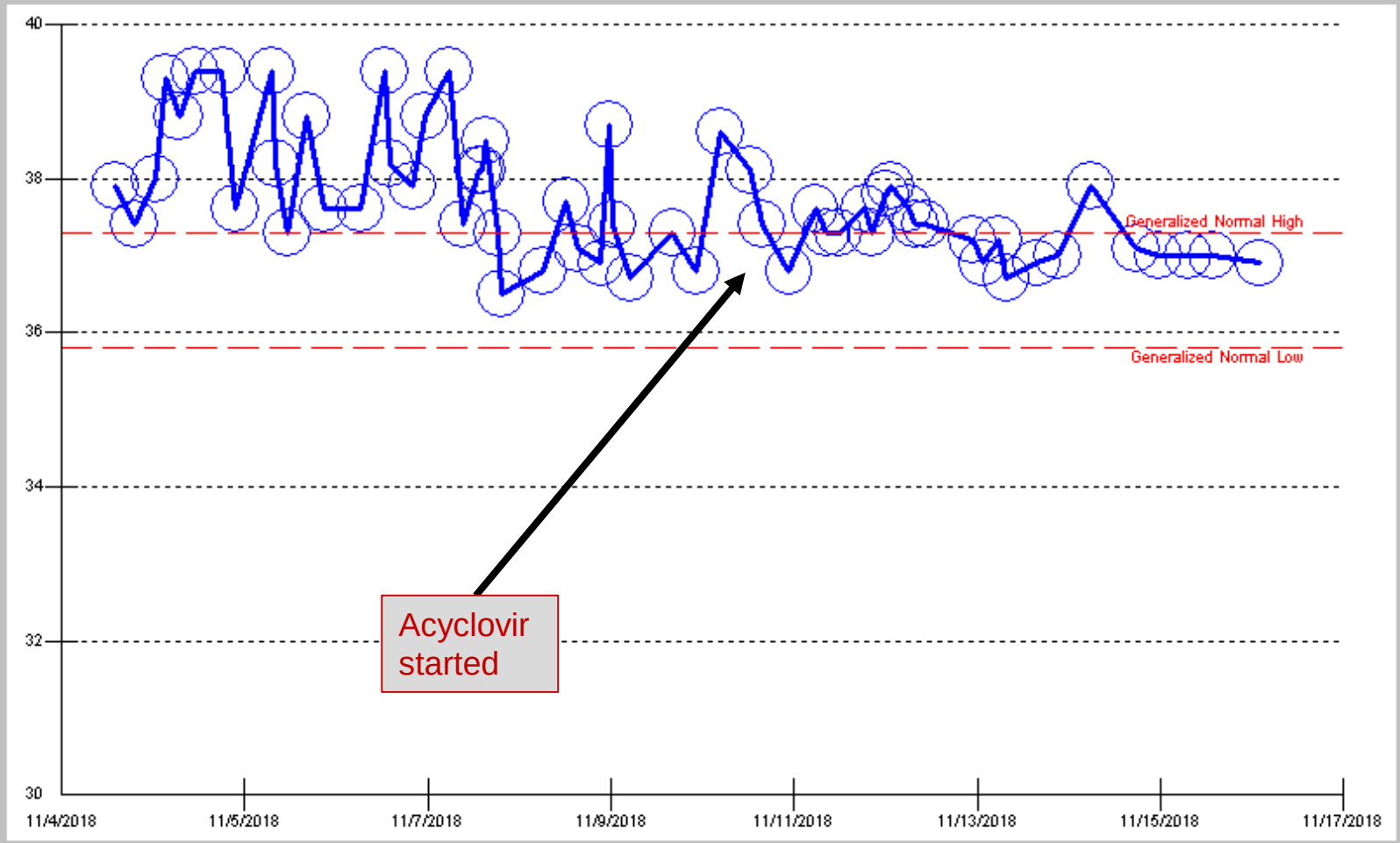
HSV1 IgM negative

HSV2 IgM positive, titer >1:320

Serum HSV1 DNA: Not detected

Serum HSV2 DNA: Detected

Temperature Oral



HSV Hepatitis

- Incidence in acute liver failure: 0.8% to 1%
- Often seen in immunocompromised and pregnancy
- Mucocutaneous lesions may be absent
- Both HSV-1 and HSV-2 known to be causative agents

F. V. Schiødt, T. J. Davern, A. O. Shakil, B. McGuire, G. Samuel, and W. M. Lee, “Viral hepatitis-related acute liver failure,” American Journal of Gastroenterology, vol. 98, no. 2, pp. 448–453, 2003.

J. P. Norvell, A. T. Blei, B. D. Jovanovic, and J. Levitsky, “Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases,” Liver Transplantation, vol. 13, no. 10, pp. 1428–1434, 2007.

HSV Hepatitis

- HSV often overlooked as a cause of acute liver failure
- Non-specific signs
  - Fever
  - Leukopenia
  - Transaminitis
- Potential for anicteric hepatitis

L.M. Haaq, J. Hofmann, L. Kredel et al., “Herpes Simplex Virus Sepsis in a Young Woman with Crohn’s Disease.” J Crohns Colitis, vol. 9, Issue 12, pp.1169-1173, 2015

B. Grimm, B. Padberg, T. Ruhstaller et al., “Fatal herpes simplex virus hepatitis in a patient with esophageal cancer under radiochemotherapy.” Onkologie 2008;31:620-622. doi: 10.1159/000162283

HSV Hepatitis: Diagnosis

- Mostly dx made post-mortem
- Liver biopsy is the gold standard
  - Areas of necrosis
  - Intranuclear viral inclusions
  - Immunostaining for HSV
- HSV PCR is more discriminating than serology

J. Levitsky, A. T. Duddempudi, F. D. Lakeman et al., “Detection and diagnosis of herpes simplex virus infection in adults with acute liver failure,” Liver Transplantation, vol. 14, no. 10, pp. 1498–1504, 2008.

U. Navaneethan, E. Lancaster, P.G. Venkatesh et al., “Herpes Simplex Virus Hepatitis - It’s High Time We Consider Empiric Treatment,” Journal Gastrointestinal Liver Disease, vol 20, no. 1, pp. 93-96, 2011

HSV Hepatitis: Treatment

Early initiation of high-dose acyclovir shows a trend towards improved survival and avoidance of liver transplantation

- Optimal treatment and duration are unknown
  - Reports of effective treatment has ranged from 1 week to lifelong
  - Prolonged course commonly administered to transplant recipients and immunosuppressed patients

J. P. Norvell, A. T. Blei, B. D. Jovanovic, and J. Levitsky, “Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases,” Liver Transplantation, vol. 13, no. 10, pp. 1428–1434, 2007.

Thank You