Castleman Disease in an Immunocompromised Patient

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Introduction

- HHV-8 MCD is a lymphoproliferative disorder that can affect one or more large lymph nodes in multiple regions of the body at the same time
- Incidence: 6500-7700 new cases/year
- 75% of them associated with HHV-8
- Prevalence: 30,000-100,000 in the US
- All patients with HIV and MCD were found to have HHV-8 association

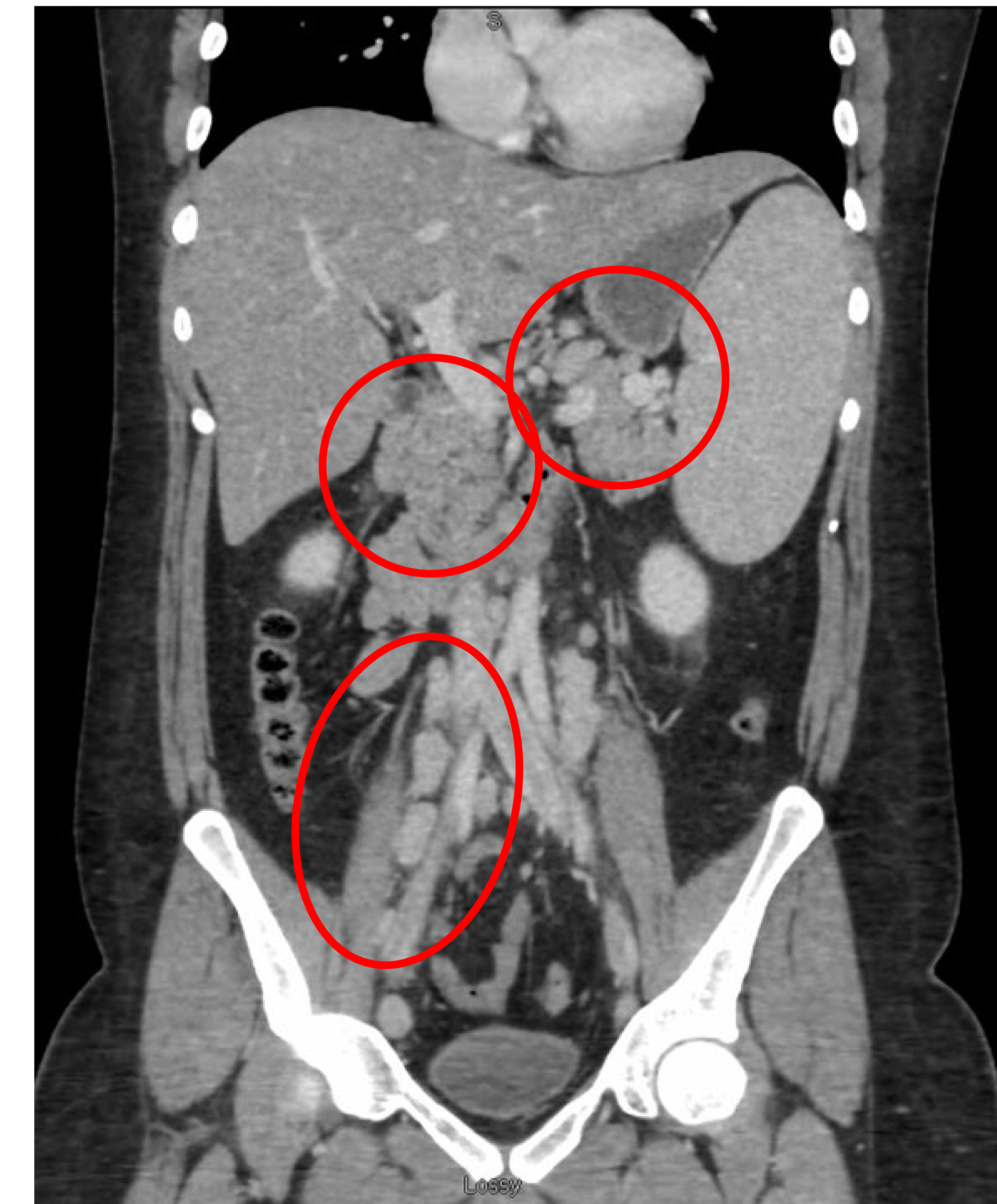
Case Presentation

- 28 yo male presenting with 5 days of fever, bilateral flank pain, nausea, vomiting, dysuria, and dark urine
- PMHx: HIV diagnosed 6 years ago, non-compliant with antiretroviral therapy (ART) for 2 years
- Vitals: T: 38.8ºC, BP 161/96 mmHg, HR 145 bpm, RR: 22 bpm
- Exam: hepatosplenomegaly, and non-tender axillary & inguinal lymphadenopathy.
- Initial labs: pancytopenia (hgb 7.8 g/dL, WBC 2.3 x10^3/mcL, Platelets 113 x10^3/mcL), high HIV viral load (95200 copies/ml), low CD4 count (27 cells/ mcL (6%)),
- Imaging: Bilateral lymphadenopathy diffuse and hepatosplenomegaly
- Right inguinal excisional biopsy: Interfollicular plasma cells and/or germinal centers with vascularization and "onion-skin" and infected with HHV-8
- Serum labs also revealed an elevated level of HHV-8 DNA PCR
- Dx: HHV-8 associated MCD
- Tx: 6 cycles of Rituximab
- Follow up: decreased splenomegaly and all lymph nodes decreasing in size. He also responded to ART and his viral load diminished to 40 copies/mL.

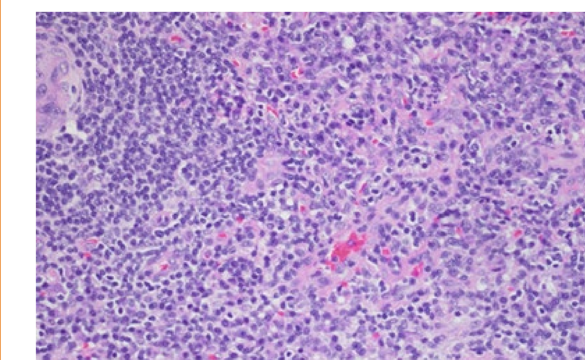
Laboratory

Table 1: Labs and cultures, Infectious disease work up				
SARS-COV2 RNA PCR (Nasopharyngeal swab)	Negative		Coccidioidomycosis Serology IgM and IgG immundiffusion and complement fixation (serum)	Non-reactive, Titer<1:2
Syphilis Ab (serum)	Non-reactive		Cryptococcal Ag (serum)	Not detected
Rapid Plasma Reagin (serum)	Non-reactive		QuantiFERON®-TB Gold (serum)	Negative
Gonorrhea/ Chlamydia rRNA (urine)	Non-reactive		Toxoplasma IgG (serum)	Negative
Hepatitis A Ab total, Hepatitis B surface Ag, Hepatitis B core Ab total, Hepatitis C Ab (serum)	Non-reactive		Acid-Fast Bacilli Grocott Methenamine Silver (GMS) stain of bone marrow	Negative
Cytomegalovirus (CMV) IgG (serum)	Positive		Cytomegalovirus DNA PCR (serum)	<200
Giardia antigen EIA (stool)	Negative		Bartonella quintana and henselae panel (serum)	Negative
Shigella, salmonella, campylobacter (stool)	Negative		Brucella IgM and IgG (serum)	Negative
Parvo-B19 IgG (serum)	Positive		Parvo-B19 DNA PCR (serum and bone marrow)	<100
Toxoplasmosis IgM (serum)	Negative		Histoplasmosis Ag (Serum and urine	Negative
Coxiiella burnetii serology (serum)	Negative		Cryptosporidium (Stool)	Negative
Clostridioides difficile (stool)	GHD Antigen positive; Toxin A & B positive		EBV DNA PCR (serum)	30360 copies/mL (normal<200)
HIV RNA PCR (serum) normal <20	95200 copies/ml		HHV-8	2,288,277 copies/ml (Normal <1,000)
Urinalysis: Unremarkable				
CSF Analysis: Glucose of 61 mg/dL, protein of 28 mg/dL, WBC count of 8 cells/mcL, Crypto Ag negative, HSV 1,2 DNA PCR not detected				
Cultures: Blood: Bacterial, fungal and mycobacterial: No growth Urine: No growth Bone marrow aspirate: Bacterial, fungal, viral and mycobacterial: No growth Cerebrospinal fluid: Bacterial, fungal, and mycobacterial: No growth				

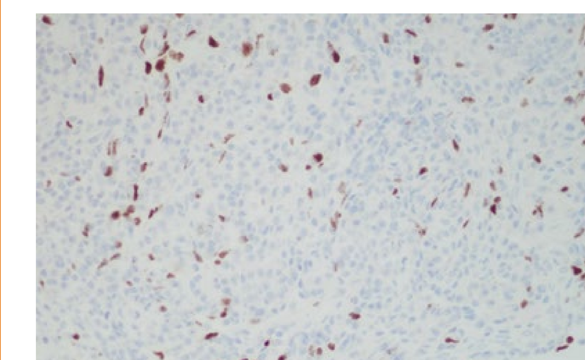
Imaging



CT Abdomen/Pelvis Coronal plane with adenopathy is seen in the region of the hilum of spleen, retroperitoneum and iliac chain, splenomegaly



H&E stain of right inguinal lymph node at 20x magnification



HHV-8 immuno stain of right inguinal lymph node at 20x magnification

Discussion

1: Molecular

- HHV8's ability to infection of B cells is consistent with the marked plasmacytosis in the lymph nodes and the clinical presentation of B-symptoms
- Molecular: HHV8 upregulates the IL-6 receptor signaling pathway via viral IL-6 (vIL-6) and LANA-1, promoting lymphoproliferation and angiogenesis

2: Therapy

- Rituximab targets against CD20 B cells inducing apoptosis via Natural Killer Cells
- W/ Rituximab: 94% survival rate at 2 years (control 42%) and 90% survival rate at 5 years (control 33%)
- If there is life-threatening organ failure or relapse of CD, pegylated liposomal doxorubicin or etoposide is administered with rituximab until a response is achieved
- In patients with poor HIV control, ART should be restarted and Gancyclovir can be used to directly target the HHV-8 virus
- IL-6 inhibitors such as Siltuximab and Tocilizumab have not demonstrated efficacy

References

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