

Acute Hepatitis A with concomitant Syphilis.

Marilian Canals Rivera, MD PGY1, HCA healthcare
Nicholas D'Angelo, MD, HCA healthcare

Introduction

-Hepatitis A is a self-limiting viral infection that causes liver inflammation. It typically spreads via fecal-oral route and has an average incubation period of 28 days. Infection confers lifelong immunity. Hepatitis A disease is often asymptomatic in young children, whereas in adults most of cases present with acute symptoms.

-Since 2006, hepatitis A vaccine has been recommended for all children at age 1 year. Hepatitis A vaccine is also recommended for certain high-risk groups of adults including injection and non-injection drug use, persons experiencing homelessness, and men who have sex with men.

-Hepatitis A virus (HAV) has substantially since the implementation of vaccination. Recent studies have shown an increase incidence in the state of Florida, with more than 3,200 cases, making HAV a public health emergency.

-The most common risk factor for transmission is travel outside of the US. In Florida the most common risk factors was Drug abuse (58% of the cases). Other relevant risk factors where homelessness and men who have sex with men.

-Differentiation of the cause of hepatitis requires an extensive history taking, physical exam, including a broad laboratory tests.

-We are reporting a clinical case of HAV in a patient with high risk factors. Pt was found to have a concomitant infection with Syphilis and who subsequently developed the Jarisch-Herxheimer reaction after antibiotic treatment

Case

The patient was a Caucasian male in his early 30s with significant past medical history for thalassemia, who presented to the Emergency Department complaining of 1 week of malaise, jaundice, epigastric discomfort, nausea, joint pains, dark urine and pale stools. Patient reported recently moving to the state of Florida and a cruise vacation to the Caribbean 1 month prior to presentation. Risk factors include IV-drug abuse and sexually active with male partner, recent travel and moving to Florida.

Vital signs:	T	HR	RR	BP	O2
	98.1	108	17	131/90	99

Remarkable laboratory workup:

Liver function Panel

Lab	Results
ALT	1834
AST	710
ALK-Pho	262
Total Bilirubin	17.9
Direct Bilirubin	12.9
Indirect Bilirubin	5.2

Hepatitis Panel & Others

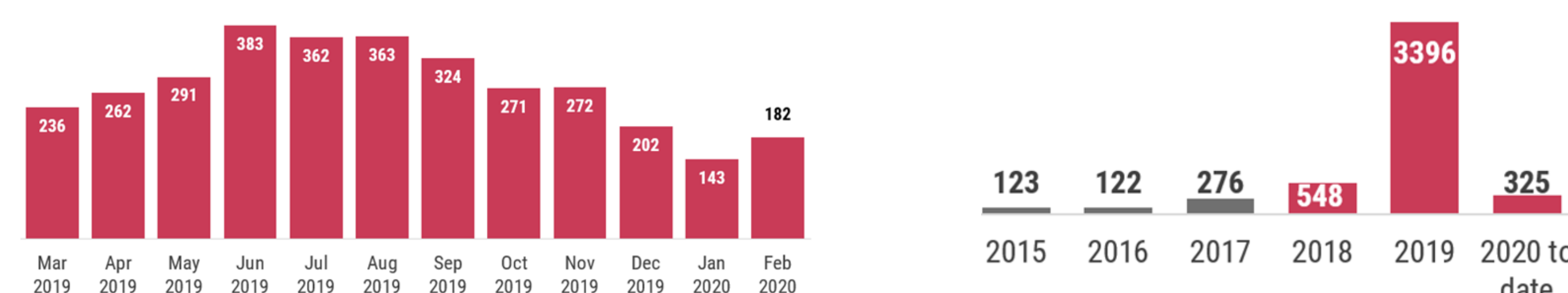
Lab	Result
Hep A IGM	Positive H
RPR	Reactive 1:64 H
FTA-Abs	Reactive H
HepBsAb	5.6 L (nl >10)
HepBsAg	Negative
HepBcore-Ab	Negative
HepC-Ab	Negative
HIV (1&2) Ag/Ab	Negative

Imaging:
Ultrasound and MRI of the abdomen did not identified a source of jaundice.

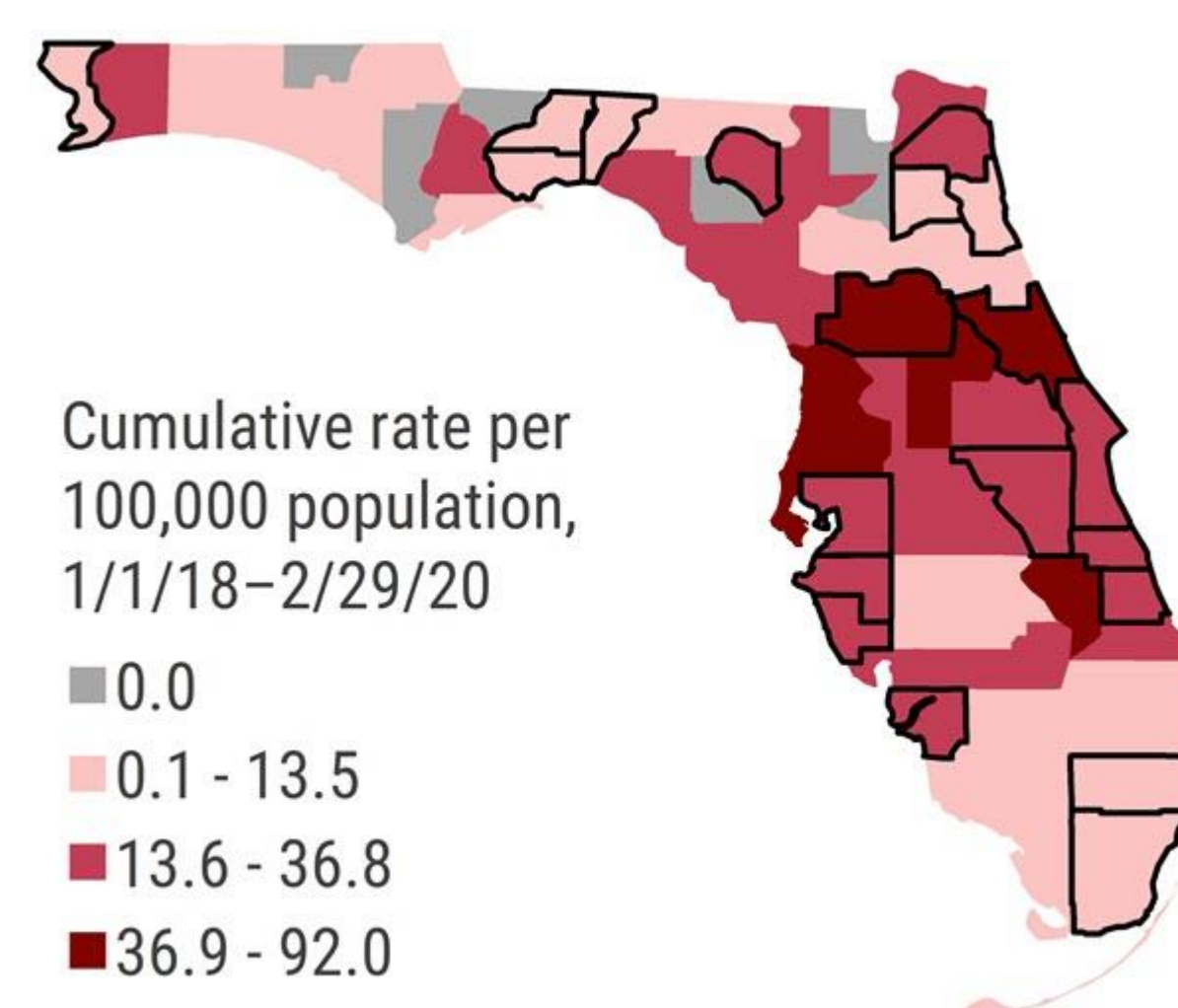
Literature Review

Hepatitis A in Florida

From Jan 01/2018- Feb/2020, 4,225 Hepatitis A cases were reported.



The number of reported hepatitis A cases more than doubled from 2016 to 2017 and nearly doubled again in 2018. From 2018 to 2019, cases increase over 500%.



01/01/2020 - 2/29/2020: Duval County in Jacksonville, FL has the highest incidence of cases with a total of 72, followed by

From 2018 to 2020, approximately 96%-97% of the cases where un-vaccinated against Hep A.

Jarisch-Herxheimer: An underdiagnosed event following treatment for Syphilis.

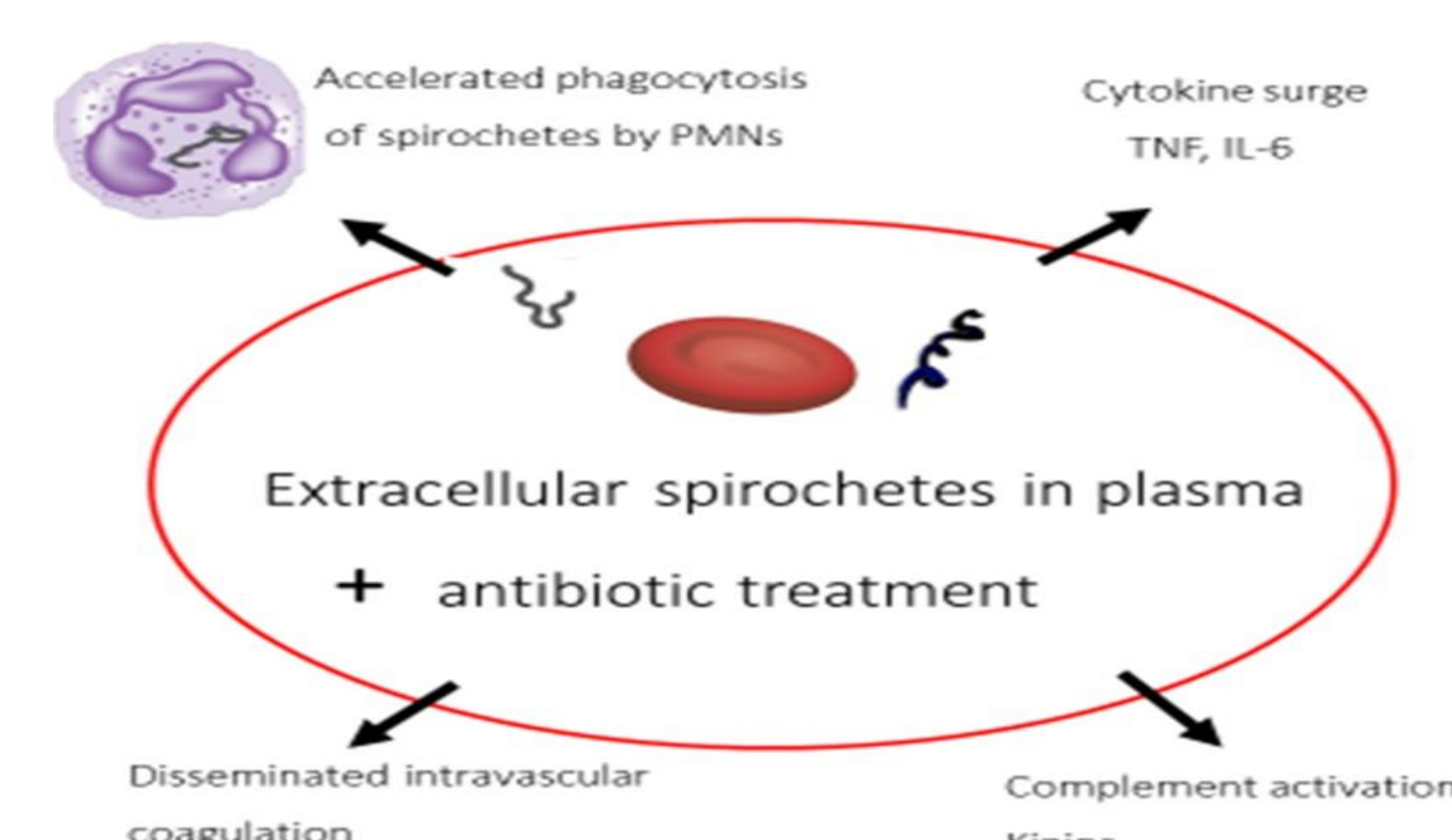
In syphilis, JHR typically starts approximately at 4 hours after starting antibiotics, peaks at 8 hours and subsides by 16hrs. Patients typically experience, fever, malaise, chills, headache and myalgias. Common associated antibiotics include, Penicillins and Tetracyclines. JHR can be regarded as an adverse effect of antibiotics necessary for achieving a cure of spirochetal infections.

- Syphilis is the leading spirochetal infection that gives rise to a JHR.
- Rarely fatal, except in neonates and in pregnancy.
- Experimental evidence indicates it is caused by non-endotoxin pyrogen and spirochetal lipoproteins
- Treatment for JHR is supportive, by monitoring vital signs and administering fluids.
- JHR is underdiagnose and underreported. It is also mistakenly diagnosed as an antibiotic allergic reaction

Pathogenesis:

In *T. Pallidum*, lipoproteins have been identified as the responsible factor for the inflammatory reaction. This is due to their effect on Macrophages resulting in increase production of TNF. Other mechanism via interleukin (IL)-6, IL-8 and complement activation have been proposed.

Mechanism of Inflammatory response has been shown to vary depending on the Spirochetal infection.



Outcome

Patient was treated for Hepatitis A infection with supportive care. Given the incidental finding of Syphilitic infection (late latent) and h/o of allergic reaction to penicillin, patient was started on a 28 days course of doxycycline. After stabilization, patient was discharge to follow up with PCP in 2-3 days. On follow up visit, patient had discontinued doxycycline due to an "allergic" reaction described as "burning, myalgias, chills". We diagnosed the patient with with Jarisch-Herxheimer reaction and recommended Naproxen 500mg before restarting antibiotics. Close follow up, revealed resolution of symptoms and continuation of antibiotic. He was advised to follow up in 1 month for re-checking Hepatitis Panel and further evaluation. Brief counseling regarding the use of IV-drugs and high risk behavior was provided, as well as information and resources in substance abuse intervention efforts.

Discussion

This patient presented with classical symptoms of Hepatitis A virus infection. He had multiple risk factors such as IV-drug abuse, homosexual, restaurant worker and recent travel, all which increased the suspicion of Hepatitis A infection. Evaluation for other communicable disease, yield the diagnosis of Syphilis. Is important to keep in mind that communicable disease share common risk factors. We concluded it is prudent to evaluate for other communicable diseases such as HIV, Hep-B, Hep-C and sexual transmitted diseases.

Clinical Relevance and Recommendations

- Vaccination remains the best method to prevent Hepatitis A infection.
- We encourage PCPs to actively offer the Hep A vaccine to individuals with risk factors.
- We recommend assessing concomitant infections in patients with multiple risk factors and becoming familiarized of current local epidemiological trends.
- JHR often goes unrecognized and is underreported. Its symptoms of chills, fever, myalgia, and skin rash are present or worsens after antibiotic treatment for spirochetal infection, JHR reaction must be consider
- Physicians need to anticipate a JHR when treating spirochetal diseases to provide supportive care of monitoring vital signs and administering fluids, as well as recognizing the appropriate diagnosis.
- Individuals with high risk factors/behaviors can benefit from other interventions to prevent transmissible disease, such as HIV. PrEP has been proved in multiple studies to prevent HIV transmission in MSM and individuals with multiple partners. A recent study showed that the implementation of PrEP could avert up to 63% of total new MSM infections.
- The use of PrEP could contribute to HIV epidemic control worldwide.

References

- 1-Centers for Disease Control and Prevention. Viral Hepatitis Surveillance: United States, 2013. US Department of Health and Human Services, Atlanta, GA 2016. https://www.cdc.gov/hepatitis/statistics/2014surveillance/pdfs/2014HepSurveillanceRpt_Rev2016-09-26.pdf
- 2-Centers for Disease Control and Prevention. Hepatitis A Questions and Answers for Health Professionals. <http://www.cdc.gov/hepatitis/hav/havfaq.htm#general> (Accessed on July 13, 2016)
- 3-Belum GR, Belum VR, Arudra SKC, Reddy BSN. The Jarisch-Herxheimer reaction revisited. *Travel Med Infect Dis.* 2013;11:231-237
- 4-SAMUEL C. MATHENY, MD, MPH, and JOE E. KINGERY, DO, University of Kentucky College of Medicine, Lexington, Kentucky. *Am Fam Physician.* 2012 Dec 1;86(11):1027-1034.
- 5-Aronson IK, Soltani K. The enigma of the pathogenesis of the Jarisch-Herxheimer reaction. *Br J Vener Dis.* 1976;52:313-315
- 6-http://www.floridahealth.gov/diseases-and-conditions/vaccine-preventable-disease/hepatitis-a/surveillance-data/_documents/2020-february-hep-a-summary.pdf-Figure 1
- 7-<http://www.floridahealth.gov/diseases-and-conditions/vaccine-preventable-disease/hepatitis-a/surveillance-data/-Figure 2>
- 8-The Jarisch-Herxheimer Reaction After Antibiotic Treatment of Spirochetal Infections: A Review of Recent Cases and Our Understanding of Pathogenesis. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5239707/>-Figure 3