Puzzles In Acute Care: Febrile Illness

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Disclosures

- No conflicts of interest or affiliations to disclose.

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Chief Complaint

- Fever, chills, headache, myalgias

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HPI

- 33-year-old male presents to the ED in Central Missouri hospital in early May for the 2nd time in 3 days. Initially he presented with fever, myalgias of 24 hours. He was noted to have erythema and edema to 2nd and 3rd PIP joints of right hand. He admitted to an altercation three weeks prior that resulted in a laceration and injury to his right hand. He had been treated in the local County Jail Infirmary with a 7-day course of Bactrim that he completed 2 weeks prior to the ED visit. X-rays obtained were negative for fracture and he was dismissed on po Keflex for suspected cellulitis.

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HPI

- He returned to the ED with worsening fever, chills, myalgias, and now severe headache. He has completed 3 of 7 days of his Keflex and symptoms continued to worsen. Nothing seems to exacerbate his symptoms and nothing has alleviated- including Tylenol for fever and myalgias as well as the Keflex for antimicrobial therapy. Denies any sick contacts or international travel.

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Past Medical/Surgical History

- Hypertension-untreated
- Asthma in childhood
- Tonsillectomy- childhood
- Arthroscopy to right knee-2015

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Home Medications/Allergies

- Keflex 500mg PO BID x 7 days, started 3 days prior
- Tylenol 1gm PO every 6 hours prn fever, pain
- Ibuprofen 400 mg every 6 hours prn fever, pain
- No Known Drug Allergies

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Social History

- Single, Lives alone in a camper in a campground at the Lake
- Smokes 1 PPD for 15 years, with 15 pack year history
- Drinks Alcohol-Whiskey few drinks several times a week

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Social History

- History of Methamphetamines (inhaled and IV), Marijuana. Last used Meth 1 month ago, last used Marijuana 7 days ago
- Recently in County Jail for 2 weeks and has been out for 2 weeks now.
- Self-employed as a Handy Man

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Family History

- Father deceased from CAD at age 55
- Mother alive with HTN, DM type 2
- One brother deceased from Suicide
- One sister alive and well

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Physical Exam

- General: Ill appearing, unkempt in appearance, well nourished male who appears his stated age. Alert, oriented, restless and in mild distress.
- HEENT: Head normocephalic, atraumatic. Conjunctiva pale, sclera non-icteric. PERRLA. Nasal Mucosa pink, no drainage. Oral mucosa dry, no exudates. Posterior pharynx pink.

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Physical Exam

- Neck Supple, with cervical lymphadenopathy. No nuchal rigidity. No JVD
- CV: Tachycardic rate, regular s1,s2, no murmur, rub or thrill.
- Lungs: Clear to auscultation bilaterally, symmetric expansion, non-labored
- Abdomen: Soft, nontender, normoactive, no hepatosplenomegaly

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Physical Exam Continued

- Extremities: no clubbing, cyanosis or edema. DP/PT +2 bilat
- Musculoskeletal: swelling/tenderness to 2nd and 3rd right PIP joint. No joint effusions, Full ROM , strength 5/5 bilaterally. No muscle spasms
- Neurological; Alert, oriented x 3, CN 2-XII grossly intact. No focal deficits, no dysarthria.

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Physical Exam Continued

- Lymphatic: mild lymphadenopathy to bilateral axilla, cervical.
- Skin: hot, diaphoretic, no rashes to hands, face, trunk, or feet. No open wounds
- Psychological: Anxious, restless, oriented x 3. Denies SI,HI.
- Vital Signs: Temp 39 C, Heart rate 122, Resp 24, BP 110/68 02 sat 96% RA

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Laboratory

CBC May 5, 2019	CBC May 2, 2019
WBC: 2.1	WBC: 8.0
HGB: 11.6	HGB: 13.8
HCT: 32.5%	HCT: 40.6%
PLT: 60	PLT: 160
NEUT: 56%	
ANC: 1.2	
LYMPH: 15%	
EOSIN: 4%	

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Laboratory

CMP May 5, 2019	CMP May 2, 2019
NA: 128 (136-145)	NA: 137
K+: 5.1 (3.5-5.1)	K+: 3.9
CL: 106 (96-106)	CL: 99
C02: 23 (23-29)	C02: 26
BUN: 33 (6-20)	BUN: 19
Cr: 1.6 (0.6-1.3)	Cr: 1.0
GLU: 108 (70-99)	GLU: 90
ALT: 215 (7-40)	ALT: 55
AST: 225 (10-34)	AST: 70
ALK: 305 (44-147)	ALK: 147

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Additional Diagnostics

- CXR: No acute cardiopulmonary abnormality
- Previous x-ray from 5/2/19 of right hand: Soft tissue swelling to 2nd and 3rd PIP, no osteomyelitis, no fracture or dislocation.
- CT head: No acute intracranial abnormality, neg for bleed/mass/ischemia

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Diagnostics Continued

- EKG: tachycardia with no ST or T-wave abnormalities
- Lactic acid 5/5/19: 2.6 (H)
- Blood cultures pending
- UA Specific Gravity 1.045, neg nitrites, neg leuk est, blood neg, WBC 0. Glu neg

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Admitting Diagnoses

- Severe Sepsis with evidence of end organ dysfunction
- Acute Kidney Injury
- Pancytopenia
- Transaminitis
- Hyponatremia
- Headache/Fever
- Substance abuse

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Differential Diagnosis

- Meningitis
- Malignancy
- Endocarditis
- Bacteremia
- Rickettsial Disease: Rocky Mountain Spotted Fever, Rickettsiosis, Anaplasmosis, Ehrlichiosis
- Viral: Mono, West Nile, Hepatitis A, Influenza, HIV

(Biggs, 2016)(Dumler, Madigan,Pusterla & Bakken, 2007)

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Hospital Course

- Patient was admitted to ICU and treated with empiric doxycycline, IV fluids of LR, and prn medications for symptom support.
- Repeat lactic acid 3 hours after admit showed lactic had normalized
- Had an LP after accepted by Hospitalist for admit, while still in ED. Meningitis panel neg.
- Blood cultures x 2 showed no growth. HIV negative, Hepatitis neg. UDS +marijuana

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Hospital Course

- After 24 hours patient remained febrile, had persistent pancytopenia. NA had normalized with IV fluids. AKI resolved. He was hemodynamically stable and transferred to the floor. Clinically improving and tolerating po. HA resolved
- At 48 hours patient was afebrile and changed to po doxycycline. Plts and WBC trending up.

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Admit Orders

Admit to ICU

Code status: Full Code

Diet: regular

Lab: Tick panel by PCR, Lactic acid q 3 hours x 2,HIV panel, Hepatitis panel, RVP,UDS

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Admit Orders Continued

AM Labs: CBC with diff, CMP, Lactic acid

Medications: Doxycycline 100mg IV q12 hours

IV fluids of LR at 150ml/h x1 liter then 125ml/h.

Prn Meds: Tylenol 650mg po q 4 hour prn,

Zofran 4mg IV q4 hour prn, Norco 5mg/325mg 1 po q4 hour prn,

Morphine 1-2 mg IV q2 hour prn breakthrough pain.

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Hospital Course Continued

- 72 hours: WBC 4.5, HGB 11.8, PLT 145. Afebrile. Tolerating oral medications. Dismissed home with 4 more days of po doxycycline 100mg BID

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Hospital Course Continued

- Follow up with PCP 1 week post hospitalization for repeat labs. Return to hospital for fever >100.5, headache, nausea/emesis if unable to keep down fluids or antibiotics.
- 5 days post hospitalization Tick Panel finalized and positive for Ehrlichiosis

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Discussion: Ehrlichiosis

- *E. Chaffeensis* is causative agent of Human Monocytic Ehrlichiosis (HME)
- 1st described in 1987, and Nationally reportable sine 1999.
- Transmitted by Lone Star Tick, encountered in South East United States, some areas of Midwest, and New England.
- The White-Tailed Deer is the major host of Lone Star Ticks

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Discussion Continued

- Epidemiological Risk factors: outdoor activities (occupational or recreational), Travel or Residence in Known area of transmission, Male gender.

Source: (Biggs, et al., 2016) (Heitman, Dahlgren, Drexler, Massung, & Behravesh, 2016)

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Discussion- Confirmation

- Treatment should not be withheld while awaiting confirmation
- PCR on whole blood during acute illness is the most specific over serology
- Most labs have Tick Borne disease Panels which test for all Rickettsia diseases using PCR and Electrospray Ionization Mass Spectrometry
- Many facilities confirmation may take an average of 3-7 days

Sources: (Heitman, Dahlgren, Drexler, Massung, & Behravesh, 2016)
(Sharo, et al., 2010)

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Discussion: Pharmacology

- CDC 2016 Guidelines for Tick Borne Disease: Doxycycline 100mg IV/PO with recommended to continue >3 days after fever resolved and clinically improving, with minimum of 5-7 days duration.
- Oral is appropriate for outpatient treatment in mild cases or early detection

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Pharmacology Continued

- IV is recommended for severely ill, requiring hospitalization, unable to tolerate oral medications due to n/v. Total duration remains the same
- Fevers resolved within 24-48 hours of doxycycline treatment. Lack of response is indication that disease is not likely Tick Borne.

Source: (Biggs, et al., 2016)

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Pharmacology Continued

- Tetracyclines: Only antibiotics recommended for all Tick Borne Rickettsial Diseases
- Rifampin: in vitro activity against *E. Chaffeensis*. No clinical trials have been conducted. Rifampin is NOT effective in Rocky Mountain Spotted Fever

Source: (Biggs, et al., 2016)

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Pharmacology Continued

- Fluoroquinolones: In vitro activity against RMSF. However, delayed cessation of fever, increased LOS, and increased disease severity. Shown resistance in HME.
- Sulfonamides have been associated with increased severity of illness when administered prior to suspicion of Tick-Borne Disease.

Source: (Biggs, et al., 2016)

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Pharmacology: What If?

- Pregnancy: Rifampin is the only alternative to try with reports of success, but no randomized clinical trials of efficacy
- Allergies/Adverse Reactions: Challenging due to lack of equally effective, proven treatment.

Source: (Biggs, et al., 2016)

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Pharmacology: What If?

- Assess type of reaction and whether it is life threatening (Anaphylaxis, Steven Johnsons)
- If non life threatening CDC recommends starting treatment with Doxy observed inpatient with close monitoring
- Life threatening reactions: Consult Allergist/Immunology for rapid desensitization

Source: (Biggs, et al., 2016)

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Discussion: In or Out? ICU or Floor?

- 3% fatality in HME, higher in immunocompromised
- Hospitalize: Evidence of end organ dysfunction, severe thrombocytopenia, mental status changes, need for supportive therapy, ability to tolerate and obtain oral doxycycline

Source: (Kuriakose, Petit, Schmitz, Moncayo, & Bloch, 2018)

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Discussion: In or Out? Icu or Floor?

- Study of 155 confirmed cases of HME in a tertiary teaching hospital in Nashville showed 28% required ICU. Increased number of days from 1st contact with healthcare system to initiation of treatment with doxycycline was associated with increased risk of requiring ICU. Also, recent treatment with sulfa was correlated with need for ICU. Surprisingly, immunocompromised and advance age were less likely to require ICU.
- Why do you think that would be?

Source: (Kuriakose, Petit, Schmitz, Moncayo, & Bloch, 2018)

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Conclusion: Don't Forget Ticks When…

- Fever with Neutropenia, thrombocytopenia, transaminitis
- Other factors: Known tick bite, environmental exposure in endemic areas, travel to endemic area within 3 weeks of symptom onset, pets with similar symptoms, other members of household with similar symptoms
- Early disease: Leukopenia, thrombocytopenia, transaminitis
- Later in clinical course: Anemia , Hyponatremia
- Severe complications: ARDS, Septic Shock, Renal Failure, Hepatic Failure, Coagulopathies.

Source: (Engleberg,2019) (Biggs, et al., 2016)

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References

Abukamsmour, W. (2018, October 15). *Ehrlichiosis Workup*. Retrieved from Medscape: https://www.medscape.com

Biggs, H. M., Behravesh, C. B., Bradley, K. K., Dahlgren, F. S., Drexler, N. A., Dumler, J. S., . . . Traeger, M. S. (2016). Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, and Anaplasmosis-United States. *MMWR. Recommendations and Reports*, 1-44.

Centers for Disease Control and Prevention. (2019, January 10). *Ehrlichiosis*. Retrieved from CDC: https://www.cdc.gov/ticks/tickbornediseases/ehrlichiosis

Dahlgren, F., Mandel, E. J., Krebs, J. W., Massung, R. F., & Mcquiston, J. H. (2011). Increasing incidence of Ehrlichia chaffeensis and Anaplasmosis phagocytophilum in the United States, 2000-2007. . *The American Journal of Tropical Medicine and Hygiene, 85(1)*, 124-131.

Engleberg, C. N. (2019). *Infectious Disease Ehrlichia and Anaplasma*. Retrieved from Infectitious Disease Advisor: https://www.infectiousdiseaseadvisor.com

Eshoo, M. W., Crowder, C. D., Li, H., Matthews, H. E., Meng, S., Sefers, S. E., . . . Tang, Y.-W. (2010). Detection and Indentification of Ehrlichia Species in Blood by Use of PCR and Electrospray Ioaization Mass Spectrometry. *Journal of Clinical Microbiology, 48(2)*, 472-478.

Heimer, K. N., Dahlgren, F. S., Drexler, N. A., Massung, R. F., & Behravesh, C. B. (2014). Increasing Incidence of Ehrlichiosis in the United States: A Summary of National Surveillance of Ehrlichia chaffeensis and Ehrlichia ewingii Infections in the United States, 2008-2012. *The American Journal of Tropical Medicine and Hygiene, 94(1)*, 52-60.

Human ehrlichiosis and anaplasmosis. (2019, April 19). Retrieved from Up To Date: https://www.uptodate.com/home

Kuriakose, K., Petit, A., Schmitz, J., Moncayo, A., & Bloch, K. (2018). Factors Associated with the Need for ICU Care Among Patients with Human Ehrlichiosis. *Public Health: Epidemiology and Outbreaks* (p. S240). Nashville: Open Forum Infectitious Disease.

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